Aus der

Herzchirurgischen Klinik und Poliklinik

der Ludwig-Maximilians-Universität München

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Einblicke in die Therapie komplexer thorakaler Aortenpathologien aus chirurgischer Sicht

Habilitationsschrift

vorgelegt von

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Inhaltsverzeichnis

1. Einleitende Zusammenfassung

1.1 Hintergrund

Die offene und endovaskuläre thorakale Aortenchirurgie stellt einen bedeutenden Teilbereich der beiden Fachgebiete Herz- und Gefäßchirurgie dar. Die offen-konventionelle Aortenchirurgie mit Anwendung der Herz-Lungen-Maschine ist nach wie vor der Goldstandard zur Behandlung von Pathologien der aufsteigenden Aorta (Aorta ascendens) und des Aortenbogens [1]. Im Bereich der absteigenden Aorta (Aorta descendens) hat sich hingegen die sogenannte „Thoracic endovascular aortic repair"-Technik (TEVAR) – ursprünglich als Notfall-Therapieverfahren – mittlerweile als Standardtherapie, insbesondere bei akuten und traumatisch-bedingten Pathologien, durchgesetzt [2]. Komplexe Pathologien der thorakalen Aorta, welche eine offen-chirurgische Behandlung erfordern, umfassen im Wesentlichen die akute Typ A Dissektion, Pathologien mit Beteiligung des Aortenbogens sowie Wiederholungseingriffe nach stattgehabter offener oder endovaskulärer Aortenoperation. Letztere sind oft mit einem besonders hohen Morbiditäts- und Letalitätsrisiko vergesellschaftet, da es sich hierbei zumeist um Notfalloperationen bei drohender oder akuter Aortenruptur, anhaltenden Blutungen, mediastinalen Infektionen oder Malperfusion von nachgeschalteten Organsystemen handelt. Trotz modernster Bildgebungsverfahren und Kathetertechniken ist die rein endovaskuläre Therapie von diesen komplexen Notfällen, insbesondere bei Infektionen von eingebrachten Aortenprothesen, oft nur in Ausnahmefällen oder übergangsweise (als sog. „Bridge-to-surgery") möglich und mit einem deutlich erhöhten perioperativen Risiko vergesellschaftet [3].

Durch die kontinuierliche Entwicklung von neuen chirurgischen Techniken und Behandlungsstrategien konnte die klassische thorakale Aortenchirurgie als Therapie der Wahl von komplexen Aortenpathologien weiter verbessert und die postoperativen Morbiditäts- und Letalitätsraten weiter gesenkt werden [4]. Die intraoperativen Neuerungen der modernen thorakalen Aortenchirurgie betreffen vor allem verschiedene Kannülierungstechniken zum Anschluss an die Herz-Lungen-Maschine sowie Perfusions- und

Temperaturstrategien für die Organprotektion, welche nunmehr besondere Anforderungen an das perioperative Management stellen [5,6].

Die vorliegende kumulative Habilitationsschrift soll neue Einblicke in die Therapie, insbesondere im Hinblick auf postoperative Ergebnisse, aktueller Behandlungsstrategien und das perioperative Management, von komplexen thorakalen Aortenpathologien im Bereich des Aortenbogens und der Aorta descendens aus herzchirurgischer Sicht zusammentragen.

1.2 Pathologien der thorakalen Aorta

Anatomisch und therapeutisch kann die thorakale Aorta in vier verschiedene Abschnitte unterteilt werden. Diese umfassen die Aortenwurzel (Bulbus aortae), die aufsteigende Aorta (Aorta ascendens), den Aortenbogen und die absteigende Aorta (Aorta descendens). Pathologien des Aortenbogens können je nach ihrer Lokalisation als proximal, distal, oder total beschrieben werden (**Abbildung 1**).

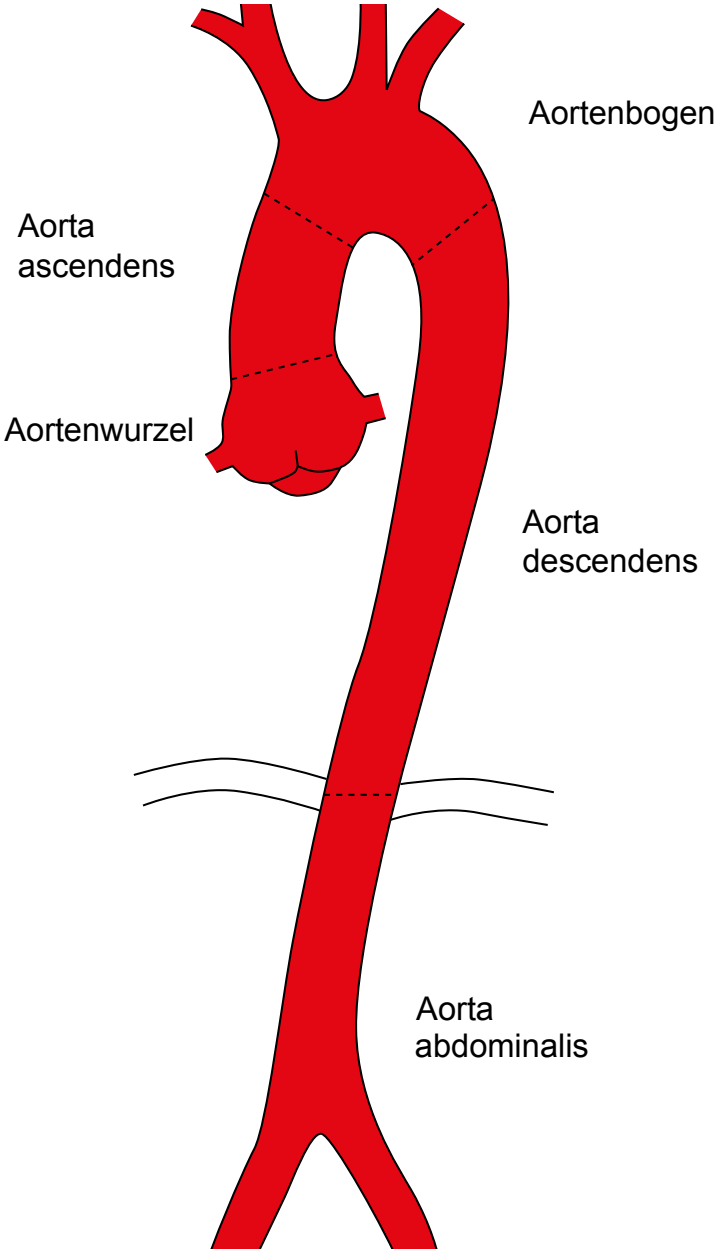

Abbildung 1:
Anatomische Einteilung der Aorta (aus Lühr [7] mit freundlicher Genehmigung der Albert-Ludwigs-Universität Freiburg i. Br.).

1.2.1 Akute thorakale Aortenpathologien

Akute Aortenpathologien sind potentiell lebensbedrohlich (Ruptur der Hauptschlagader) und können alle Abschnitte der thorakalen Aorta betreffen. Allgemein werden diese Erkrankungen, aufgrund der Ähnlichkeit der klinischen Leitsymptome, unter dem Begriff „akutes thorakales Aortensyndrom“ zusammengefasst [8]. Klassischer Weise geht das akute thorakale Aortensyndrom initial mit einem akuten und reißenden thorakalen „Vernichtungsschmerz“ einher, welcher im weiteren klinischen Verlauf persistieren oder nachlassen kann. Zusätzlich können weitere klinische Symptome durch die resultierende Veränderung des Blutstroms in der Aorta—beispielsweise Pulsdefizite zwischen den oberen und unteren Extremitäten, neurologische Ausfälle (transitorische ischämische Attacke, Schlaganfall, Paraplegie, etc.) und Durchblutungsstörungen nachgeschalteter Organsysteme—auftreten.

Die Dissektion stellt mit einer Inzidenz von 2 bis 3,5 Fälle/100.000 Einwohner die häufigste und prognostisch ungünstigste akute thorakale Aortenpathologie dar [9]. Bei der Dissektion kommt es—meist im Zusammenhang mit einer hypertensiven Krise—zu einem lokalen Einriss der innersten Schicht der Aorta (Intima) und in der Folge zu einer Einblutung mit Aufspaltung der mittleren Gefäßmuskelschicht (Media) [10]. Je nach Lokalisation kann sich die Einblutung innerhalb der aortalen Gefäßschichten nach antegrad oder retrograd ausdehnen, während diese nur noch durch die bindegewebige äußerste Gefäßschicht (Adventitia) begrenzt wird. Dissektionen werden hinsichtlich ihres Entstehungsortes (sog. „Entry“) und der jeweiligen Ausdehnung nach Stanford (Typ A und B) oder DeBakey (Typ I-III) klassifiziert (**Abbildung 2**). Im klinischen Alltag hat sich jedoch die Einteilung nach Stanford weitestgehend durchgesetzt. Aufgrund der hohen Rupturgefahr bei Patienten mit akuter Stanford Typ A Dissektion ist bis heute stets die notfallmäßige offene Operation indiziert, während bei der akuten (unkomplizierten) Typ B Dissektion zunächst konservative Therapieansätze (Schmerzlinderung, Blutdrucksenkung, etc.) im Vordergrund stehen [9]. Im Falle von drohenden Komplikationen (z.B. Ruptur oder Organmalperfusion) ist jedoch auch bei der akuten Typ B Dissektion eine offene oder endovaskuläre Operation der Aorta descendens indiziert [2].

Das intramurale Hämatom (IMH) und das penetrierende Aortenulkus (PAU) sind eben-

falls unter dem Begriff akutes Aortensyndrom subsumiert, treten aber deutlich seltener als die Aortendissektion auf. Während bei der Entstehung eines IMH am ehesten eine Einblutung aus den Vasa vasorum innerhalb der Aortenmedia vermutet wird (welche sich ebenfalls zirkulär innerhalb der Aorta im Sinne einer Dissektion ausbreiten kann), so liegt dem PAU ursächlich eine Ulzeration auf dem Boden einer fokalen Arteriosklerose zu Grunde [8,9,11]. Beide Pathologien zeichnen sich durch ein hohes Ruptur- und Dissektionsrisiko aus, welches insbesondere bei einer Lokalisation im Bereich der Aorta ascendens und des Aortenbogens stark erhöht ist (IMH bis 35%; PAU bis 40%), und stellen somit je nach Befund ebenfalls dringliche bis notfallmäßige Operationsindikationen dar [12]. Die traumatische (loco typico, meist nach Dezelerationstrauma) oder iatrogene Verletzung (z.B. im Rahmen einer Herzkatheteruntersuchung) der Aorta kann ebenfalls zum akuten Aortensyndrom gezählt werden.

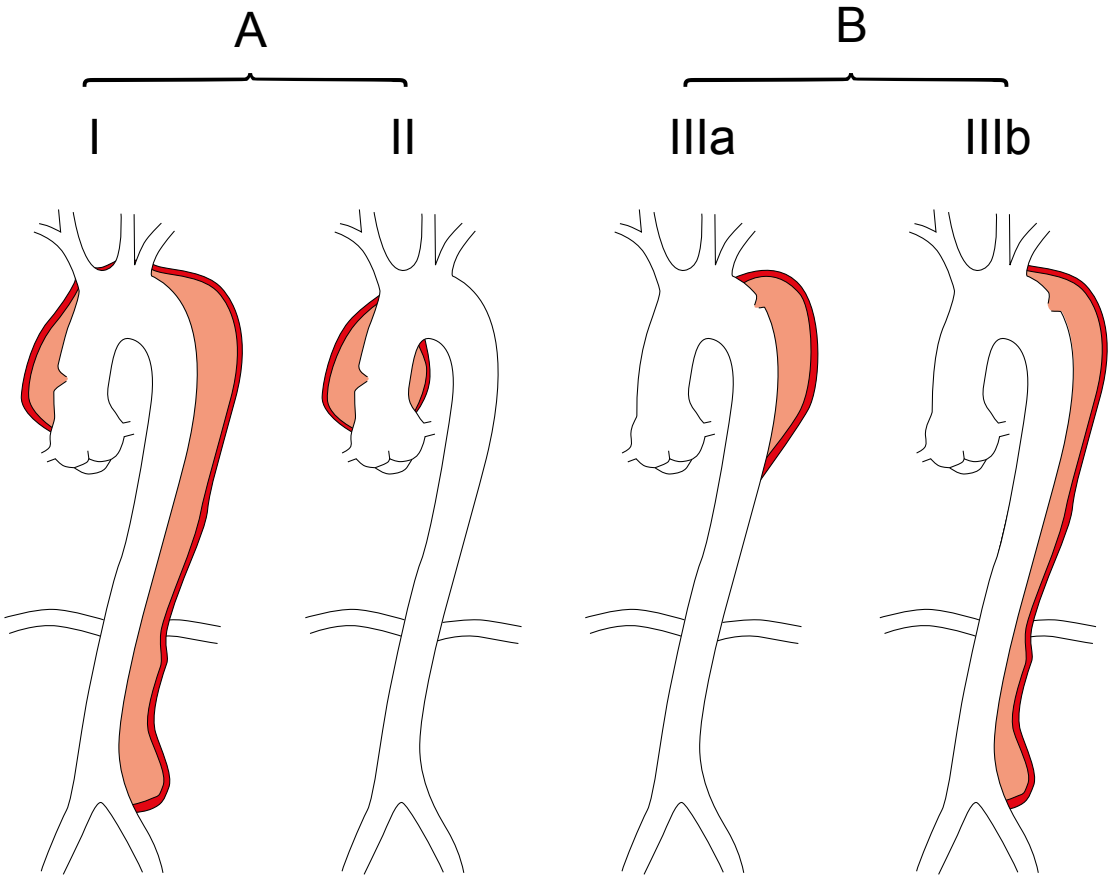

Abbildung 2: Klassifikationen der akuten Aortendissektion nach Stanford (A und B) und DeBakey (I-III) (aus Lühr [7] mit freundlicher Genehmigung der Albert-Ludwigs-Universität Freiburg i. Br.).

1.2.2 Chronisch-degenerative Aortenpathologien

Chronisch-degenerative Aortenpathologien sind in der Regel mit einer Erweiterung aller Wandschichten der Aorta (Intima, Media, Adventitia) assoziiert, welche ab entsprechender Größe (>150% des erwarteten geschlechts-, alters- und körpergrößenabhängigen Durchmessers) als Aneurysma bezeichnet werden [13]. Thorakale Aortenaneurysmen treten mit verschiedenen Häufigkeiten in den jeweiligen Abschnitten auf: Aorta ascendens (60%), Aorta descendens (40%) und Aortenbogen (10%) [14]. Das durchschnittliche Wachstum beträgt je nach Lokalisation zwischen 0,1 cm (Aorta ascendens) und 0,29 cm (Aorta descendens) pro Jahr [15]. Ursächlich können Aneursymen der thorakalen Aorta degenerativ (Atherosklerose), syndromal (Marfan Syndrom, Ehlers-Danlos Syndrom, Loeys-Dietz Syndrom, Erdheim-Gsell Syndrom, Turner Syndrom), genetisch (uni-/ bicuspide Aortenklappe, nicht-syndromal/ familiär) oder inflammatorisch (z.B. Aortitis, Riesenzellarteritis, Takayasu Arteritis, Wegner Granulomatose, Lues, etc.) bedingt sein [8,13,16,17].

Die Entstehung von thorakalen Aneurysmen verläuft in der Regel asymptomatisch. Klinische Symptome, bei entsprechender Größenzunahme mit Kompression von umgebenden Strukturen des Mediastinums, sind meist unspezifisch (Schluck- und Stimmstörung, obere Einflussstauung), so dass die Diagnose in der Regel erst spät oder als Zufallsbefund gestellt wird [8]. Die jährliche Inzidenz thorakaler Aneurysmen beträgt 5 bis 10 Fälle/100.000 Einwohner mit steigender Tendenz [18].

Die progediente Zunahme der Wandspannung bei gleichzeitiger Abnahme der Dehnbarkeit im Bereich der aneurysmatischen Erweiterung der Aorta erhöht das Risiko einer Ruptur bzw. das Auftreten einer Dissektion. Das jährliche Risiko beträgt demnach bei Aortendurchmessern von 4,0 bis 4,9 cm ca. 2% und steigt rapide auf 6,9% bei Aneurysmen ab 6 cm in der Aorta ascendens bzw. 7 cm in der Aorta descendens [8,19]. Dementsprechend sehen die europäischen und US-amerikanischen Leitlinien eine chirurgische Indikation bereits ab einem Aortendurchmesser 5,0 cm bzw. 5,5 cm vor [9,20]. Im Falle von schnell wachsenden (>0,5 cm/ Jahr) Aneurysmen, syndromalen Erkrankungen (z.B. Marfan Syndrom) oder elektiven Eingriffen an der Aortenklappe kann die OP-Indikation entsprechend früher gestellt werden (ab 4,5 cm Aortendurchmesser) [16].

1.3 Offene und endovaskuläre Aortenchirurgie

Seit den 1950er Jahren konnten die operativen Ergebnisse bei offenen Eingriffen an der thorakalen Aorta durch die Entwicklung von neuen und bahnbrechenden operativen Techniken und Strategien—insbesondere durch die klinische Einführung des tiefen hypothermen Kreislaufstillstands, der selektiven zerebralen Hirnperfusion und der sogenannten Elephant Trunk-Technik—stetig verbessert und optimiert werden [21–25]. Heutzutage werden bei ausgedehnten Pathologien der thorakalen Aorta, insbesondere mit Beteiligung des Aortenbogens und der Aorta descendens, zwei-zeitige offene Operationsverfahren oder Hybridtechniken favorisiert [26,27]. Eine komplette endovaskuläre Versorgung aortaler Pathologien im Bereich der Aorta ascendens und des Aortenbogens sind bislang, aufgrund der anatomischen Gegebenheiten der proximalen thorakalen Aorta und weiterhin bestehenden technischen Limitationen, auf wenige Fallberichte und kleine Fallserien beschränkt [28,29]. Demzufolge ist die offene Chirurgie nach wie vor als der Goldstandard für die Behandlung von Pathologien der proximalen thorakalen Aorta (Aortenbulbus, Aorta ascendens und Aortenbogen) zu sehen [5,8].
Durch die erfolgreiche Entwicklung und klinische Etablierung von aortalen Stentprothesen, welche eine thorakale endovaskuläre Aortenreparatur (TEVAR) ermöglichten, hat sich die chirurgische Therapie im Bereich der Aorta descendens in den vergangenen Jahren jedoch maßgeblich verändert [2,30]. Die TEVAR stellt heutzutage die Standardtherapie bei Patienten mit traumatischer Aortenverletzung und akuter komplizierter Stanford Typ B Dissektion dar [2,31]. Im Vergleich zum offenen Ersatz der Aorta descendens wurde bei der TEVAR-Methode zwar eine niedrigere perioperative Letalität und Morbidität nachgewiesen, jedoch birgt diese Technik ein potentielles Risiko für mehr Langzeitkomplikationen durch Verletzung benachbarter mediastinaler Strukturen (Rigidität der aortalen Stentprothese) bei vergleichbarem Querschnittsrisiko (Paraplegie) [2,32,33] (**Abbildung 3**).

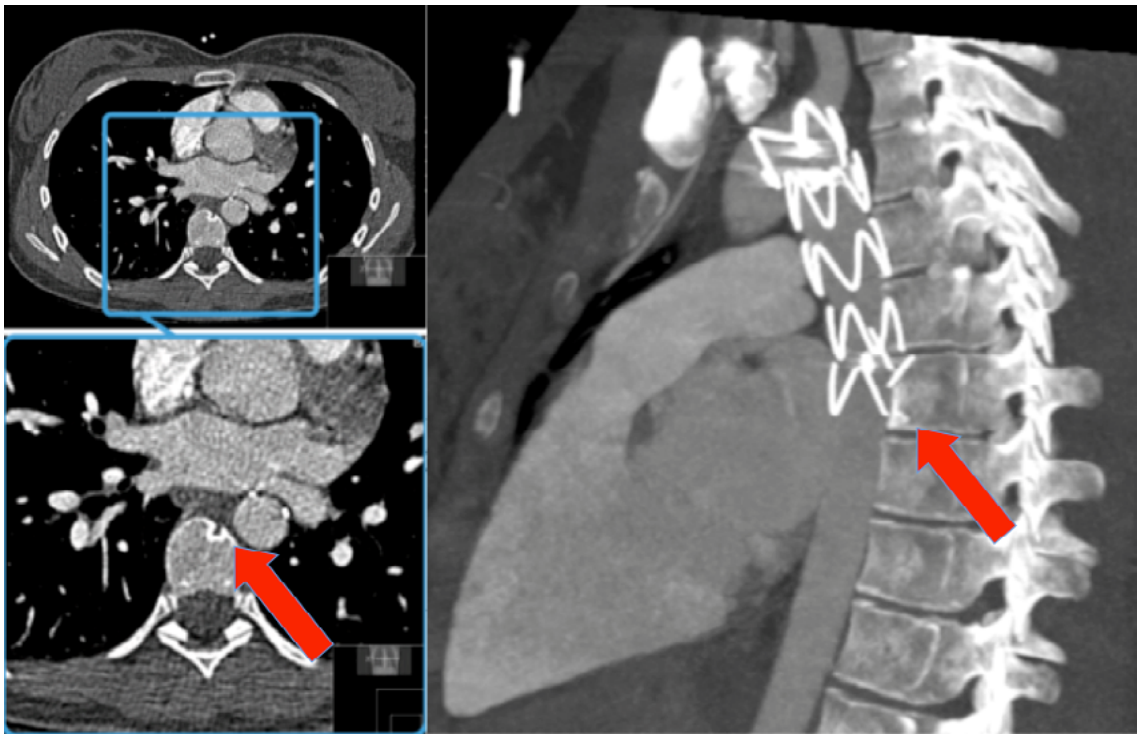

Abbildung 3: Computertomographische Darstellung einer gedeckten Ruptur der Aorta descendens nach dorsal mit Erosion des 7. thorakalen Wirbelkörpers (rote Pfeile) bei Materialversagen einer endovaskulären Stentprothese (aus Luehr M et al. [33] mit freundlicher Genehmigung von Wolters Kluwer Health, Inc.).

2. Offene Eingriffe am Aortenbogen

Komplexe Pathologien der thorakalen Aorta können heutzutage erfolgreich offen chirurgisch, endovaskulär oder als Hybridprozeduren behandelt werden. Mitte des vergangenen Jahrhunderts stellte die offene Aortenbogenchirurgie, wegen des hohen technischen Aufwands, der limitierten Anwendungsindikationen und einem gesteigerten Risiko für zerebrale und postoperative Komplikationen, jedoch eine chirurgisch extrem anspruchsvolle und für den Patienten sehr gefährliche Operation dar [34]. Die Erkenntnis, dass eine Erniedrigung der Körperkerntemperatur auf unter 20°C zumindest sehr kurze Phasen eines Kreislaufstillstandes ohne gravierende neurologische Schäden erlaubt, bildete die Grundlage der modernen Aortenbogenchirurgie. Die klinische Einführung des tiefen hypothermen Kreislaufstillstands Mitte der 1970er Jahre (Temperaturabsenkung auf unter 20°C; Erstbeschreibung durch Hans G. Borst bereits im Jahr 1964 in München [35]) erlaubte fortan routinemäßige Eingriffe am Aortenbogen mit relativer Sicherheit für perioperative Komplikationen [22].

Die Einführung additiver zerebraler Perfusionsstrategien (retrograd vs. antegrad) in Kombination mit tiefer Hypothermie stellte die zweite grundlegende Neuerung in der Entwicklung hin zur modernen Aortenbogenchirurgie dar [23,36]. Insbesondere durch die Einführung der antegraden, selektiven zerebralen Perfusion („antegrade selective cerebral perfusion“, ASCP) konnte eine erhebliche Reduzierung perioperativer (zentraler) neurologischer Schäden bei gleichzeitiger Anhebung der Körperkerntemperatur des Patienten erreicht werden. In jüngster Zeit wurden neue Operationsstrategien mit einer Kombination aus ASCP (18–22°C) unter lediglich moderaten (28–32°C) Körperkerntemperaturen zunehmend eingesetzt, um hypothermie-assoziierte Komplikationen (z.B. Störungen der Gerinnungskaskade) und prolongierte Abkühlungs- und Aufwärmzeiten beim Einsatz extrakorporaler Zirkulation zu vermeiden [34]. Bislang existiert jedoch hinsichtlich des optimalen Temperatur-, Kannülierungs- und Perfusionsmanagements beim Aortenbogenersatz kein einheitlicher Konsens—und folglich eine große Anzahl von in der Fachliteratur beschriebenen Strategien und empfohlenen chirurgischen Techniken [5].

Die Behandlung von ausgedehnten Aortenbogenaneurysmen, insbesondere mit Beteiligung der Aorta descendens und der Notwendigkeit für eine Zweitoperation über eine linkslaterale Thorakotomie, war in der Vergangenheit einem sehr hohen Risiko für perioperative Letalität und Ischämie des Rückenmarks mit potentieller Querschnittslähmung (Paraplegie) assoziiert. Im Jahre 1983 wurde jedoch, ebenfalls durch Borst, ein weiterer Meilenstein durch die sogenannte „Elephant Trunk"-Technik (ET) gelegt, welche die distale Anastomose beim Aortenbogenersatz vereinfachte und gleichzeitig als potenzieller proximaler Anschluss (offen) oder als Landezone (endovaskulär) für einen Zweiteingriff zur Versorgung der deszendierenden Aorta dient (Reduktion der OP-Dauer bzw. Vermeidung einer offenen Zweitoperation) [25]. Die Einführung endovaskulärer Stentprothesen in den 1990er Jahren schaffte die technischen Voraussetzungen, um die zweitzeitig konzipierte konventionelle ET-Technik als sogenannte „Frozen Elephant Trunk"-Technik (FET) zu einem einzeitigen Eingriff weiter zu entwickeln [26,37]. Die heutige FET-Technik stellt ein Hybridverfahren zwischen konventioneller und endovaskulärer Technik dar und erlaubt somit die definitive Behandlung von ausgedehnten Aortenbogenpathologien als einzeitige Operation via Sternotomie bei deutlich kürzeren Kreislaufstillstandszeiten [37,38] (**Abbildung 4**).

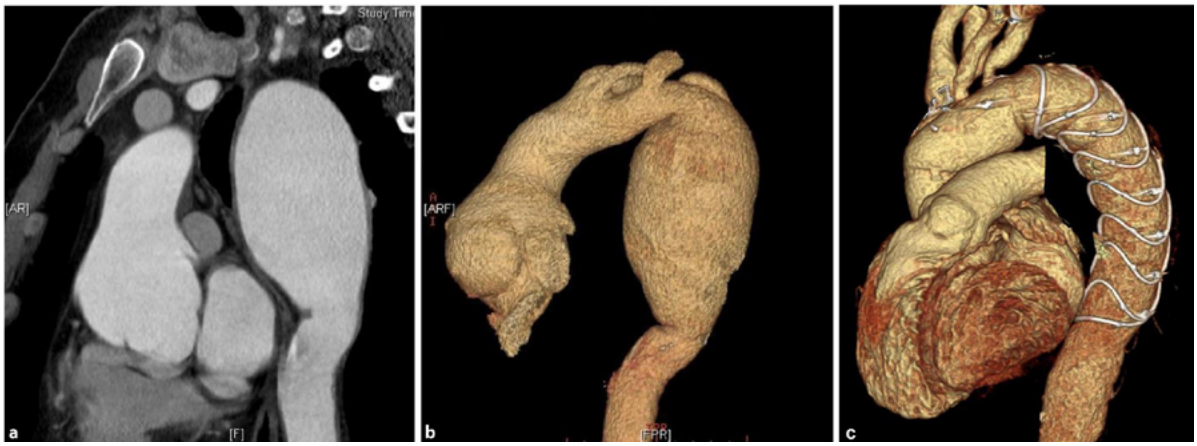

Abbildung 4: Computertomographie der thorakalen Aorta: Aneurysma der Aortenwurzel und der Aorta descendens mit Beteiligung des distalen Bogens (a + b); postoperative Erfolgskontrolle (c) (aus Luehr M et al. [37] mit freundlicher Genehmigung von Springer-Verlag Berlin Heidelberg).

2.1 Multizentrische Analyse von aktuellen Therapiestrategien und Ergebnissen bei offenen Eingriffen am Aortenbogen (Originalarbeit 6.1)

Hintergrund

Die chirurgische Technik des offenen Aortenbogenersatzes konnte, ebenso wie das perioperative Management, in den vergangenen Jahrzehnten durch deutliche Ergebnisverbesserungen, mit weniger perioperativen Komplikationen und höheren Überlebensraten, kontinuierlich weiterentwickelt werden. Allerdings ist die chirurgische Therapie des Aortenbogens—in Ermangelung klarer chirurgischer Leitlinien bei einer Vielzahl von zur Verfügung stehenden Behandlungsstrategien und Operationstechniken—oft zentrumsspezifisch und (insbesondere in nicht-spezialisierten Kliniken) auch weiterhin mit einer hohen perioperativen Morbidität und Letalität vergesellschaftet [5,6].

Die Anwendung neuer Techniken und Strategien für Aortenbogenoperationen (einhergehend mit niedrigeren perioperativen Komplikations- und Letalitätsraten) sind in der Fachliteratur fast ausschließlich von einzelnen spezialisierten Kliniken, als sog. „Single Center Experience", beschrieben. Multi-zentrische Studienansätze, welche als Basis für Empfehlungen und zukünftige fachübergreifende Leitlinien dienen könnten, sind bislang jedoch die Ausnahme [39].

Das Ziel des Forschungsprojektes war die retrospektive Analyse aktueller klinischer Ergebnisse, im Hinblick auf angewandte chirurgische Techniken und Perfusionsstrategien, nach elektivem kompletten Aortenbogenersatz an verschiedenen Referenzzentren in Europa.

Methodik

Es erfolgte eine retrospektive Datenauswertung im Zeitraum 2003 bis 2013 aus den folgenden elf europäischen Aortenzentren: Ludwig-Maximilians-Universität München, Herz- und Gefäßklinik Bad Neustadt, S. Orsola-Malpighi Krankenhaus der Universität Bologna (Italien), Europa Krankenhaus Rom (Italien), Humanitas Gavazzeni Krankenhaus Bergamo (Italien), Universität Birmingham (UK), Herzzentrum – Universität Leipzig, Ruprecht-Karls-Universität Heidelberg, Medizinische Hochschule Hannover, Albert-Lud-

wigs-Universität Freiburg, Westdeutsches Herzzentrum – Universität Duisburg-Essen, Johann-Wolfgang-Goethe Universität Frankfurt.

Alle Aortenbogenoperationen mit drei (total), zwei (subtotal) oder einer (partiell) zirkulären Anastomose der hirnversorgenden Gefäße (sog. supraaortale Abgänge der Aorta) wurden eingeschlossen. Akute Aortenpathologien (z.B. Dissektionen, iatrogene Verletzungen, Traumata, Notfälle, etc.) wurden ausgeschlossen. Als primäre Endpunkte wurden 30-Tage- und Langzeit-Sterblichkeit (ursachenunabhängig) sowie neuaufgetretene postoperative neurologische Defizite (innerhalb von 7 Tagen oder nach prolongierter Aufwachphase) definiert.

Ergebnisse

Insgesamt konnten 1232 elektive Aortenbogenoperationen für die multizentrische Analyse identifiziert und eingeschlossen werden. Die 30-Tage- und Krankenhausletalität der gesamten Studienkohorte betrug 8,8% bzw. 11,6%. Im Langzeitverlauf (mittlerer Nachverfolgungszeitraum: 3,3 ± 2,9 Jahre; entsprechend 4020 Patientenjahren) zeigte sich eine Gesamtüberlebensrate nach 5 und 8 Jahren von 72,0 ± 1,5% und 64,0 ± 2,0% (**Abbildung 5**).

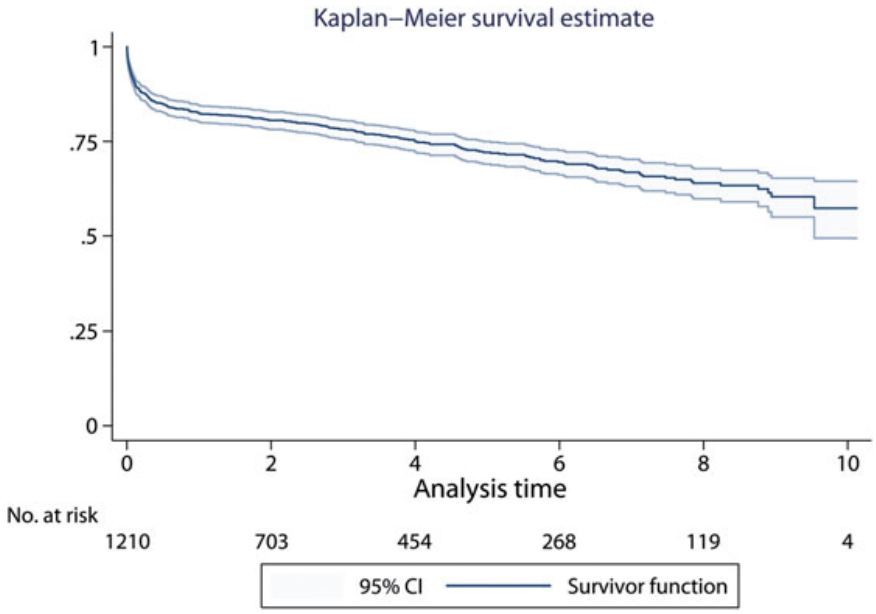

Abbildung 5: Kaplan-Meier-Überlebensschätzung von Patienten nach elektivem Aortenbogenersatz mit 95%-Konfidenzintervall (aus Urbanski PP, Luehr M, et al. [39] mit freundlicher Genehmigung von Oxford University Press).

Neuaufgetretene neurologische Defizite wurden als zerebral fokal permanent /-temporär, Paraplegie (Querschnittslähmung) oder als temporär-postoperatives Delir in 5,7% (n=70), 3,3% (n=40), 1,1% (n=13) und 7,9% (97) der Fälle festgestellt.

In der anschließenden multivariaten Risikofaktoranalyse (logistische Regressionsanalyse) konnten die Parameter hohes Patientenalter (p<0.001), die Anzahl vorheriger Herzoperationen (p=0.016) und eine gleichzeitig stattfindende koronare Bypassoperation (p=0.029) als unabhängige Risikofaktoren für 30-Tage-Sterblichkeit identifiziert werden. Zusätzlich wurden auch einzelne Studienzentren—am ehesten bei stark variierenden Patientenzahlen (eingeschlossene Patienten pro Zentrum zwischen 17 und 237)—als unabhängige Risikofaktoren für elektive Aortenbogenoperationen identifiziert.

Die angewandten Kannülierungstechniken zur Etablierung der extrakorporalen Zirkulation (Herz-Lungen-Maschine) im Studienzeitraum variierten deutlich hinsichtlich der favorisierten Lokalisation zwischen den verschiedenen Kliniken: A. axillaris dextra (37,7%), Aorta (24,8%), A. carotis dextra/ sinistra (13,7%), Trunkus brachiocephalicus (12,1%), A. femoralis (10,6%) und andere Lokalisationen (1,1%). Als Perfusionsstrategie wurde vor-

nehmlich die antegrade Hirnperfusion (ASCP) angewendet (96,7%), während der tiefe hypotherme Kreislaufstillstand ohne (6,0%) oder mit retrograder Hirnperfusion (0,1%) äußerst selten herangezogen wurde. Auf die geplante Risikoanalyse von perfusionsspezifischen Parametern der selektiven Hirnperfusion—u.a. Temperatur (°C), Druck (mmHg) und Fluss (ml/min)—hinsichtlich des Auftretens von postoperativen neurologischen Komplikationen musste jedoch bei lückenhafter Datenlage einzelner Zentren verzichtet werden.

Diskussion

Diese multi-zentrische Analyse konnte zeigen, dass die perioperative Letalität und Morbidität bei offenen Eingriffen am Aortenbogen zwar im Vergleich zu den Ergebnissen aus den vergangenen Jahrzehnten (tiefer Kreislaufstillstand ohne Hirnperfusion) heutzutage deutlich niedriger liegt, jedoch mit über 10% weiterhin als substanziell zu bezeichnen ist. Die perioperative Letaliät ist insbesondere bei älteren, bereits voroperierten Patienten oder bei notwendigen Kombinationseingriffen (z.B. Aortenbogenersatz mit notwendiger Bypassoperation) erhöht. Ebenso sind temporäre oder permanente neurologische Defizite durch die notwendige Manipulation an den hirnversorgenden Gefäßen (Anastomosierung, Kreislaufstillstand, selektive Perfusion, etc.) nicht unwahrscheinlich, wenngleich auch hier das Risiko im Vergleich zu früheren Ergebnissen insgesamt weiter gesunken ist.

Im Gegensatz zu den in der Studienkohorte sehr unterschiedlich angewendeten Kannülierungstechniken für den elektiven Aortenbogenersatz, konnte bei den intraoperativen Perfusionsstrategien zur zerebralen Protektion ein eindeutiger Paradigmenwechsel hin zur antegraden Hirnperfusion (96,7%; ASCP) registriert werden, während der tiefe hypotherme Kreislaufstillstand ohne (6,0%) oder mit retrograder Hirnperfusion (0,1%) bei den teilnehmenden Studienzentren seinen Stellenwert weitestgehend verloren hat.

2.2 Aortale Ereignisse und Reoperationen nach elektivem Aortenbogenersatz: Inzidenz, chirurgische Strategien und Ergebnisse (Originalarbeit 6.2)

Hintergrund

Offene elektive Eingriffe am Aortenbogen werden seit Jahrzehnten routinemäßig an spezialisierten Zentren weltweit mit guten Ergebnissen durchgeführt, wobei heutzutage—insbesondere bei ausgedehnten Aortenbogenpathologien—zunehmend Hybridverfahren (z.B. FET-Technik) zum Einsatz kommen. Nach stattgehabtem elektivem Aortenbogenersatz bleibt jedoch oftmals ungeklärt, ob die Primäroperation den Patienten tatsächlich geheilt hat, oder ob es im postoperativen Kurz- und Langzeitverlauf im Bereich des Aortenersatzes oder den angrenzenden Aortensegmenten verstärkt zu neuen Pathologien oder Komplikationen (sog. „aortale Ereignisse“) mit der Notwendigkeit zur Re-Operation kommt.

Das Ziel der Studie war die retrospektive Analyse im Kurz- und Langzeitverlauf nach elektivem komplettem Aortenbogenersatz hinsichtlich der Inzidenz neuer aortaler Ereignisse (mit oder ohne Re-Operationsindikation) und postoperativer Ergebnisse nach Sekundäreingriff.

Methoden

Die bereits bestehende Datenbank mit 1232 elektiven Aortenbogenoperationen von elf europäischen Aortenzentren (**s. Kapitel 2.1**) wurde für die Datenauswertung herangezogen [39]. Retrospektiv wurden alle Patienten mit einem aortalen Ereignis im Kurz- bis Langzeitverlauf nach elektivem Aortenbogenersatz eingeschlossen. Es erfolgte eine deskriptive Analyse zur Bestimmung der Inzidenz von aortalen Ereignissen, notwendigen Re-Operationen, angewandten OP-Techniken und potentiellen Risikofaktoren für Krankenhausmortalität bei Sekundäreingriff. Die Patienten ohne aortales Ereignis wurden ausgeschlossen.

Ergebnisse

Insgesamt konnten 155 Patienten (mittleres Alter 64,9 Jahre; 66,5% Männer) mit einem aortalen Ereignis nach elektivem Aortenbogenersatz identifiziert werden. Das mittlere Intervall von Primäroperation zu aortalem Ereignis betrug 11,3 Monate (IQR: 4,2 - 38,4). Am häufigsten war die Aorta descendens (79,4%) betroffen, gefolgt von Aorta abdominalis (10,3%) und Aorta ascendens/ Bogen (9,0%).

Re-Operationen wurden bei insgesamt 133 Patienten (85,8%), entweder offen (43,6%) oder endovaskulär (56,4%), durchgeführt. In den verbliebenen 22 Fällen bestand entweder eine Kontraindikation für einen Sekundäreingriff oder die Operation/Intervention konnte nicht rechtzeitig durchgeführt werden.

Insgesamt lag die Krankenhaus- und die Langzeitletalität nach Re-Operation an der Aorta bei 17,3% bzw. 8,3%. Nach einem, drei und fünf Jahren lagen die Überlebensraten bei 81,2%, 79,0% und 76,7% (**Abbildung 6**). Postoperative permanente neurologische Komplikationen traten als Paraplegie und Schlaganfall in jeweils 6,0% und 1,5% der Fälle auf.

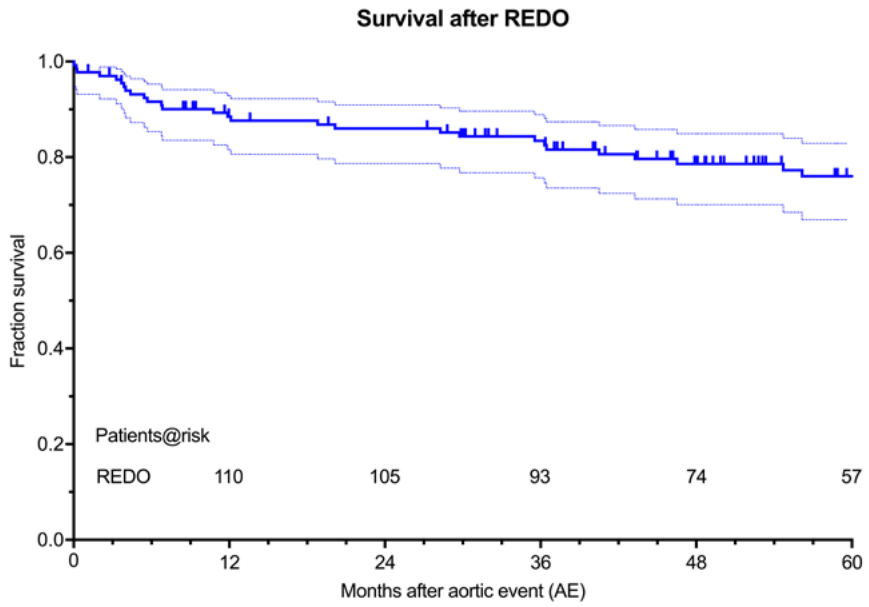

Abbildung 6: Kaplan-Meier-Überlebensschätzung: Re-Operation nach stattgehabtem primären Aortenbogenersatz inkl. 95%-Konfidenzintervall (aus Luehr M, et al. [40] mit freundlicher Genehmigung von Oxford University Press).

In der multivariaten Analyse konnte einzig das Alter der operierten Patienten als unabhängiger Risikofaktor identifiziert werden (p=0,008; 95%-CI: 1,005 - 1,176). Die Kaplan-Meier-Überlebensschätzung lieferte keinen statistisch signifikanten Unterschied zwischen offen operierten Patienten hinsichtlich der Lokalisation (Aorta ascendens/ Bogen vs. A. descendens; p=0,613) (**Abbildung 7**).

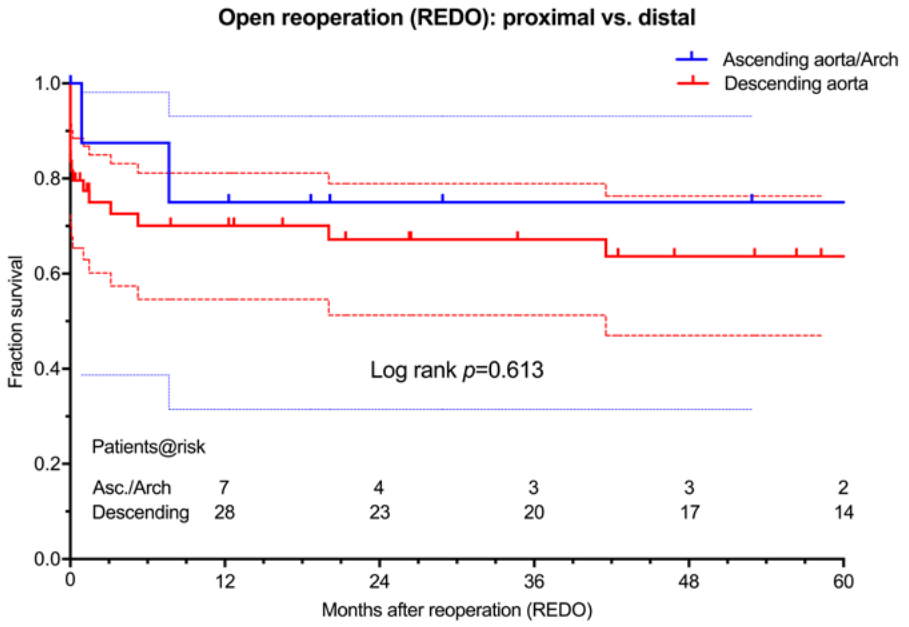

Abbildung 7: Kaplan-Meier-Überlebensschätzung: Offene Re-Operation nach stattgehabtem primären Aortenbogenersatz im Bereich der Aorta ascendens/ Bogen vs. Aorta descendens mit 95%-Konfidenzintervall (aus Luehr M, et al. [40] mit freundlicher Genehmigung von Oxford University Press).

Auch der direkte Vergleich von offener und endovaskulärer Therapie im Bereich der Aorta descendens lieferte keinen statistisch signifikanten Überlebensvorteil für die endovaskuläre Therapie (p=0,059) (**Abbildung 8**).

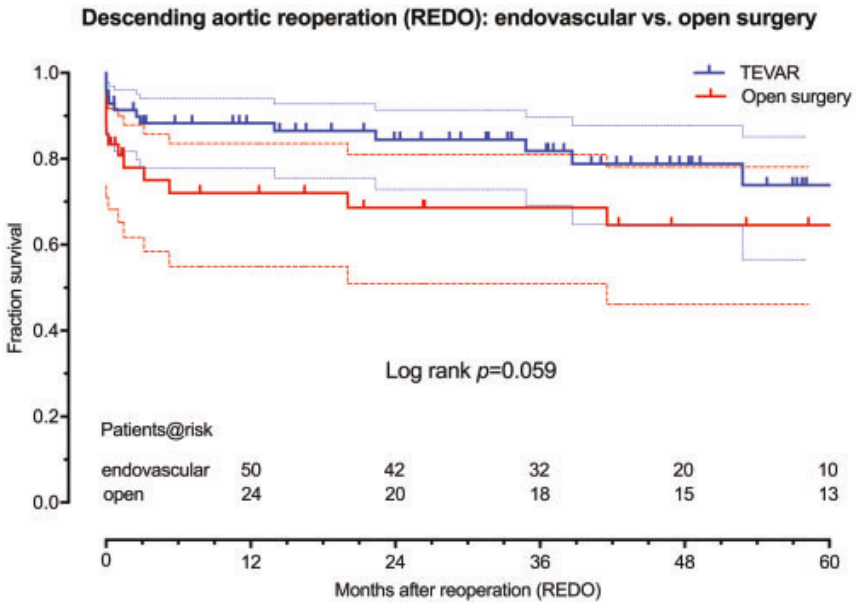

Abbildung 8: Kaplan-Meier-Überlebensschätzung: Offene vs. endovaskuläre Re-Operation nach stattgehabtem primären Aortenbogenersatz im Bereich der Aorta descendens mit 95%-Konfidenzintervall (aus Luehr M, et al. [40] mit freundlicher Genehmigung von Oxford University Press).

Diskussion

Aus der Studienkohorte von 1232 elektiven Aortenbogenoperationen entwickelten insgesamt 12,6% ein aortales Ereignis im Zeitraum 2003 bis 2013. Im voroperierten Bereich des Primäreingriffs (Aorta ascendens/ Aortenbogen) waren Re-Operationen jedoch in nur 0,7% der Fälle notwendig. Dieses Ergebnis bestätigt den elektiven konventionellen Aortenbogenersatz weiterhin als Goldstandard, insbesondere da die Mehrzahl der neuen aortalen Ereignisse in den unbehandelten distalen Aortenabschnitten (Aorta descendens und abdominalis) auftraten. Bei den endovaskulären Sekundäreingriffen im Bereich der Aorta descendens zeichnete sich ein Trend—hin zu einem früh-postoperativen Überlebensvorteil (p=0,059)—ab, so dass die Vorbereitung einer TEVAR-Landungszone im Rahmen des offenen Primäreingriffs am Aortenbogen, im Sinne eines ET oder FET, gerechtfertigt erscheint.

Trotz der insgesamt niedrigen Anzahl von aortalen Ereignissen sollten Patienten, nach stattgehabter Aortenbogenchirurgie, idealerweise an eine Aortensprechstunde mit regelmäßigen Verlaufskontrollen der gesamten Aorta angebunden werden.

2.3 Extra-anatomische Revaskularisation bei distalem Verschluss der Arteria carotis und resultierender zerebraler Malperfusion bei der akuten Typ A Dissektion (Originalarbeit 6.3)

Hintergrund

Im Rahmen der akuten Typ A Dissektion kann es (entsprechend der Ausdehnung) durch eine Verlegung (falsches Lumen) bzw. Involvierung von aortalen Gefäßabgängen (periphere Dissektion) zu einer Malperfusion mit Ischämie von nachgeschalteten Organsystemen kommen [41]. Eine Beteiligung der supraaortalen Äste (Trunkus brachiocephalicus, A. carotis communis links und A. subclavia links) wird aufgrund des potentiellen Schlaganfallrisikos als besonders kritisch bewertet und in der Literatur mit einer variablen Inzidenz von 5 bis 43% der Fälle beschrieben [42]. Das Risiko ist insbesondere bei präoperativ bereits nachgewiesenen (hämorrhagischen) Schlaganfällen oder komatösen Patienten mit unklarem neurologischen Status erhöht [43,44] (**Abbildung 9**).

Primäres Ziel der offenen Operation ist die schnellstmögliche Wiederherstellung des Blutflusses durch den Ersatz der disseziierten thorakalen Aorta mit Anschluss des richtigen Gefäßlumens (sog. „wahres Lumen“). Die Erfolgsaussichten für die Wiederherstellung einer vollständigen zerebralen Durchblutung können jedoch bei langstreckiger Dissektion mit distaler Verlegung der Carotiden, z.B. durch Kollaps des falschen Lumens mit oder ohne Thrombusbildung, limitiert oder schlichtweg nicht mehr gegeben sein. In Einzelfällen wurde hier die Möglichkeit einer Revaskularisierung mittels eines uni- oder bilateralen extra-anatomischen Bypasses—u.a. zur Frühzeitigen Initiierung der selektiven antegraden Hirnperfusion—beschrieben [45–47].

Das Ziel dieser retrospektiven Untersuchung war die Identifikation und deskriptive Analyse der postoperativen Ergebnisse von Patienten mit akuter Typ A Dissektion und einer präoperativen Okklusion der linken und/oder rechten A. carotis communis, welche zusätzlich mittels extra-anatomischem Bypass behandelt wurden.

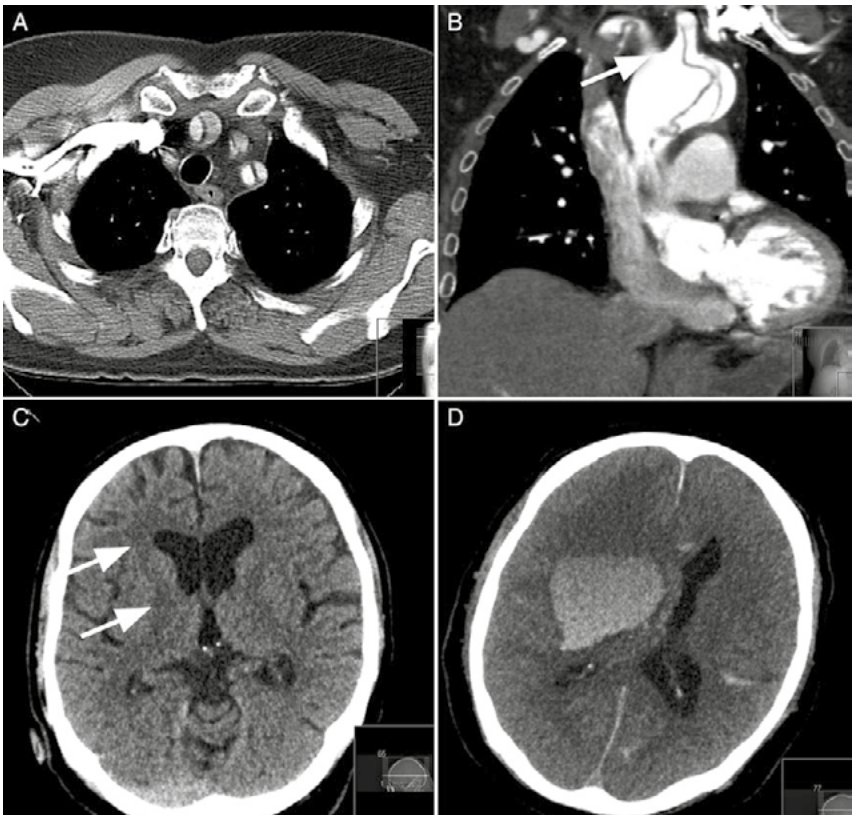

Abbildung 9: Präoperatives CT: Dissektion aller drei supraaortalen Äste (A), Malperfusion des Tr. brachiocephalicus und Dissektion der linken A. carotis communis (B), präoperativer Schlaganfall (C) und postoperative links-zerebrale Einblutung im präoperativen Ischämiegebiet (D) (aus Luehr M, et al. [48] mit freundlicher Genehmigung von Oxford University Press).

Methodik

Im Zeitraum 2005 bis 2013 wurden insgesamt 354 Patienten mit akuter Typ A Dissektion am Herzzentrum Leipzig – Universität Leipzig operiert. Ausschließlich Patienten mit einer präoperativen Okklusion der linken oder rechten A. carotis communis und nachgewiesener zerebraler Malperfusion (Klinik und Bildgebung) wurden in die Analyse mit eingeschlossen (**Abbildung 10**). Die perioperativen Daten der eingeschlossenen Patienten wurden retrospektiv aus den Krankenakten und OP-Berichten zusammengetragen und anschließend ausgewertet. Für die Überlebensschätzung nach Kaplan-Meier wurde ein aktuelles Follow-up durchgeführt. Patienten mit einer Dissektion der supraaortalen Äste ohne Carotisokklusion wurden ausgeschlossen.

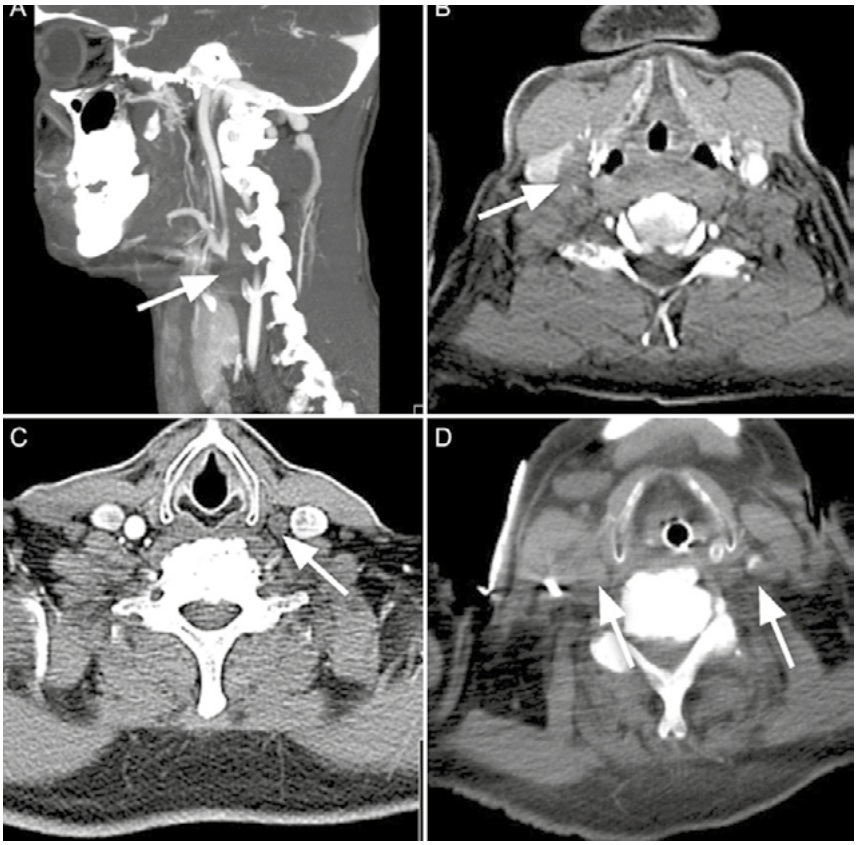

Abbildung 10: Präoperative Computertomographie (CT): Verschluss der rechten A. carotis communis auf Höhe der Bifurkation und retrograder Füllung (A), kompletter Kollaps des wahren Lumens bei unilateraler (B and C) und bilateraler Okklusion der A. carotis communis (D) (aus Luehr M, et al. [48] mit freundlicher Genehmigung von Oxford University Press).

Ergebnisse

Insgesamt konnten 23 Hochrisiko-Patienten (Inzidenz: 6,5% von 354 Patienten) mit einer distalen Okklusion der A. carotis communis links (n=11) oder rechts (n=13) bei Typ A Dissektion identifiziert und analysiert werden (mittleres Alter 66,3 Jahre; 78,3% männlich). Ein Patient wurde präoperativ mit einem bilateralen Verschluss der A. carotis communis aufgenommen.

Drei Patienten mit ausgeprägtem präoperativen Schlaganfall entwickelten postoperativ eine intrazerebrale Blutung (n=2) bzw. ein Multi-Organ-Versagen (n=1). Die resultierende Krankenhausletalität betrug 13,0%. Nach einem mittleren postoperativen Zeitraum von 15,2 Monaten (IQR: 4,8–34,1) lag die Überlebensrate der Studiengruppe bei 69,6%. Im Vergleich zu Patienten ohne Carotisokklusion, die im selben Zeitraum wegen

einer akuten Typ A Dissektion am Herzzentrum Leipzig operiert wurden (Überlebensrate 72,5%), zeigte die Kaplan-Meier-Überlebensschätzung—nach Entlassung aus dem Krankenhaus—über einen Zeitraum von 36 Monaten keinen statistisch signifikanten Unterschied (p=0,90) (**Abbildung 11**).

Die registrierte postoperative Schlaganfallrate in der Studienkohorte betrug 34,8%. Neue permanente bzw. fatale neurologische Komplikationen traten in 26,1% (n=6) der Fälle auf, wohin gegen sich acht Patienten (34,8%) von neuaufgetretenen, temporären neurologischen Defiziten im postoperativen Verlauf vollständig erholten. In den verbleibenden neun Fällen (39,1%) wurden bei unauffälligem Verlauf keine relevanten neurologischen Komplikationen registriert. Die Intensivstations- und Krankenhausverweildauer lag im Mittel bei 7 (IQR: 2,0–16,5) bzw. 16 (12,5–26,0) Tagen.

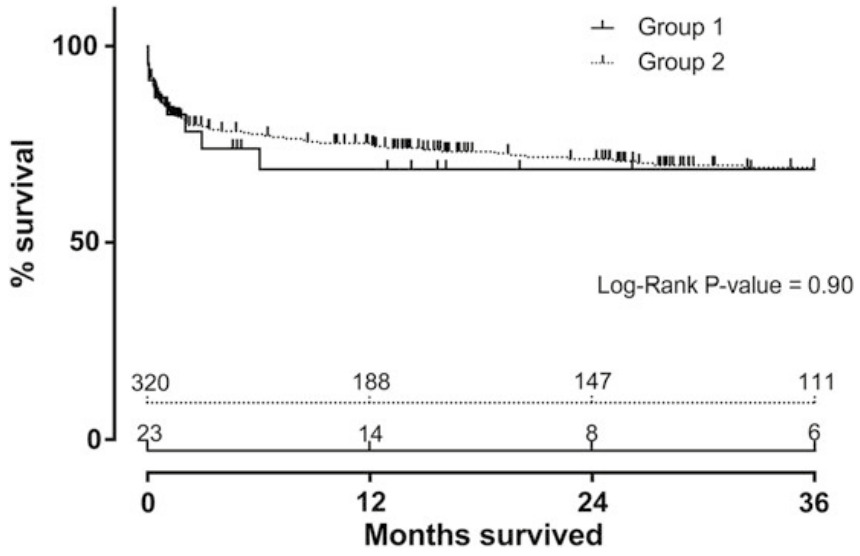

Abbildung 11: Kaplan-Meier-Überlebensschätzung bei Patienten mit Typ A Dissektion (intraoperativ verstorbene Fälle ausgeschlossen): präoperative Carotisokklusion (Gruppe 1) vs. keine Carotisokklusion (Gruppe 2) (aus Luehr M, et al. [48] mit freundlicher Genehmigung von Oxford University Press).

Diskussion

Patienten mit Carotisokklusion und einer präoperativen zerebralen Malperfusion bei akuter Typ A Dissektion stellen eine Hochrisikogruppe mit deutlich erhöhter Krankenhausletalität (14,6% bis 30,5%) dar und haben postoperativ, im Vergleich zu Patienten ohne Endorganischämie, eine signifikant erhöhte Langzeitsterblichkeit [41,49,50]. Dennoch konnte in der Studie gezeigt werden, dass eine frühzeitige offene Operation mit einem extra-anatomischen Bypass (zur schnellen Wiederherstellung der zerebralen Perfusion über die Herz-Lungen-Maschine) im Vergleich mit Patienten ohne distale Carotisokklusion nicht zwangsläufig mit einer signifikant erhöhten Verlaufsletalität einhergeht. Vielmehr ist davon auszugehen, dass in der untersuchten Patientengruppe—ohne die angewandte OP-Technik—ein zusätzlicher Anstieg der Krankenhaus- und Verlaufsletalität sowie eine signifikant höhere Rate von permanenten und fatalen neurologischen Komplikationen aufgetreten wäre.

2.4 Schlussfolgerungen

1) Bei elektiven offenen Eingriffen am Aortenbogen ist die perioperative Letalität und Morbidität mit über 10% weiterhin als substanziell zu bezeichnen und, insbesondere bei älteren, bereits voroperierten Patienten oder Kombinationseingriffen, signifikant erhöht.
2) In den vergangenen Jahren hat ein Paradigmenwechsel hinsichtlich der zerebralen Protektion hin zur antegraden Hirnperfusion stattgefunden. Der tiefe hypotherme Kreislaufstillstand und die retrograde Hirnperfusion haben ihren Stellenwert in Europa weitestgehend verloren.
3) Nach stattgehabtem elektivem Aortenbogenersatz liegt die Inzidenz von Re-Operationen im Bereich der Primäroperation bei unter 1% der Fälle. Dieses Ergebnis bestätigt den konventionellen Aortenbogenersatz weiterhin als Goldstandard.
4) Im postoperativen Verlauf nach elektivem Aortenbogenersatz ist die Aorta descendens am häufigsten von aortalen Ereignissen und Re-Operationen betroffen. Insbesondere bei ausgedehnten Aneurysmen des Aortenbogens mit Beteiligung der Aorta descendens sollte deshalb eine Landungszone zur endovaskulären Weiterbehandlung, im Sinne eines ET oder FET, in Erwägung gezogen werden.
5) Patienten mit akuter Typ A Dissektion und zerebraler Malperfusion stellen eine Hochrisikogruppe mit erhöhter Letalität und Morbidität dar. Die konsequente Behandlung der distalen Carotisokklusion mittels extra-anatomischem Bypass, zur frühzeitigen Wiederherstellung der antegraden zerebralen Perfusion, ist mit akzeptablen postoperativen Ergebnissen bei vergleichbaren Überlebensraten im mittelfristigen Verlauf assoziiert.

3. Endovaskuläre Eingriffe im distalen Aortenbogen und in der Aorta descendens

Die endovaskuläre Chirurgie mittels Stentgraftprothese (TEVAR) stellt heutzutage die Therapie der Wahl bei den meisten Pathologien der Aorta descendens dar [2,30]. Eine offene Operation kommt dementsprechend nur bei Patienten in Frage, die für einen TEVAR-Eingriff aus sonstigen Gründen nicht geeignet sind. Dies kann insbesondere dann der Fall sein, wenn die anatomischen Gegebenheiten das Einbringen der endovaskulären Stentprothese erschweren oder verhindern (Atherosklerose, starkes Abknicken der Aorta,), die aortale Grunderkrankung infektiösen Ursprungs ist (z.B. Aortitis, aorto-ösophageale Fistel, etc.) oder eine Verankerung des proximalen Prothesenanteils in Ermangelung einer ausreichenden Landungszone von mindestens zwei Zentimetern (z.B. bei aneurysmatischer Erweiterung) schlichtweg nicht möglich ist [30,51].
Im letzten Fall kann jedoch eine Verlagerung der proximalen Landezone bis in den distalen Aortenbogen (sog. Ishimaru Landungszonen 2 und 3) durchgeführt werden, um einen TEVAR-Eingriff trotzdem noch zu ermöglichen [52,53] (**Abbildung 12**).

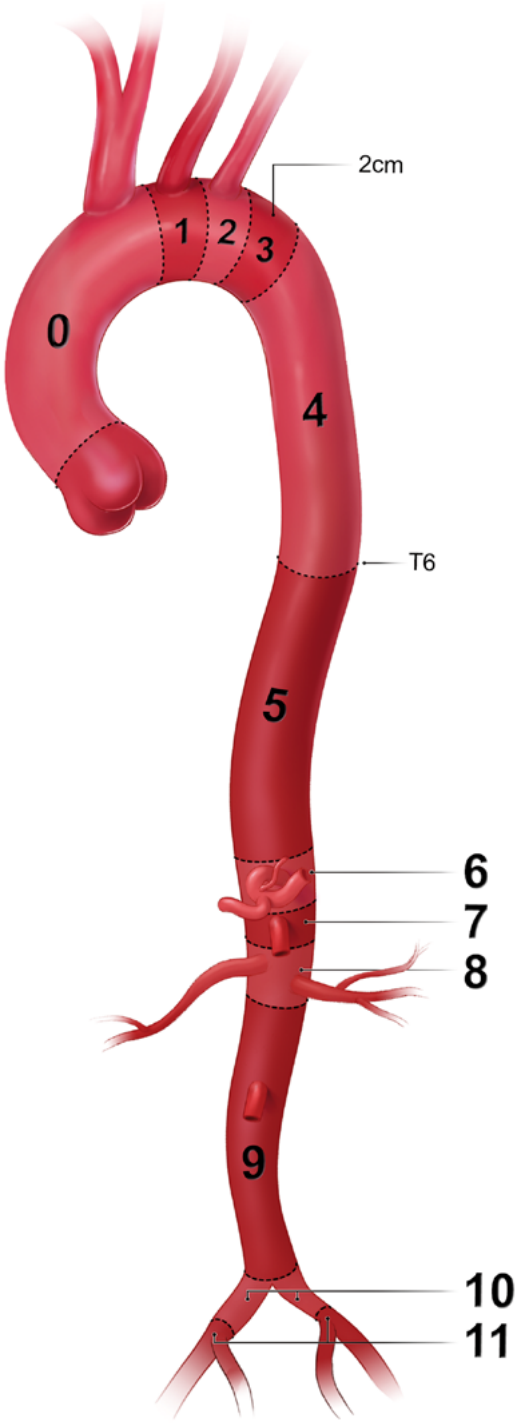

Abbildung 12: Modifizierte Ishimaru Landezonen (LZ) im Bereich der thorakalen (LZ 0-5) und abdominalen (LZ 6-9) Aorta (aus Czerny et al. [52] mit freundlicher Genehmigung von Oxford University Press).

3.1 Inzidenz von neurologischen Komplikationen nach endovaskulärem Verschluss der linken Arteria subclavia (Originalarbeit 6.4)

Hintergrund

Eine Verlagerung der TEVAR-Landezone bis in den Aortenbogen (Landezone 2 und 3, **Abbildung 12**) erlaubt auch eine endovaskuläre Behandlung von sehr proximal gelegenen Pathologien der Aorta descendens [30]. Diese Behandlungsmethode ist jedoch oftmals nur unter Inkaufnahme einer partiellen oder vollständigen Verlegung (sog. Überstenten) der linken A. subklavia (LSA; Landezone 2) möglich, wobei das Risiko für zentrale neurologischen Komplikationen durch eine Minderperfusion der linken oberen Extremität mit einem Subclavian-Steal-Syndrom (SSS) erhöht zu sein scheint [54].
Das Ziel dieser frühen Studie war die deskriptive Analyse der postoperativen Früh- und Spätergebnisse hinsichtlich des Auftretens neurologischer Komplikationen nach TEVAR mit partieller oder vollständiger Überstentung der LSA.

Methodik

Im Zeitraum Dezember 2001 bis März 2006 wurden 265 Patienten mit TEVAR an der Albert-Ludwigs-Universität Freiburg i. Br. behandelt. Insgesamt konnten 20 Patienten (10 Männer, 10 Frauen; mittleres Alter: 64.3±12.2 Jahre) in die Studie eingeschlossen werden: bei 14 Patienten erfolgte eine vollständige und in 6 Patienten eine partielle Überstentung der LSA.
Die primären Endpunkte der Studie waren das postoperative Auftreten von klinisch relevanten zentralen und peripheren neurologischen Komplikationen im Früh- und Langzeitverlauf sowie der positive Nachweis eines SSS (Grad I-III). Alle überlebenden Patienten wurden postoperativ in regelmäßigen Abständen (3, 6 und 12 Monate) einer diagnostischen (CT/ MRT) sowie neurologischen Verlaufsuntersuchung (inkl. Gefäß-Doppler-Untersuchung) zugeführt. Anschließend erfolgte die Auswertung der klinischen Daten.

Ergebnisse

Alle Patienten konnten erfolgreich mittels TEVAR behandelt werden. Das Follow-up betrug 100%. Zwei Patienten verstarben im Verlauf (nicht OP-assoziiert). Neue zentrale neurologische Ereignisse traten verspätet in zwei Patienten (10%) mit kompletter Überstentung der LSA auf: Hirnstamminfarkt (n=1) und transitorische Ischämische Attacke (TIA) mit beidseitiger Visusminderung (n=1). Bei 10 der 14 Patienten (71%) mit vollständiger Überstentung der LSA wurde ein SSS im Verlauf festgestellt: Grad I (n=1), Grad II (n=2) und Grad III (n=7). Fünf Patienten mit vollständiger Überstentung der LSA und SSS Grad III (36%) entwickelten periphere neurologische Komplikationen im Sinne von sensorischen und/oder motorischen Defiziten der linken oberen Extermität. Mit Ausnahme eines Patienten, welcher mittels Bypass zur LSA (Ausgehend von der linken A. carotis communis) im Verlauf behandelt werden musste, waren diese Symptome jedoch rückläufig. In den sechs Patienten mit partieller Überstentung der LSA wurden keine relevanten neurologischen Komplikationen bzw. ein SSS festgestellt.

Diskussion

Eine Erweiterung der Landungszone bis in den Aortenbogen mit partieller oder kompletter Überstentung der LSA erlaubt eine Behandlung mittels TEVAR bei Hochrisikopatienten mit Pathologien der proximalen Aorta descendens und des distalen Aortenbogens. Im Gegensatz zur partiellen Überstentung der LSA muss jedoch bei einem vollständigen LSA-Verschluss mit Durchblutungsstörungen der oberen linken Extremität (SSS) und potentiellen neurologischen Komplikationen—insbesondere bei einem SSS Grad III—gerechnet werden. Dementsprechend sollte präoperativ bei TEVAR mit geplanter LSA-Überstentung möglichst immer eine bildgebende Diagnostik der supraaortalen und zerebralen Gefäßanatomie durchgeführt werden, um anatomische Variationen (z.B. Stenosen/ Unterbrechungen im Circulus arteriosus cerebri) oder supraaortale Gefäßpathologien (z.B. Hypoplasie/ Stenose der A. vertebralis rechts), welche eine vorherige Revaskularisierung der LSA mittels Bypass bzw. Transposition erfordern, sicher auszuschließen.

3.2 Postoperative Ergebnisse nach endovaskulärer Stentgraft-Therapie der Aorta mit komplettem Verschluss der linken Arteria subclavia (Originalarbeit 6.5)

Hintergrund

Die komplette Überstentung der LSA mittels TEVAR ermöglicht bekanntermaßen die Behandlung von Patienten mit ausgedehnten Aortenpathologien der proximalen Aorta descendens bis in den distalen Aortenbogen hinein. Allerdings birgt dieses Therapiekonzept ein nicht zu unterschätzendes Risiko für das Auftreten von perioperativen neurologischen Komplikationen [30,55,56]. Eine prophylaktische Revaskularisation der LSA bei elektiven Fällen, wie von einigen Klinikern gefordert, ist jedoch nicht ohne Risiko und wird in der Literatur mit einer postoperativen Sterblichkeit von 1,2% bis 5% beschrieben [57–59]. Aus diesem Grund befürworten einige Chirurgen die prophylaktische LSA-Revaskularisation nur in Ausnahmefällen mit nachweislich erhöhtem Risikoprofil des Patienten (atypische/ pathologische supraaortale Gefäßanatomie, Ausdehnung der Aortenpathologie, etc.) [60,61]. Die bislang veröffentlichten Studien einzelner Zentren zu diesem Thema sind jedoch widersprüchlich, so dass ein gemeinsamer Konsens innerhalb der wissenschaftlichen Fachgesellschaften hinsichtlich der prophylaktischen Revaskularisation der LSA weiterhin aussteht.

Das Ziel der vorliegenden multi-zentrischen Studie war die statistische Analyse aktueller Patientendaten und chirurgischer Ergebnisse nach TEVAR mit kompletter Überstentung der LSA, mit besonderem Fokus auf den Einfluss der prophylaktischen LSA-Revaskularisation, zur Identifikation möglicher perioperativer Risikofaktoren für neurologische Komplikationen.

Methodik

Es erfolgte eine retrospektive Datenauswertung an der Ludwig-Maximilians-Universität München, der Albert-Ludwigs-Universität Freiburg i. Br. und am Herzentrum Leipzig – Universität Leipzig. Einschlusskriterien waren alle konsekutiv behandelten Patienten mit einem kompletten Verschluss der LSA mittels TEVAR (Landezone 2; **Abbildung 12**) im Zeitraum 2001 bis 2016. Patienten mit einer partiellen Überstentung der LSA (Landezo-

ne 2) oder mit Landungszonen 0, 1 und 3 wurden ausgeschlossen. Für die statistische Auswertung wurden vorab zwei Gruppen definiert: „LSA-Revaskularisation“ (Gruppe 1) und „Keine LSA-Revaskularisation“ (Gruppe 2).

Neben der Krankenhausletalität wurde das einzelne oder kombinierte Auftreten von prozedurspezifischen Komplikationen nach TEVAR mit LSA-Verschluss als primärer Endpunkt festgelegt: (1) linksseitiger Schlaganfall, (2) permanente Querschnittslähmung sowie (3) klinisch-relevante Malperfusion der linken oberen Extremität.

Ergebnisse

An den drei Studienzentren konnten zwischen den Jahren 2001 und 2016 insgesamt 176 Patienten (mittleres Alter: 61,3 Jahre) in die Studie eingeschlossen werden. In 55 (31,3%) Fällen erfolgte eine Revaskularisation mittels LSA-Bypass bzw. -Transposition vor der TEVAR-Prozedur (Gruppe 1), während bei den verbliebenen 121 (68,7%) Patienten die LSA ohne Revaskularisation komplett überstentet wurde (Gruppe 2).

Die Krankenhausletalität für die gesamte Studienkohorte lag bei 8,5% (einschließlich Notfalleingriffen) und war zwischen beiden Gruppen nicht signifikant unterschiedlich (p=0,779). In elektiven Fällen lag die postoperative Letalität bei 4,5%. In der Kaplan-Meier-Überlebensschätzung über einen postoperativen Zeitraum von sieben Jahren zeigte sich ebenfalls kein statistisch signifikanter Unterschied zwischen beiden Studiengruppen (p=0,570; **Abbildung 13**).

Postoperativ lag die Schlaganfall- und Paraplegierate für alle Studienpatienten bei insgesamt 6,8% bzw. 6,3%, ohne signifikante Unterschiede zwischen revaskularisierten (Gruppe 1) und nicht-revaskularisierten (Gruppe 2) Patienten. Im Gegensatz dazu traten Malperfusionen der linken oberen Extremität mit einer Inzidenz von 9,9% ausschließlich in Gruppe 2 auf (p=0,018). In diesen Patienten mit klinisch-relevanter Malperfusion wurde zudem eine vierfach häufigere Inzidenz von Schlaganfällen der linken Hemisphäre festgestellt (16,7% vs. 3,7%; p=0,095).

In der multivariaten Analyse konnten die Nicht-Revaskularisation der LSA (OR: 3,779; 95%-CI: 1,096 - 13,029; p=0,035), die Platzierung von mehr als zwei endovaskulären Stentprothesen (OR: 3,814; 95%-CI: 1,557 - 9,343; p=0,003) und das Vorhandensein einer koronaren Herzerkrankung (OR: 3,276; 95%-CI: 1,262 - 8,507; p=0,015) als unab-

hängige Risikofaktoren für eine prozedurspezifische Komplikation (linksseitiger Schlaganfall, permanente Querschnittslähmung oder klinisch-relevante Malperfusion der linken oberen Extremität) identifiziert werden.

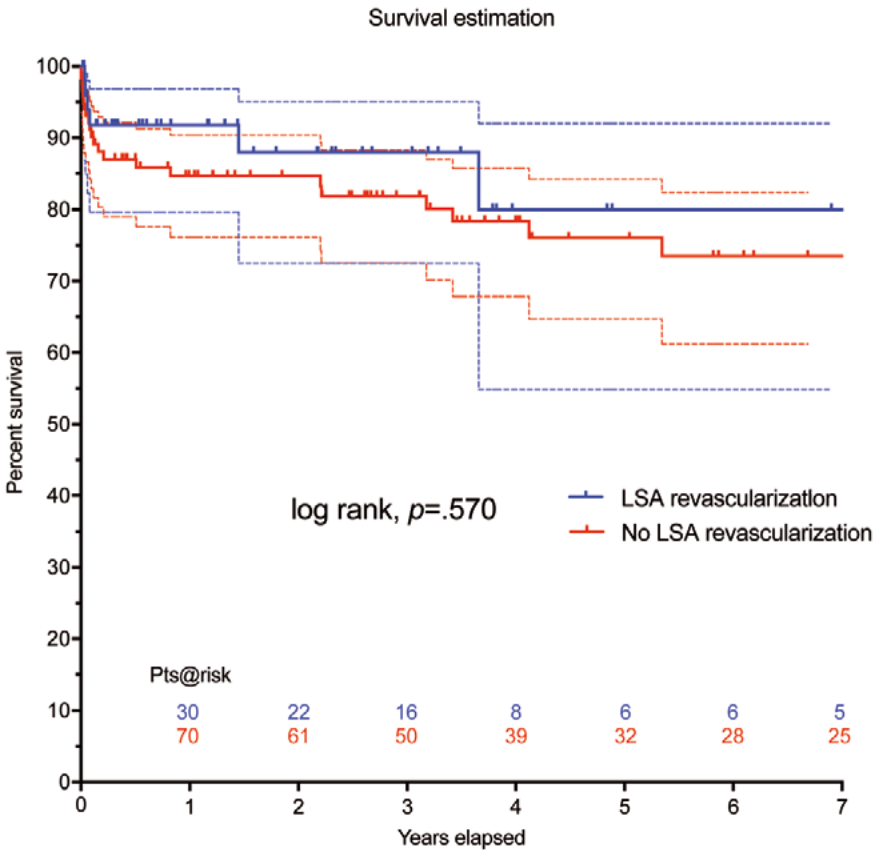

Abbildung 13: Kaplan-Meier-Überlebensschätzung von Patienten nach TEVAR mit (blaue Linie) oder ohne (rote Linie) prophylaktische LSA-Revaskularisation inkl. 95%-Konfidenzintervall (aus Luehr M, et al. [62] mit freundlicher Genehmigung von Elsevier).

Diskussion

In dieser multi-zentrischen Studie konnte erfolgreich gezeigt werden, dass eine prophylaktische Revaskularisation der LSA (im Vergleich zur Nicht-Revaskularisation) nicht zwangsläufig mit einer erhöhten Krankenhausletalität einhergeht. Vielmehr zeigte sich, dass die Nicht-Revaskularisation der LSA bei TEVAR-Patienten mit einem signifikant erhöhten Risiko für die Entwicklung einer klinisch-relevanten Malperfusion der

linken oberen Extremität (mit gesteigertem Risiko für einen linksseitigen Schlaganfall) vergesellschaftet ist. Die Tatsache, dass die o.g. prozedurspezifischen Komplikationen (Schlaganfall und Querschnittslähmung) signifikant gehäuft bei Patienten mit ausgeprägten Gefäßverkalkungen (koronare Herzerkrankung) und nach der Implantation von mehreren Stentprothesen auftreten, unterstreicht die Notwendigkeit der präoperativen bildgebenden Diagnostik und interdisziplinären OP-Planung.

In der Konsequenz sollte die prophylaktische Revaskularisation der LSA, insbesondere bei Patienten mit koronarer Herzerkrankung sowie ausgedehnten Aortenpathologien (welche mehrere Stentprothesen zur Behandlung erfordern), vor der TEVAR-Prozedur erfolgen, um assoziierte links-zerebrale neurologische Komplikationen zu vermeiden und eine Perfusion der linken oberen Extremität sicher zu stellen.

3.3 Schlussfolgerungen

1) Im Vergleich zu Patienten mit einer partiellen Überstentung der LSA (antegrade Perfusion ist weiterhin gegeben) ist das perioperative Risiko für periphere und zentrale neurologische Komplikationen bei einem vollständigen LSA-Verschluss nach TEVAR erhöht. Dies trifft insbesondere auf Patienten mit einem ausgeprägten postoperativen Subclavian-Steal-Syndrom (Grad III) zu.
2) Die Überstentung der LSA ohne prophylaktische Revaskularisation, die Platzierung von mehr als einer endovaskulären Stentprothese und das Vorhandensein einer koronaren Herzerkrankung stellen unabhängige Risikofaktoren für prozedurspezifische Komplikationen bei TEVAR-Patienten mit einer Landungszone 2 dar.
3) Bei einer geplanten Überstentung der LSA sollte eine prophylaktische Revaskularisierung mittels Bypass/ Transposition angestrebt werden, um links-zerebrale neurologische Komplikationen zu vermeiden und eine Perfusion der linken oberen Extremität sicher zu stellen.

4. Sekundäreingriffe im Bereich des Aortenbogens und der Aorta descendens nach stattgehabter endovaskulärer Therapie

Während die endovaskuläre Therapie von Pathologien im Bereich der Aorta thorako-abdominalis oftmals eine mehrwöchige Vorlaufzeit erfordert (Maßanfertigung einer individuellen Stentprothese), können akute und chronische Erkrankungen mit Beschränkung auf die Aorta descendens meist schnell und erfolgreich mittels TEVAR behandelt werden [2,30]. Zudem bietet die endovaskuläre Therapie der Aorta descendens im Vergleich zur offenen Chirurgie Vorteile hinsichtlich der frühpostoperativen Mortalität und Letalität [20]. Dementsprechend hat die Anzahl von TEVAR-Eingriffen in den vergangenen Jahren stetig zugenommen.

Allerdings ist die Inzidenz von TEVAR-assoziierten Komplikationen im Mittel- und Langzeitverlauf und deren Behandlung als Sekundäreingriff—mit besonderer Relevanz für jüngeren Patienten—bislang jedoch nur unzureichend untersucht worden.

4.1 Ergebnisse von Sekundäreingriffen nach primär endovaskulärer Stentgraft-Therapie der Aorta (Originalarbeit 6.6)

Hintergrund

Durch die klinische Etablierung von TEVAR hat sich die Behandlung von Pathologien der Aorta descendens, weg von einer reinen Notfallprozedur und hin zur Standardtherapie entwickelt [2,30,52]. Durch die starke Zunahme von TEVAR ist jedoch auch das Risiko für mögliche Verlaufskomplikationen im Bereich der Aorta descendens sowie der angrenzenden Aortenabschnitte (Aortenbogen, Aorta abdominalis) weiter angestiegen, welche ggf. mittels offenem oder endovaskulären Sekundäreingriff behandelt werden müssen [63]. Erfahrungen mit TEVAR-Komplikationen sind jedoch begrenzt und postoperative Ergebnisse von Sekundäroperationen wurden in der Fachliteratur bisher nur einzeln (z.B. als Fallberichte) oder in kleineren Fallserien veröffentlicht.

Das Ziel der Forschungsarbeit war daher die Bestimmung der Inzidenz von relevanten Verlaufskomplikationen nach stattgehabter primärer TEVAR, die Beschreibung der durchgeführten Sekundäreingriffe sowie die Analyse der postoperativen Ergebnisse an einem großen aortenchirurgischen Referenzzentrum.

Methodik

Die Datenbank des Herzzentrum Leipzig – Universität Leipzig wurde retrospektiv ausgewertet und alle Patienten mit Sekundäreingriff bei Komplikation nach primärer TEVAR evaluiert. Als Sekundäreingriffe wurden alle offenen, endovaskulären oder Hybrid-Operationen im klinischen Verlauf nach Primäreingriff definiert. Zum direkten Vergleich wurden zwei Gruppen hinsichtlich der Art von Sekundäreingriff gebildet: Reintervention (endovaskulär) und Operation (offen konventionell). Alle Patienten mit bereits zum Zeitpunkt des Primäreingriffs geplanten Operationen oder Reinterventionen als Zweiteingriff (sog. „staged repair“) wurden ausgeschlossen.

Ergebnisse

Insgesamt konnten 56 (15,1%) von 371 Patienten (mittleres Alter: 61,3 Jahre) mit einem ungeplanten Sekundäreingriff nach TEVAR im Zeitraum 2002 bis 2013 identifiziert und

eingeschlossen werden. Es wurden 25 Operationen (44,6%) und 31 Reinterventionen (55,4%) nach einem mittleren Zeitraum von 3,8 bzw. 1,6 Monaten durchgeführt. Die Indikationen für Sekundäreingriffe in der gesamten Studienkohorte umfassten relevante Undichtigkeiten (Endoleaks; n=28; 7,5%), Zunahme des Aneurysmadurchmessers (n=3; 0,8%), Malperfusionssyndrome (n=9; 2,4%), retrograde Typ A Dissektionen (n=2; 0,5%), aorto-bronchiale/ -ösophageale Fistelbildungen (n=9; 2,4%), Stentprotheseninfekte (n=4; 1,1%) sowie einen Fall mit iatrogener Aortenklappeninsuffizienz (katheterinduziert; n=1; 0,3%).

Die Krankenhausletalität betrug insgesamt 10,7%. Allerdings konnte kein signifikanter Unterschied zwischen Patienten mit Operation oder Reintervention gefunden werden (4% vs. 16%; p=0,14). Auch zeigten sich keine signifikanten Unterschiede—mit Ausnahme der respiratorischen Insuffizienz—im Hinblick auf postoperative Komplikationen (siehe **Tabelle 1**).

Im postoperativen Verlauf über einen Zeitraum von 36 Monaten konnte mittels Überlebensschätzung nach Kaplan-Meier ebenfalls kein statistisch signifikanter Unterschied zwischen offen operierten oder reintervenierten Patienten gefunden werden (p=0,60; **Abbildung 14**).

Tabelle 1: Postoperative Ergebnisse nach Sekundäreingriff (n=56): Operation vs. Reintervention

Komplikation, n (%)	**Operation (n=25)**	**Reintervention (n=31)**	***p*-Wert**
Krankenhausletalität	1 (4)	5 (16)	0.14
Paraplegie	1 (4)	2 (6)	0.68
Schlaganfall	2 (8)	3 (9)	0.82
Niereninsuffizienz	4 (16)	1 (3)	0.09
Respiratorische Insuffizienz	3 (12)	-	0.04*
Sepsis	4 (16)	1 (3)	0.09
Malperfusion	1 (4)	1 (3)	0.87

*=statistisch signifikant

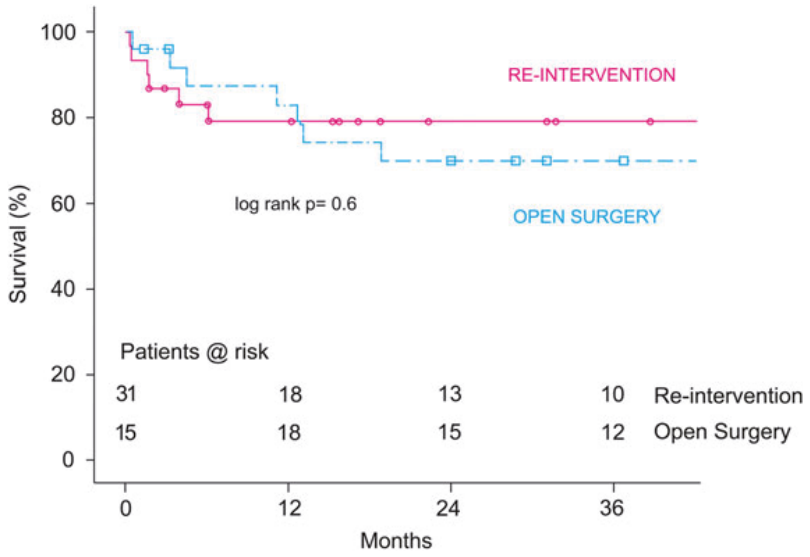

Abbildung 14: Kaplan-Meier-Überlebensschätzung: Operation vs. Reintervention nach TEVAR (aus Nozdrzykowski M, Luehr M et al. [64] mit freundlicher Genehmigung von Oxford University Press).

Diskussion

Sekundäreingriffe nach TEVAR aufgrund von früh oder spät auftretenden Verlaufskomplikationen sind nicht selten und wurden in der aktuellen Studienkohorte in über 15% der Fälle notwendig. Die am häufigsten auftretenden Verlaufskomplikationen stellen Endoleaks (insbesondere vom Typ Ia), Stentprotheseninfektionen, aorto-bronchiale/-ösophageale Fisteln und Malperfusionen nachgeschalteter Organsysteme dar. Während sich Endoleaks und Malperfusionen oftmals gut mittels Reintervention behandeln lassen, ist eine offene Operation bei Infektionen mit oder ohne Fistelbildung, drohenden Rupturen oder retrograden Typ A Dissektionen unumgänglich, um das Leben von betroffenen Patienten zu retten.

Zusammenfassend lässt sich feststellen, dass Sekundäreingriffe nach TEVAR bei entsprechender individueller Planung mit sehr akzeptablen Ergebnissen durchgeführt werden können. Jedoch sollte in den behandelnden Zentren eine engmaschige Verlaufskontrolle bei TEVAR-Patienten durchgeführt werden, um drohende oder akute Komplikationen frühzeitig diagnostizieren und optimal therapieren zu können.

4.2 Chirurgische Therapie bei verzögert auftretender retrograder Typ A Dissektion nach endovaskulärer Stentgraft-Therapie des Aortenbogens mit kompletter supraaortaler Revaskularisierung (Originalarbeit 6.7)

Hintergrund

Die konventionelle offene Operation ist nach wie vor der Goldstandard bei der Therapie des Aortenbogens. Aufgrund von zunehmender klinischer Erfahrung und weiteren technischen Verbesserungen von TEVAR kamen in der jüngsten Vergangenheit jedoch zunehmend endovaskuläre Techniken bei Hochrisikopatienten zum Einsatz, welche einer konventionellen Aortenbogenoperation nicht zugeführt werden konnten [65–67]. Ein Konzept, das sog. „supraaortale Debranching", generiert eine ausreichende Landungszone im Aortenbogen (Landungszonen 0, 1, 2; **Abbildung 12**) durch eine Absetzung und extra-anatomische Revaskularisierung von Truncus brachiocephalicus, der A. carotis communis sinistra und der A. subclavia sinistra [65]. Anschließend werden eine oder mehrere Stentprothesen retrograd über die A. femoralis in der Aorta ascendens bzw. im Aortenbogen platziert. Diese Technik kann auch ohne Herz-Lungen-Maschine und Kreislaufstillstand durchgeführt werden. Allerdings birgt diese Technik die Gefahr einer „retrograden" Typ A Dissektion, welche entweder verzögert oder akut auftreten kann und mit einer sehr hohen Letalität von 50% bis 70% assoziiert ist [68].
In dieser Analyse wurden die ersten Erfahrungen mit dieser neuen Hybrid-Technik in Bezug auf die Durchführbarkeit und die postoperativen Ergebnisse—mit speziellem Fokus auf die Behandlung der retrograden Typ A Dissektion—hin untersucht.

Methodik

Die Datenbank des Herzzentrum Leipzig – Universität Leipzig wurde hinsichtlich der Behandlung von Aortenbogenpathologien retrospektiv ausgewertet. Als Einschlusskriterium wurde die Behandlung mittels Hybrid-Technik (supraaortales Debranching und TEVAR) herangezogen. Patienten mit einem konventionellen Aortenbogenersatz wurden ausgeschlossen.

Ergebnisse

Im Zeitraum 2010 bis 2012 wurden 118 Patienten mit Aortenbogenpathologien behandelt. Insgesamt konnten neun (7,6%) Hochrisikopatienten mit ausgedehnten Pathologien des Aortenbogens und Beteiligung der proximalen Aorta descendens (mittlerer logistischer EUROScore: 26), welche mit einem komplettem supraaortalen Debranching (Landungszone 0) versorgt worden waren, in die Studie eingeschlossen werden.

Bei allen Patienten konnte die Hybrid-Prozedur erfolgreich durchgeführt werden. Die Krankenhausletalität lag bei 0%. Die mittlere Intensiv- und Krankenhausverweildauer lang im Mittel bei 11,3 Tagen und 19,5 Tagen. Die postoperativen Komplikationen umfassten neue Schlaganfälle (n=2), respiratorische Insuffizienz (n=5), Nachblutungen (n=3), Bypassverschluss (n=1) und Sternuminstabilität (n=1). Darüber hinaus entwickelten zwei Patienten (22,2%) während ihres weiteren Krankenhausaufenthalts verzögert eine retrograde Typ A Dissektion, welche in beiden Fällen notfallmäßig mit einem totalen Aortenbogenersatz in konventioneller Technik behandelt werden mussten (**Abbildung 15**).

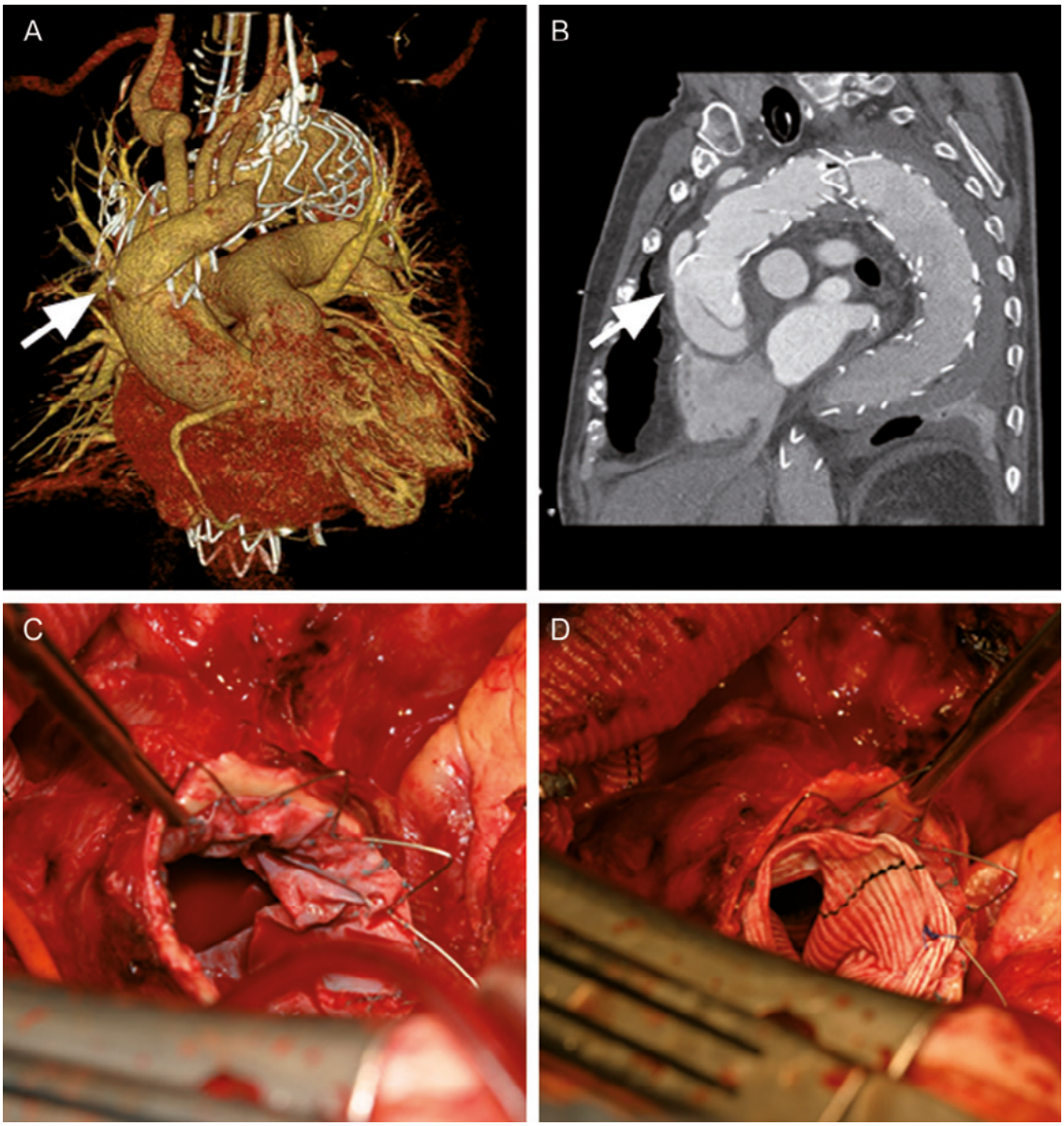

Abbildung 15: Computertomographie mit Darstellung einer retrograden Typ A Dissektion durch Perforation des proximalen nicht-bedeckten Anteils der Stentprothese (A und B). Intraoperativer Blick auf den unbedeckten Anteil der Stentprothese vor (C) und nach Einnähen einer Aortenprothese (D) zur Versorgung mittels totalem Aortenbogenersatz in ET-Technik (aus Luehr M, et al. [69] mit freundlicher Genehmigung von Oxford University Press).

Diskussion

Im Hinblick auf die Ergebnisse dieser Studie stellt sich die Frage, ob die angewandte Hybrid-Technik für jeden vermeintlichen Hochrisikopatienten auch immer die optimale Strategie darstellt. Dies wird insbesondere durch die Tatsache verdeutlicht, dass beide Patienten mit retrograder Typ A Dissektion erfolgreich konventionell re-operiert werden konnten. Dementsprechend sollten für eine Therapieentscheidung präoperativ immer alle zur Verfügung stehenden Behandlungsoptionen in Betracht gezogen und stets individuell auf den Patienten angepasst werden.

Die retrograde Typ A Dissektion stellt eine neue und möglicherweise in ihrer Inzidenz stark unterschätzte Komplikation der neuen Hybrid-Technik des supraaortalen Debranchings dar. Insbesondere Stentprothesen mit unbedeckten proximalen Anteilen (Stentgerüst) sollten, ebenso wie unnötiges Überdimensionieren und Nachballonieren der Stentprothese, im nativen Aortenbogen und der Aorta ascendens keine Anwendung finden. Ebenso sollte ein elektiver Ersatz der Aorta ascendens (Landungszone 0) bei Patienten mit einer Ektasie der Aorta ascendens vor dem TEVAR-Eingriff durchgeführt werden, um eine retrograde Typ A Dissektion sicher zu verhindern und eine ausreichende Landungszone zu gewährleisten [66].

4.3 Notfallmäßige offene Chirurgie bei aorto-ösophagealen und aorto-bronchialen Fisteln nach endovaskulärer Stentgraft-Therapie der Aorta (Originalarbeit 6.8)

Hintergrund

Sekundäre aorto-bronchiale (ABF) und aorto-ösophageale (AÖF) Fisteln stellen ungewöhnliche (Inzidenz 1,7%) aber fatale Komplikationen nach offenem thorakalen und thorakoabdominellen Aortenersatz dar [70]. In jüngster Zeit wurden diese Komplikationen jedoch auch bei Patienten nach TEVAR mit einer steigenden Inzidenz von 1,5% bis 1,9% beschrieben [70]. Eine aortale Fistelbildung kann mit zerebralen Luftembolien einhergehen oder zu freien Blutungen in die Speiseröhre (AÖF) bzw. ins Bronchialsystem (ABF) führen. Zudem kommt es zu einer Infektion der Stentprothese, die eine offene Reoperation mit Entfernung von Fremdmaterial sowie umgebendem Gewebe erfordert und mit einer postoperativen Letalität von 26% bis 64% assoziiert ist [51,70]. Während in den Fachgesellschaften übergreifend Einigkeit darüber besteht, dass ein konservatives Vorgehen mit einer Letalität von 100% einhergeht, wird von einigen Autoren, zumindest für ABF, alternativ zur offenen Operation eine endovaskuläre Reintervention kritisch diskutiert [67,71]. In Ermangelung von großen klinischen Untersuchungen beschränkt sich die Erfahrung bei der Behandlung von ABF und AÖF allerdings nur auf einige wenige Fallberichte und kleinere Fallserien.

Das Ziel dieser Studie war die retrospektive Analyse von Patienten mit ABF und AÖF zur Bestimmung der Inzidenz, Beschreibung der klinischen Präsentation und Evaluation von postoperativen Ergebnissen.

Methodik

Es erfolgte eine retrospektive Datenbankauswertung am Herzzentrum Leipzig – Universität Leipzig im Zeitraum 2002 bis 2013. Ausschließlich Patienten mit einer AÖF oder ABF nach stattgehabter TEVAR wurden in die Studie eingeschlossen. Alle TEVAR-Patienten ohne eine aortale Fistel im postoperativen Verlauf wurden ausgeschlossen.

Ergebnisse

Insgesamt wurden 374 Patienten (mittleres Alter: 67,6 Jahre) mittels TEVAR im Zeitraum 2002 bis 2013 behandelt. Postoperativ entwickelten 10 (2,6%) Patienten eine AÖF (n=8; 2,1%) und zwei eine ABF (0,5%) nach einem mittleren Zeitraum von 18,1 Monaten.

Die klinischen Symptome bei Aufnahme von Patienten mit AÖF oder ABF umfassten Hämatemesis (n=4), Hämoptysis (n=4) oder Melena (n=1) mit oder ohne hämorrhagischem Schock (n=4), neu-aufgetretenes Fieber (n=3), Dysphagie (n=1), Dyspnoe (n=1), Brustschmerz (n=1), Schwindel (n=1) und Präsynkope (n=1). Alle Patienten zeigten zudem pathologisch erhöhte Entzündungswerte im präoperativen Labor (n=10) mit positiven Blutkulturen in 8 Fällen. Die definitive Diagnosestellung erfolgte einzeln oder in Kombination mittels Endoskopie (n=7), Bronchoskopie (n=1), Ösophagographie (n=1) oder Computertomographie (n=4) (**Abbildung 16 und 17**).

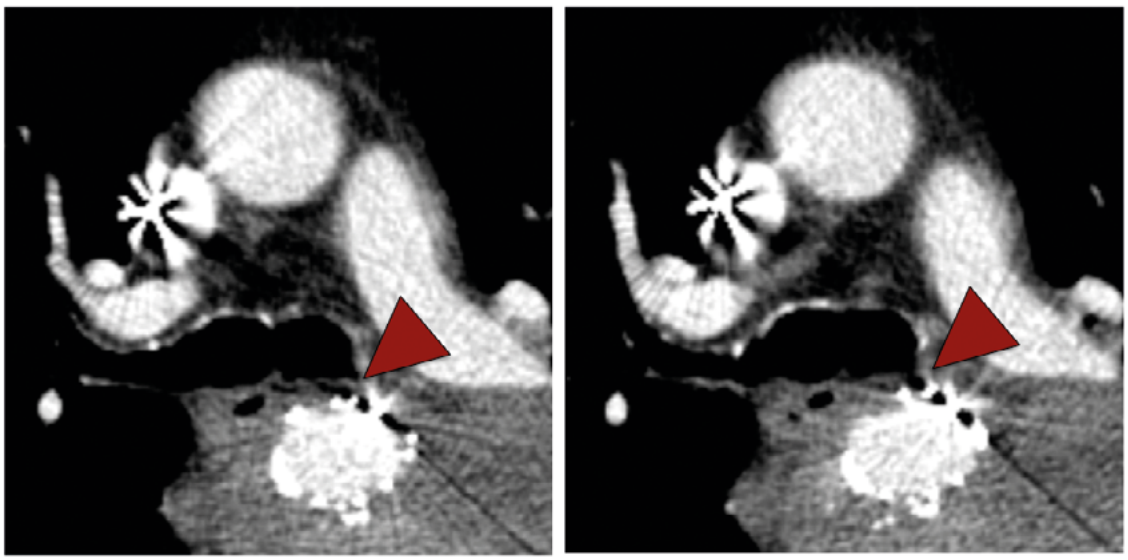

Abbildung 16: Darstellung einer aorto-bronchialen Fistel (AÖF; s. rote Pfeilspitze) mittels Computertomographie (aus Luehr M, et al. [3] mit freundlicher Genehmigung von Oxford University Press).

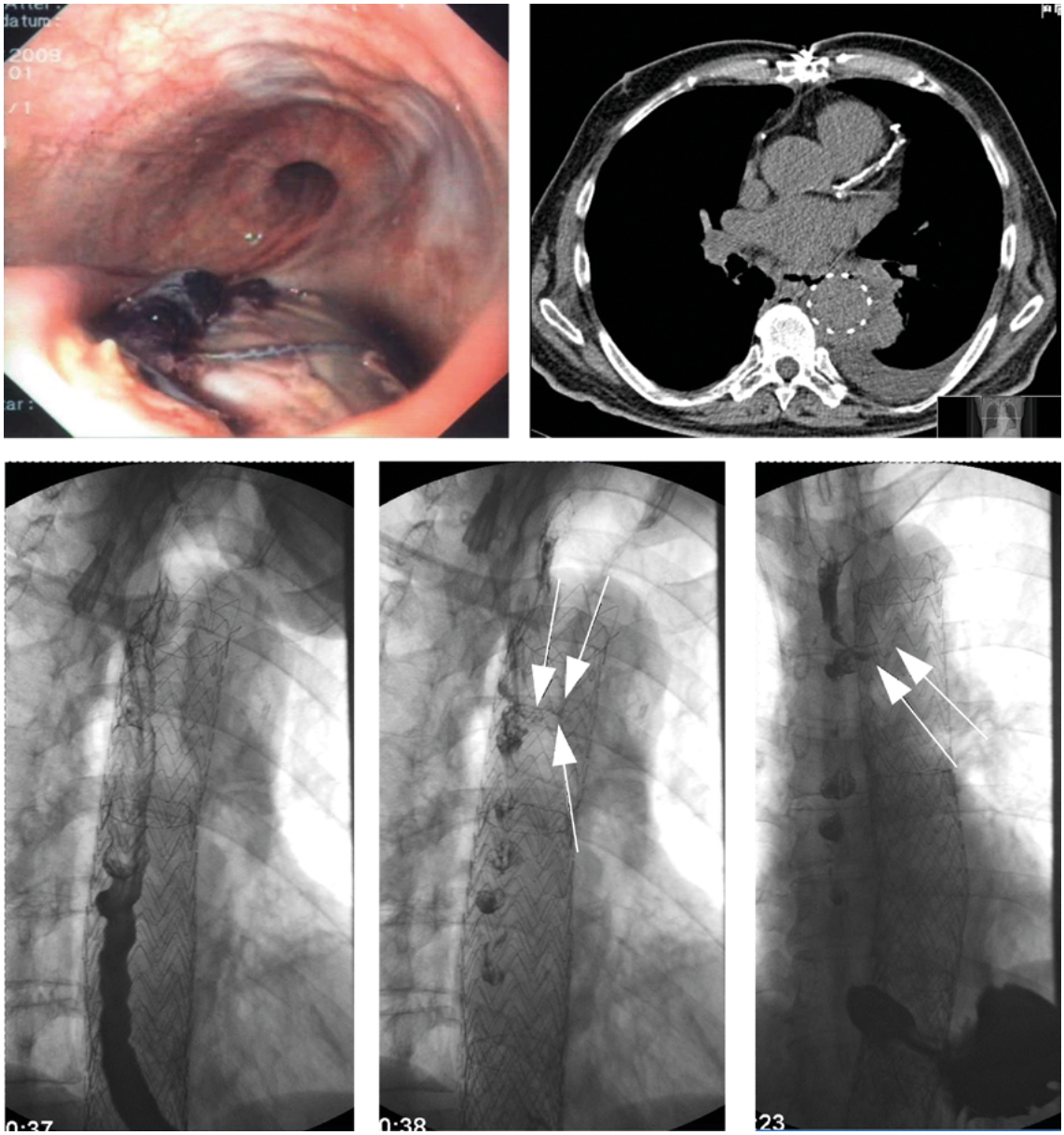

Abbildung 17: Darstellung von aorto-ösophagealen Fisteln (AÖF) mittels Endoskopie (A), Computertomographie (B) oder Ösophagographie (C) (aus Luehr M, et al [3] mit freundlicher Genehmigung von Oxford University Press).

Insgesamt wurden acht Patienten mit AÖF (n=7) und ABF (n=1) offen operiert. Die Operationstechnik umfasste die vollständige Entfernung der Stentprothese und des umgebenden infizierten Gewebes (**Abbildung 18**). Die Krankenhaus- und Ein-Jahresletalität lagen jeweils bei 25% (n=2) bzw. 37,5% (n=3). Postoperative Komplikationen umfassten Re-Operationen bei Nachblutung (n=4) sowie temporär auftretendes Nieren- (n=2) und Lungenversagen (n=2). Die Krankenhausverweildauer nach stattgehabter Operation bei AÖF/ABF betrug im Mittel 30 (±21,4) Tage.

Zwei der zehn Patienten wurden zum Zeitpunkt der Diagnose als inoperabel eingestuft und verstarben akut (n=1) oder nach konservativer Therapie im weiteren Verlauf (n=1).

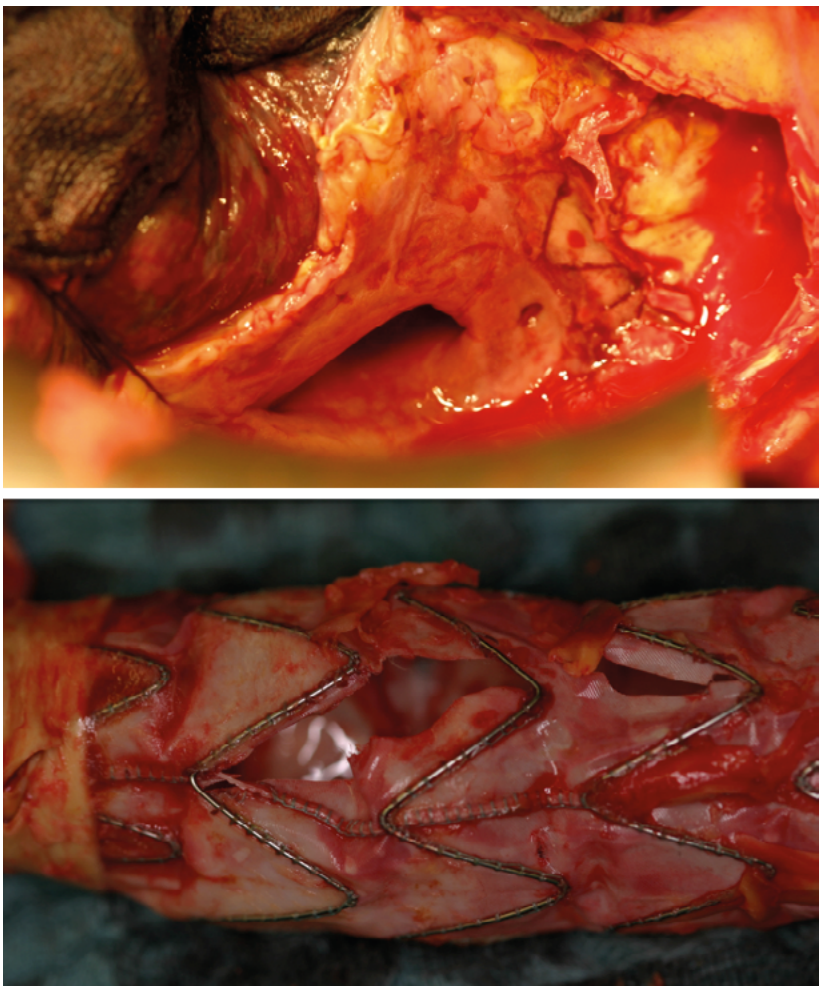

Abbildung 18: Intraoperativer Blick auf eine aorto-ösophageale Fistel (A) und die explantierte Stentprothese (B) (aus Luehr M, et al. [3] mit freundlicher Genehmigung von Oxford University Press).

Diskussion

Durch die zunehmende endovaskuläre Therapie der Aorta descendens mittels TEVAR wurde in der Literatur zuletzt ein deutlicher Anstieg von zuvor als extrem selten geltenden Komplikationen registriert. Obwohl in der Fachliteratur die Inzidenz von aortalen Fisteln in die Speiseröhre (AÖF) bzw. in das Bronchialsystem (ABF) nur mit 1,5% bis 1,9% beschrieben wird [70], lag die Inzidenz in der Studienkohorte mit 2,6% fast doppelt so hoch.

Die Ergebnisse der Studie legen nahe, dass AÖF und ABF weitaus häufiger nach TEVAR auftreten als bislang angenommen. Zudem ist der initiale Verlauf dieser fatalen Komplikationen oft unspezifisch, so dass eine sichere Diagnose oft nur in Kombination von verschiedenen Untersuchungstechniken und bildgebenden Verfahren möglich ist. Da späte Diagnosen oder rein medikamentöse Therapieansätze oftmals fatal enden und eine infizierte Stentprothese nicht dauerhaft mittels erneuter TEVAR saniert werden kann, stellt die offene und radikale Operationstechnik, mit vollständiger Entfernung von Fremdmaterialen und Geweben, die derzeit einzige kurative Therapie von Patienten mit AÖF und ABF dar. In erfahrenen Zentren können bei der operativen Behandlung von AÖF und ABF jedoch sehr akzeptable Ergebnisse, mit einer postoperativer Krankenhausletalität von 25% bis 27% [3,72], erreicht werden.

4.4 Schlussfolgerungen

1) Die Inzidenz von Sekundäreingriffen nach TEVAR aufgrund von Verlaufskomplikationen liegt bei über 15%. Häufige Verlaufskomplikationen stellten Endoleaks (insbesondere vom Typ Ia), Stentprotheseninfektionen, Fisteln und Malperfusionen nachgeschalteter Organsysteme dar.
2) Offene und endovaskuläre Sekundäreingriffe nach TEVAR können mit akzeptablen Ergebnissen durchgeführt werden. Engmaschige Routineuntersuchungen sind jedoch notwendig, um drohende oder akute Komplikationen im postoperativen Verlauf frühzeitig zu diagnostizieren und optimal behandeln zu können.
3) Das supaaortale Debranching stellt eine neues Hybrid-Verfahren für Hochrisikopatienten mit ausgedehnten Aortenbogenpathologien dar. Allerdings birgt diese Technik ein erhöhtes Risiko für das Auftreten von retrograden Typ A Dissektionen.
4) Um das Risiko einer retrograden Typ A Dissektion zu senken, sollte bei TEVAR im Aortenbogen bzw. in der Aorta ascendens ein Überdimensionieren und Nachballonieren vermieden werden, ebenso wie Stentprothesen mit unbedeckten proximalen Anteilen. Bei Patienten mit Ektasie der Aorta ascendens sollte ein elektiver Ersatz Aorta ascendens in Erwägung gezogen werden.
5) Aortale Fisteln in die Speiseröhre (AÖF) und in das Bronchialsystem (ABF) treten mit steigender Inzidenz (bis 2,6%) nach TEVAR auf. Eine offene Operation—mit vollständiger Entfernung von Fremdmaterial und infiziertem Gewebe—stellt derzeit die einzige kurative Therapie von AÖF und ABF dar und kann in spezialisierten Zentren mit akzeptablen Ergebnissen durchgeführt werden.

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6. Schriftenverzeichnis der kumulativ zusammengefassten Originalarbeiten

6.1 Multicentre analysis of current strategies and outcomes in open aortic arch surgery: heterogeneity is still an issue

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Multicentre analysis of current strategies and outcomes in open aortic arch surgery: heterogeneity is still an issue

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Abstract

OBJECTIVES: The study was conducted to evaluate, on the basis of a multicentre analysis, current results of elective open aortic arch surgery performed during the last decade.

METHODS: Data of 1232 consecutive patients who underwent aortic arch repair with reimplantation of at least one supra-aortic artery between 2004 and 2013 were collected from 11 European cardiovascular centres, and retrospective statistical examination was performed using uni- and multi-variable analyses to identify predictors for 30-day mortality. Acute aortic dissections and arch surgeries not involving the supra-aortic arteries were not included.

RESULTS: Arch repair involving all 3 arch arteries (total), 2 arch arteries (subtotal) or 1 arch artery (partial) was performed in 956 (77.6%), 155 (12.6%) and 121 (9.8%) patients, respectively. The patients' characteristics as well as the surgical techniques, including the method of cannulation, perfusion and protection, varied considerably between the clinics participating in the study. The in-hospital and 30-day mortality rates were 11.4 and 8.8% for the entire cohort, respectively, ranging between 1.7 and 19.0% in the surgical centres. Multivariable logistic regression analysis identified surgical centre, patient's age, number of previous surgeries with sternotomy and concomitant surgeries as independent risk factors of 30-day mortality. The follow-up of the study group was 96.5% complete with an overall follow-up duration of 3.3 ± 2.9 years, resulting in 4020 patient-years. After hospital discharge, 176 (14.3%) patients died, yielding an overall mortality rate of 25.6%. The actuarial survival after 5 and 8 years was 72.0 ± 1.5% and 64.0 ± 2.0, respectively.

CONCLUSIONS: The surgical risk in elective aortic arch surgery has remained high during the last decade despite the advance in surgical techniques. However, the patients' characteristics, numbers of surgeries, the techniques and the results varied considerably among the centres. The incompleteness of data gathered retrospectively was not effective enough to determine advantages of particular cannulation, perfusion, protection or surgical techniques; and therefore, we strongly recommend further prospective multicentre studies, preferably registries, in which all relevant data have to be clearly defined and collected.

Keywords: Aortic arch • Aortic surgery • Cerebral protection

INTRODUCTION

Since Griepp and associates first described the use of deep hypothermic circulatory arrest for prosthetic replacement of the aortic arch in 1975, the number of centres performing these procedures has continued to grow and it has become a routine surgery in many units [1]. However, various reports throughout the last decades demonstrate that aneurysms of the arch still remain a

challenging task, requiring thoughtful preoperative and intraoperative planning. Changes in operative techniques and technical progress have led to a substantial improvement in survival and outcomes [2–5]. On the other hand, there is also a rapid growth in alternative techniques and evolving technologies, including debranching of the aortic arch with subsequent thoracic endovascular aortic repair that should be benchmarked adequately [6–10]. With novel perfusion methods, improved neuroprotective strategies, and further technical advances, the success rates should continue to improve in the future. However, the determination of the impact of those advanced techniques on surgical outcomes should be based on the conclusive analysis of data gathered from several aortic referral sites to build a foundation for future recommendations and guidelines. Taking into account that no or very limited multicentre trials exist to date, the aim of this study was to evaluate the operative and clinical outcomes after conventional total or subtotal aortic arch replacement, using current perfusion and surgical techniques at several aortic referral centres in Europe.

PATIENTS AND METHODS

To assess the surgical and mid-term clinical outcomes after a conventional aortic arch surgery performed in several European aortic referral centres during the last 10 years, 18 aortic centres from 5 European countries were asked to report on their respective surgical strategies and postoperative results after elective aortic arch surgery performed between January 2004 and December 2013. Eleven centres (Supplementary material, Table S1) responded to the call and provided their data for a retrospective analysis. To keep an anonymous character of this analysis, the order of the centres as provided in tables and Supplementary tables does not correspond to the alphabetical order in the list of principal investigators and the centre list describing particular perfusion and protection strategies, which are provided in Supplementary material, Tables S1 and S4.

Inclusion criteria

The analysis includes all scheduled (elective and urgent) aortic arch surgeries performed due to any pathology (also including chronic dissections or re-do surgeries after conventional or thoracic endovascular aortic repair—TEVAR) with at least one circular aortic anastomosis and reimplantation of at least one aortic arch branch, regardless of the proximal or distal extent of the thoracic aorta repair. The extent of arch repair was defined as partial, subtotal or total:

- Arch repair with reimplantation of one arch artery (partial arch repair)
- Arch repair with reimplantation of two arch arteries (subtotal arch repair)
- Arch repair with reimplantation of three arch arteries (total arch repair)

To give an exact overview of the various methods for conventional aortic arch replacement, no exclusions were made with regard to the performed surgical approaches, (which, in addition to median sternotomy included median sternotomy with lateral extension [hemi-clamshell], bilateral thoracotomy [clam shell] and posterolateral thoracotomy), anastomosing techniques (conventional, elephant trunk [ET] or stented elephant trunk [so-called frozen elephant trunk—FET]) or any concomitant cardiac or cardiovascular procedures. For supra-aortic reconstruction, all surgical methods of reimplantation were included (e.g. island technique, singular reimplantation, supra-aortic translocation and extra-anatomic bypass). To analyse the potential impact of neuroprotective strategies, all participating centres were also asked to give detailed information on their arterial cannulation techniques and respective cerebral protection and, if appropriate, cerebral perfusion management. Accordingly, all available techniques were included and comprised all forms of antegrade (bilateral or unilateral) cerebral perfusion (ACP), retrograde cerebral perfusion (RCP) and deep hypothermic circulatory arrest (DHCA).

Table 1: Preoperative patient characteristics

Characteristics	No (%) or mean ± SD
Sex male	778 (63)
Age (years)	64 ± 13
Arch pathology	
Aneurysm	874 (70.9)
Chronic dissection	278 (22.6)
False aneurysm	29 (2.4)
Inflammatory/infection	21 (1.7)
Porcelain aorta	14 (1.1)
Others	16 (1.3)
Aortic valve defect	
Insufficiency	515 (41.8)
Stenosis	75 (10.0)
Mixed	51 (4.1)
Previous cardiac surgery	340 (27.6)
Previous neurological events	113 (9.2)
With residuals	66 (5.4)
Without residuals	47 (3.8)
Previous TEVAR	34 (2.8)
Creatinine (mg%)	1.1 ± 1.6

TEVAR: thoracic endovascular aortic repair.

Exclusion criteria

The only exclusion criteria were:

- open arch anastomosis (hemiarch) without involvement of any arch arteries
- acute aortic dissection
- intraoperative aortic injury necessitating unscheduled repair

Altogether, 1232 patients (mean age 64 ± 13 years) were included in the study group (Table 1). The respective numbers of included patients varied between single centres from 17 to 237. The subcohorts also varied in regard to age, gender, previous neurological event and previous surgery (Supplementary material, Table S2). Aortic aneurysm was the most frequent indication for aortic arch surgery (70.9%), followed by chronic dissection (22.6%) and other pathologies (6.5%); however, the incidences of chronic aneurysm, chronic dissection or aortic valve defect were also significantly different among the centres. Previous open cardiac surgery with sternotomy had been performed in 340 patients (27.6%), whereas 34 (2.8%) patients were initially treated by TEVAR of the thoracic aorta. The detailed preoperative patient characteristics and underlying aortic pathologies are summarized in Table 1 for the entire cohort

Table 2: Operative data

Variables	No (%) or mean ± SD
Arterial cannulation	
AXA right	464 (37.7)
Aorta	306 (24.8)
CCA	169 (13.7)
IA	149 (12.1)
Femoral	131 (10.6)
Others	13 (1.1)
Cerebral protection	
Bilateral CP	777 (63.1)
Unilateral CP	377 (30.6)
DHCA	74 (6.0)
Retrograde CP	1 (0.1)
Others[a]	3 (0.2)
CPB time (min.)	206.4 ± 64.4
CP time (min.)	58.1 ± 28.1
CA time of lower body (min.)	50.1 ± 26.0
CA time of brain (min.)	9.3 ± 11.7
Aortic cross-clamp time (min.)	120.8 ± 44.9
Lowest rectal temp. (°C)	26.1 ± 3.5

AXA: axillary artery; CCA: common carotid artery; IA: innominate artery; CP: cerebral perfusion; DHCA: deep hypothermic circulatory arrest; CPB: cardiopulmonary bypass; CA: circulatory arrest; LSA: left subclavian artery.
[a]beating heart with cross-clamping between left CCA and LSA.

and in Supplementary material, Table S2 for all sub-cohorts; whereas Supplementary material, Table S3 demonstrates that the incidences of chronic-obstructive lung disease (COLD), functional NYHA class, ejection fraction (EF) and aortic aetiology were reported incompletely limiting the evidence of statistical analysis. The complete monitoring of operative data, especially perfusion flow and pressure during cerebral perfusion, was provided by only 2 centres.

Surgical techniques, cannulation and perfusion

Surgical access was achieved via full sternotomy, partial sternotomy, bilateral thoracotomy, sternotomy with lateral extension and postero-lateral thoracotomy in 1134 (92.1%), 54 (4.4%), 14 (1.1%), 5 (0.4%) and 25 (2.0%) cases, respectively. Various techniques of arterial cannulation were also used in accordance with the preferences of the respective centre. As presented in Table 2, the right axillary artery (AxA) was the most frequently used arterial cannulation site (37.7%) followed by direct aortic (24.8%), common carotid artery (CCA, 13.7%), innominate artery (IA, 12.1%) and femoral artery (FA, 10.6%); other access routes as double cannulations were documented in only 13 patients (1.1%). The reported cerebral protection strategies comprised mainly bilateral (63.1%) or unilateral (30.6%) ACP, and DHCA (6.0%). In 3 cases (0.2%), the distal arch was performed with beating heart after cross-clamping the arch between the left CCA and left subclavian artery (LSA), and in only 1 case (0.1%) RCP was used (Table 2). However, there were relevant centre-related differences in the execution of these techniques, which could have already been observed in a survey performed by the vascular domain group of the EACTS [11]. A noverview of cannulation sites used in particular centres is demonstrated in Supplementary material, Table S4, whereas a short description of protection and perfusion techniques is provided below. Here, the order of the centres corresponds to the alphabetical list of the principal investigators (Supplementary material, Table S1), which is different from the anonymous order of the sub-cohorts in remaining tables and Supplementary tables.

- In Bologna, the preferred cannulation sites were AxA and IA followed by FA and aorta (Supplementary material, Table S4). Bilateral hypothermic ACP (blood temp. 20–24°C) applied by cannulation graft and/or, if appropriate, by inflatable perfusion catheters in the IA and left CCA with a constant flow of 15 ml per kg of body weight was used for cerebral protection. The LSA was blocked using a Fogarty catheter or, in case of FET, was cannulated with inflatable perfusion catheter and perfused. Near-infrared spectroscopy (NIRS) was used for neuro-monitoring and moderate hypothermia (24–26°C) for organ protection.
- In Bergamo, the preferred cannulation site was IA, followed in very rare cases by aorta, AxA or FA (Supplementary material, Table S4). Unilateral or bilateral moderate hypothermic ACP (blood temp. 24–26°C) applied by cannulation graft and/or, if appropriate, by inflatable perfusion catheters in the IA and left CCA with a pressure-controlled flow (targeting 40 mmHg) was used for cerebral protection. During ACP, the LSA was blocked using a Fogarty catheter. NIRS was used for neuro-monitoring and moderate hypothermia (26°C) was used for organ protection.
- In Leipzig, the preferred cannulation site was right AxA, followed by aorta, IA or FA (Supplementary material, Table S4). Mainly bilateral, or less frequently unilateral, hypothermic ACP (blood temp. 20°C) applied by cannulation graft and/or, if appropriate, by inflatable perfusion catheters in the IA and left CCA, with a flow (within the range of 8–20 ml of flow per minute/kg body weight) and pressure according to the surgeons' preferences. During ACP, the LSA was blocked using a Fogarty catheter. NIRS was used for neuro-monitoring and moderate hypothermia (24–28°C) was used for organ protection.
- In Heidelberg, the preferred cannulation site was the aorta followed by FA (Supplementary material, Table S4). Bilateral, mostly hypothermic ACP (blood temp. about 20°C) applied via 2 inflatable perfusion catheters in the IA and left CCA with a flow and pressure according to the surgeons' preferences was used for cerebral protection. During ACP, the LSA was blocked using a Fogarty catheter. NIRS was used for neuro-monitoring and moderate hypothermia (24–28°C) for organ protection.
- In Munich, until 2011, the preferred cannulation site was an FA combined with DHCA. Since 2012, a preferred cannulation site has been aorta followed by right AxA and IA (Supplementary material, Table S4). Hypothermic ACP (blood temp. 18°C) applied by cannulation graft and/or, if appropriate, by inflatable perfusion catheters in the IA and left CCA with a pressure-controlled flow (60 mmHg) was used for cerebral protection. During ACP, the LSA was blocked using a Fogarty catheter. NIRS was used for neuro-monitoring and moderate hypothermia (24–28°C) for organ protection.
- In Rome, IA or right AxA was used for arterial cannulation (Supplementary material, Table S4). Unilateral or bilateral hypothermic ACP (blood temp. 24–28°C) applied by cannulation graft and/or, if appropriate, by inflatable perfusion catheters in the IA and left CCA with a pressure-controlled flow (50–80 mmHg), resulting in a flow of about 0.7–1.0 l/min. was used for cerebral protection. During ACP, the LSA was blocked using a clamp or Fogarty catheter. NIRS and bilateral RR measurement in radial arteries were used for neuro-monitoring and moderate hypothermia (24–28°C) for organ protection.

- In Freiburg, the preferred cannulation site was the right AxA followed by an FA (Supplementary material, Table S4). Unilateral or bilateral hypothermic ACP (blood temp. 18–23°C) applied by cannulation graft and/or, if appropriate, by inflatable perfusion catheters in the IA and left CCA with a flow of 0.5–1.2 l/min., targeting a pressure of 40–50 mmHg was used for cerebral protection. During ACP, the LSA was blocked using a Fogarty catheter. NIRS was used for neuro-monitoring and deep to moderate hypothermia (about 20–22°C) for organ protection.
- In Hannover, the aorta was used for cannulation exclusively (Supplementary material, Table S4). Bilateral moderate hypothermic ACP (blood temp. 27°C) applied via 2 inflatable catheters in the IA and left CCA with a pressure-controlled flow (about 50 mmHg), targeting a flow rate of at least 500 ml/min. During ACP, the LSA was blocked using either a Fogarty catheter or a clamp. NIRS was used for neuro-monitoring and moderate hypothermia (25°C) for organ protection during ACP.
- In Essen, the preferred cannulation site was the right AxA followed by the aorta (Supplementary material, Table S4). Bilateral hypothermic ACP (blood temp. 18°C) applied by cannulation graft and/or, if appropriate, by inflatable perfusion catheters in the IA and left CCA with a pressure-controlled flow (targeting 50 mm of Hg) was used for cerebral protection. During ACP, the LSA was blocked using a Fogarty catheter. NIRS was used for neuro-monitoring and moderate hypothermia (24–26°C) for organ protection.
- In Bad Neustadt, the preferred cannulation site was the right CCA, followed by the left CCA and IA (Supplementary material, Table S4). Unilateral mild hypothermic ACP (blood temp. above 28°C) applied via cannulation graft with a pressure-controlled flow (about 80 mmHg), resulting in a flow of about 1.2 l/min. was used. All arch branches were cross-clamped with soft clamps exclusively. NIRS and bilateral RR measurement in radial arteries were used for neuro-monitoring and mild hypothermia (about 30°C) for organ protection.
- In Frankfurt, the preferred cannulation site was the right AxA, followed in very rare cases by the IA or FA (Supplementary material, Table S4). Mainly unilateral or bilateral mild hypothermic ACP (blood temp. above 28°C) applied by cannulation graft in the right AxA and/or, if appropriate, by inflatable perfusion catheters in the IA and left CCA, with a pressure-controlled flow (about 75 mmHg), resulting in a flow of about 1.1–1.4 l/min., was used. During ACP, the LSA was blocked, mainly using Fogarty catheter and NIRS was used for neuro-monitoring. Mild hypothermia (about 30°C) was used for organ protection.

Definitions and statistical analysis

The Ethics Committee of the Cardiovascular Clinic Bad Neustadt granted approval for the study. Principal investigators of each particular clinic (Supplementary material, Table S1) confirmed the validation of their respective dataset, especially that all consecutive patients who underwent arch surgery according to the study definition had been included.

The clinical charts of all patients were retrospectively reviewed if no prospectively collected data were available (depending on the respective centre). Follow-up consisted of a telephone interview with patients and/or their physicians and especially included the following variables: survival, neurological morbidity (permanent), aortic events and a need for aortic reinterventions. The primary end-points were set as: early (30 days) and late mortality for any reason, postoperative permanent neurological deficit (within 7 days after surgery or after gaining consciousness if longer ventilation was necessary). The secondary end-points included postoperative early (30 days) transient neurological deficit, late permanent neurological morbidity and all aortic events including aortic reinterventions.

Categorical variables were reported using the number and percentage of occurrences. Continuous variables were expressed as mean ± standard deviation. The impact of the available variables on the early (30-day) mortality was analysed using univariable and multivariable analyses. For the latter, several logistic regression models were built to determine the independent predictors for early (30-day) mortality. Actuarial survival was estimated by the Kaplan–Meier method. The statistical analysis was performed with the SPSS statistical software package (version 22.0; IBM, Ehningen, Germany).

Table 3: Extent of surgery

Variables	No (%) or mean ± SD
Extension of arch repair	
Repair 3 arch arteries	956 (77.6)
Repair 2 arch arteries	155 (12.6)
Repair 1 arch artery	121 (9.8)
Ascending aorta replacement	1033 (83.8)
Descending aorta replacement	44 (3.6)
Aortic valve sparing	247 (20.0)
VSRR	190 (15.4)
Aortic valve replacement	327 (26.6)
Valve conduit	218 (17.7)
Mitral valve surgery	33 (2.7)
CABG	205 (16.6)

VSRR: valve-sparing root repair; CABG: coronary artery bypass grafting.

RESULTS

Operative data

The extent of surgery depended on the extent of aortic arch disease and the coexistence of other cardiac pathologies (Table 3). Arch repair involving all 3 arch arteries (total), 2 arch arteries (subtotal) or 1 arch artery (partial) was performed in 956 (77.6%), 155 (12.6%) and 121 (9.8%) patients, respectively. The extent of aortic pathology required additional replacement of the ascending aorta in 1033 (83.8%) and descending aorta in 44 (3.6%) patients. Concomitant procedures included aortic valve and/or aortic root surgery in 574 (46.6%), coronary artery bypass grafting in 205 (16.6%) and mitral valve surgery in 33 (2.7%) patients (Table 3). There were, however, considerable differences with regard to the extent of surgery between the sub-cohorts. In some centres, the ET technique was the preferred method of arch replacement with more than 70% occurrence (Supplementary material, Table S5). Beginning in 2012, even a rate of 100% was documented in 1 centre. In contrast, only 2 centres reported about combined conventional arch and descending aorta replacement (Supplementary material, Table S5), and the rate of descending aorta replacements combined with at least partial arch replacement was only 3.6% altogether (Table 3). Also, the incidences of valve-sparing root repair, complete root replacement with valve composite graft, concomitant mitral valve surgery and coronary

Table 4: Outcome and follow-up

Variables	No (%) or mean ± SD
30-day mortality	108 (8.8)
In-hospital mortality	143 (11.6)
Re-sternotomy	150 (12.2)
Dialysis	160 (13.0)
Permanent	52 (4.2)
Transient	108 (8.8)
Myocardial infarction	18 (1.5)
Neurological defect	
Focal permanent	70 (5.7)
Focal transient	40 (3.3)
Paraplegia	13 (1.1)
Transient neuro-psychological deficit	97 (7.9)
Lost to follow-up	43 (3.5)
Follow-up duration (years)	3.3 ± (2.9)
Overall mortality	317 (25.8)

bypass grafting (CABG) were remarkably different between the sub-cohorts (Supplementary material, Table S5). Accordingly, operative data such as ischaemic time, perfusion time and temperature; which are provided in Table 2 for the entire cohort, varied considerably between particular sub-cohorts (Supplementary material, Table S6). Especially, the brain ischaemia time (9.3 ± 11.7) occurred only in patients undergoing DHCA or those patients with ACP, in whom a femoral artery or the aorta was cannulated and in whom the perfusion had to be completely interrupted during the placement of perfusion cannulas in the arch branches. Some cerebral perfusion data, especially, the flow, pressure and blood temperature during ACP, were reported incompletely, and therefore, had to be excluded from the multivariable statistical analysis (see below).

Early mortality and morbidity

Four foreign patients, who went to their countries after discharge, were lost to follow-up before the end of the 30-day postoperative period. The in-hospital and 30-day mortality rates for the remaining cohort of 1228 patients were 11.4% (140 patients) and 8.8% (108 patients) (Table 4).

Postoperative complications comprised the incidence of resternotomy for haemorrhage, reintubation, tracheostomy, renal failure (by means of temporary or permanent dialysis), myocardial infarction and transient or permanent neurological deficits. An occurrence of tracheostomy was reported incompletely and therefore was excluded from statistical analysis.

Resternotomy for haemorrhage was required in 150 (12.2%) cases. Postoperative respiratory failure occurred in 262 patients (21.3%), among whom 77 (6.3%) required prolonged ventilation primarily and 185 (15.0%) after reintubation. Renal failure with transient or permanent dialysis was required in 108 (8.8%) and 52 (4.2%) cases. The incidence of perioperative myocardial infarction was low (1.5%) despite the relatively high rate of concomitant coronary heart disease, requiring simultaneous CABG in 205 patients (16.6%), (Table 3). Focal permanent and transient defects or transient neuro-psychological deficits were noted in 70 (5.7%), 40 (3.3%) and 97 (7.9%) patients. Postoperative paraplegia occurred in 13 patients (1.1%).

Statistical analysis revealed significant differences between the surgical outcomes in particular sub-cohorts (Supplementary material, Table S7). The 30-day mortality ranged between 1.7 and 19.0%, the rate of permanent neurological deficit from 0 to 12.0% and the paraplegia rate from 0 to 3.6%. In the univariable analysis, the surgical centre, age, EF, previous CABG, number of previous surgeries means sternotomy, concomitant surgeries, cardiopulmonary bypass (CPB) time and cardiac cross-clamp time were revealed as predictors of increased 30-day mortality (Table 5). In the multivariable analysis, several models were built in which a few variables had to be excluded. For example, CCA cannulation was performed in only one centre, and the brain ischaemia occurred only in patients undergoing DHCA or those patients with ACP in whom a femoral artery or the aorta was cannulated; consequently, it was also limited to only a few centres. Lastly, as mentioned above, several preoperative and operative data were not complete and were even missing entirely in some centres. For example, 2 centres did not provide EF at all and would have been excluded completely from the analysis. Nonetheless, it has to be emphasized that in all models, the surgical centre could be revealed as the most important predictor of early mortality. Eventually, a model, adjusting the 30-day mortality with a particular centre, patient age, number of previous surgeries with sternotomy and concomitant surgeries (Table 6) revealed to be very suitable in regard to the number of observations (1129 cases equalling 88% of the study group) and in regard to the conformity between occurrences and estimated probabilities as shown in the goodness-of-fit test.

Table 5: Univariable analysis to identify risk factors for 30-day mortality

Variables	Odds Ratio	95% CI		*P*-value
		Low	High	
Centre B	3.09[a]	0.61	15.72	0.18
Centre C	6.61[a]	1.96	22.31	0.002
Centre D	7.40[a]	2.06	26.60	0.002
Centre E	2.58[a]	0.66	10.16	0.174
Centre F	12.57[a]	2.32	68.15	0.003
Centre G	8.26[a]	2.39	28.48	0.001
Centre H	5.33[a]	1.15	24.70	0.032
Centre I	7.48[a]	2.17	25.78	0.001
Centre K	13.73[a]	3.68	51.22	0.000
Centre L	5.10[a]	0.81	32.16	0.083
Age	1.03	1.01	1.05	0.001
EF	0.97	0.95	0.99	0.001
Pervious CABG	1.58	1.03	2.42	0.035
No of previous surgeries[b]	2.64	1.40	4.95	0.003
Concomitant CABG	1.71	1.05	2.79	0.030
Concomitant MVR	1.70	0.58	4.99	0.332
CPB time	1.01	1.01	1.01	0.000
Cardiac cross-clamp time	1.01	1.00	1.01	0.000

CI: confidence interval; EF: ejection fraction; CABG: coronary artery bypass grafting; MVR: mitral valve repair/replacement; CPB: cardiopulmonary bypass.
[a]in relation to centre A.
[b]cardiovascular surgeries performed through sternotomy.

Survival

The follow-up of the study group was 96.5% complete with an overall follow-up duration of 3.3 ± 2.9 years, resulting in 4,020 patient-years. Forty-three patients were lost to follow-up, including 4 who were lost after discharge but still during the 30-day

Table 6: Multivariable analysis to identify risk factor for 30-day mortality

Variables	Odds Ratio	95% CI		*P*-value
		Low	High	
Centre B	2.83[a]	0.54	14.73	0.217
Centre C	6.82[a]	1.93	24.13	0.003
Centre D	7.28[a]	1.98	26.82	0.003
Centre E	2.51[a]	0.63	10.04	0.192
Centre F	14.30[a]	2.50	81.68	0.003
Centre G	8.30[a]	2.37	29.04	0.001
Centre H	6.20[a]	1.30	29.57	0.022
Centre I	6.35[a]	1.80	22.56	0.004
Centre K	12.57[a]	3.31	47.70	0.000
Centre L	4.02[a]	0.62	26.20	0.146
Age	1.05	1.02	1.07	0.000
No of previous surgeries[b]	1.21	1.04	1.42	0.016
Concomitant CABG	1.79	1.06	3.04	0.029
Concomitant MVR	2.35	0.75	4.61	0.143

CABG: coronary artery bypass grafting; MVR: mitral valve repair/replacement; CI: confidence interval.
[a]in relation to centre A.
[b]cardiovascular surgeries performed through sternotomy.

Table 7: Cause of death

Variable	In-hospital, No (%)	After discharge, No (%)
Total	140 (11.4)	176 (14.3)
Cardiac	46 (3.7)	20 (1.6)
Non-cardiac	66 (5.4)	62 (5.0)
Aortic	11 (0.9)	17 (1.4)
Neurological	18 (1.5)	4 (0.3)
Sudden/unknown	3 (0.2)	72 (5.8)

postoperative period. After hospital discharge, 176 (14.3%) patients died, resulting in an overall mortality rate of 25.6% (Table 7). The actuarial survival after 5 and 8 years was 72.0 ± 1.5% and 64.0 ± 2.0, respectively (Fig. 1). The respective causes of death were cardiac-related in 20 (1.6%), aortic-related in 17 (1.4%), neurologic-related in 4 (0.3%) and non-cardiac-related in 62 (5.0%) patients. However, in 5.8% (72) of the cases, the causes of death were unknown (Table 7).

Aortic events

In the entire study period, a total of 130 (10.6%) aortic events occurred, including aortic dissection in 3 (0.2%), formation of a false aneurysm in a further 3 (0.2%), aortic rupture in 18 (1.5%) and others (including endoleak development after stented elephant trunk or distal aortic progression) in 106 cases (8.6%).

DISCUSSION

With the data presented, we are confronted with a fact that overall surgical risk in elective aortic arch surgery has remained high during the last decade despite the advancements in surgical techniques. The evaluation of procedural methods additionally

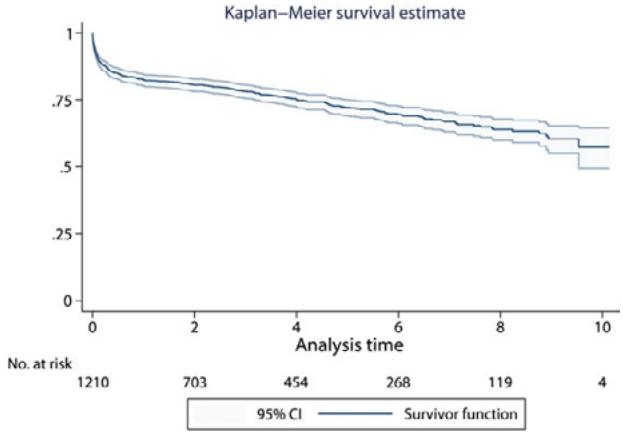

Figure 1: Actuarial survival (Kaplan–Meier) after aortic arch replacement.

supports the results of the observations from the recently published survey from the EACTS vascular domain group on current trends in cannulation and neuroprotection during surgery of the aortic arch in Europe [11]. Only a decade ago, DHCA, RCP and ACP represented three almost equally distributed strategies for cerebral and visceral organ protection [12]. More recently, a clear trend towards ACP is noticeable in the literature, and it was confirmed by our results with only 1/1232 patients (0.1%) receiving RCP and only 74/1232 patients (6.0%) using DHCA for cerebral protection. While the vast majority of patients (93.7%) were operated on employing selective ACP, presented data reveal a substantial diversity regarding the technical details, including cannulation site, ACP flow, ACP pressure and temperature management. However, even similar surgical and cerebral perfusion techniques may yield different outcomes due to the variations in cardiopulmonary bypass perfusion flow and pressure, temperature and glucose management and haematocrit profile [13]. Additionally, most of the perfusion variables vary over the duration of the surgical procedure, so continuous data recording with the advent of electronic perfusion recording systems may be needed to find out the subtle yet important changes.

Actually, we hoped that the study would enable us to identify the procedural aspects impacting the surgical outcomes; yet, the complete intraoperative monitoring data were not continuously recorded in all centres and therefore not available for retrospective analysis. Additionally, the techniques were closely connected with specific centres (mostly at a 1:1 ratio), making a separate analysis nonsensical, especially from the statistical point of view. In other words, it was not possible to differentiate if the results in particular centres were associated with the characteristics of their sub-cohorts or specific procedural methodologies. Consequently, an assessment of the impact of specific technical details on surgical outcomes will be the major task of future studies. The necessity for prospective randomized multicentre trials has been advocated several times before, but its realization seems to be very difficult for many reasons. One of them is a lack of homogenous definitions in the field of aortic arch surgery, especially the fundamental definition of the area of arch surgery. Most series reporting on aortic arch surgery include the results of simple 'hemiarch' replacement, even if it is well recognized that not only the extent of this repair but also the surgical techniques and outcomes differ substantially when compared with total aortic arch replacement [2, 5, 14, 15]. Taking this aspect into account, it is not surprising that the current guidelines do not give evidentiary

recommendations for aortic arch surgery [16, 17]. Such recommendations should not only differentiate between the extents of surgery but also consider acceptable risk, especially in such pathologies like asymptomatic chronic aneurysm (as it has been provided for decades for asymptomatic carotid stenosis [18]). Another key definition concerns the lowest core temperature since substantial differences may occur depending on whether bladder, rectal or nasopharyngeal temperatures are reported. Similarly, perfusion pressure during ACP may be understood as the pressure recorded on the arterial line or, on the right or left radial artery. In addition, the ACP flow may be reported misleadingly high in cases in which an unknown amount of the flow is directed to the right arm. It seems hardly comprehensible why cerebral perfusion in a 120-kg patient should be double that of a 60-kg patient; and therefore, the pressure measurement seems to be indispensable. When compared with a visual evaluation of the backflow from an unclamped supra-aortic artery, the pressure monitoring is objectively gaugeable, efficient and reproducible. Furthermore, it needs to be distinguished between classic clamping of non-perfused arch vessels when compared with endovascular balloon occlusion, which is less controllable and may result in accidental injuries, misplacements and thrombo-embolic events. Nevertheless, there is still a problem in conducting randomized multicentre trials that assess particular surgical methods in aortic arch surgery. There seems to be a creed among particular aortic surgeons who develop a strong attachment to their distinct perfusion and temperature management protocols with which they achieve good clinical outcomes and are not willing to switch their routine for clinical trials. Members of the EACTS vascular domain group recently experienced this renunciation when attempting to initiate a prospective multicentre trial with a random assignment to either unilateral or bilateral ACP.

In summary, the presented data reveal that the surgical risk in elective aortic arch surgery has remained high during the last decade despite the advancements in surgical techniques. Despite the widespread acceptance of ACP, a substantial heterogeneity of technical details in aortic arch surgery is still an issue. Whether the impact of one or more of these details led to the broad range of reported mortality and morbidity rates could not ultimately be delineated; and therefore, the members of the steering committee of the current investigation strongly recommend the need for further multicentre studies, preferably registries, in which all relevant variables have to be thoroughly defined and collected prospectively.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *EJCTS* online.

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Sadly, Robert Bonser, the initiator of this study died unexpectedly, before completion of the data. His fellow co-authors would like to dedicate this paper to his memory.

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6.2 Aortic events and reoperations after elective arch surgery: incidence, surgical strategies and outcomes

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Aortic events and reoperations after elective arch surgery: incidence, surgical strategies and outcomes†

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Abstract

OBJECTIVES: The true incidence of aortic events (AEs) and reoperations (REDO) following elective total aortic arch replacement remains unknown. The aim of this study was to review the incidence of AEs and surgical REDO, and its respective outcomes after 1232 elective arch repairs at 11 European aortic centres.

METHODS: Retrospective chart review (in the absence of prospective data collection) was performed for statistical analysis. Follow-up was conducted during routine clinical examination or in a telephone interview with patients and/or their respective physicians.

RESULTS: One hundred fifty-five (12.6%) patients were identified (median follow-up time 48.7 months). The recorded AEs comprised aortic dilatation (62.6%), rupture (15.5%), endoleak (11%), false aneurysm (3.9%), dissection (3.2%), infection (2.6%) and others (1.3%). REDO (open/endovascular) were performed in 85.8% of patients ($n = 133$). Intraoperative and in-hospital mortality in the REDO patients were 7.5% and 17.3%, respectively. Postoperative neurological complications comprised paraplegia (6.0%) and stroke (1.5%). Survival rates after REDO at 1, 3 and 5 years were 81.2%, 79.0% and 76.7%, respectively. Univariate analysis identified 'rupture' and 'diameter progression', 'older age at REDO' and the REDO strategies 'frozen elephant trunk' and 'no elephant trunk' as predictors of increased in-hospital mortality. Multivariate analysis identified 'older age at REDO' ($P = 0.008$) as the only independent risk factor for in-hospital mortality.

CONCLUSIONS: AEs after elective arch surgery are not irrelevant and mostly involve the distal aspects of the adjoining aorta. In accordance with the underlying pathology, open or endovascular REDO may be performed with an acceptable outcome. Preparation of an adequate proximal landing zone at the time of primary arch surgery is advisable.

Keywords: Aortic arch • Surgery • Follow-up • Aortic events • Aortic reoperation • Thoracic endovascular aortic repair

INTRODUCTION

Despite substantial improvement in survival and outcomes, elective total aortic arch surgery remains challenging and is associated with significant morbidity and mortality [1–3]. The use of thoracic endovascular aortic repair (TEVAR) in the transverse arch is still limited due to a lack of adequate proximal landing zones (LZs) and suitable aortic stent grafts, which safely match that of the arch's anatomy [4–6]. On the other hand, the use of hybrid techniques, such as the frozen elephant trunk (FET), is increasing, especially in extensive arch disease [7–9].

Although aortic surgery has been routinely performed for decades, the true incidence of aortic events (AEs) and reoperations (REDO) following elective total aortic arch replacement remains

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unknown. Therefore, the aim of this analysis was to estimate, on the basis of mid-term follow-up data after 1232 elective arch replacements, the incidence of AEs, surgical strategies and postoperative outcomes after REDO.

MATERIALS AND METHODS

As previously reported [1], the perioperative data of 1232 patients undergoing elective surgery for chronic aortic arch disease with at least 1 circular aortic anastomosis at 11 European aortic centres between January 2004 and December 2013 were retrospectively analysed (Supplementary Material, Table S1). Emergency (e.g. acute Type A aortic dissection) or unscheduled surgery (e.g. iatrogenic aortic injury) and hemiarch repairs were excluded from the primary analysis. The extent of elective arch repair was defined as partial, subtotal or total with regard to the reimplantation of 1, 2 or 3 supra-aortic arteries.

Incidence of aortic events

One hundred fifty-five (12.6%) patients with an AE during a median follow-up time of 48.7 [interquartile range (IQR) 23.7–81.9] months were identified and included in this study for further analysis. The median time interval between primary aortic arch surgery and occurrence of an AE was 11.3 (IQR 4.2–38.4) months. The median age at the time of AE and/or REDO was 64.9 (IQR 53.8–70.4) years, and 103 (66.5%) patients were men. Total arch replacement with reimplantation of all 3 supra-aortic branches was performed primarily in 149 (96.1%) cases including 41 (26.4%) with conventional elephant trunk (ET) and 79 (51%) with FET procedures, whereas 5 (3.2%) patients had had a subtotal and 1 patient (0.6%) had a partial arch replacement. Additional ascending aortic replacement during primary arch surgery was performed in supracoronary fashion ($n = 87$; 56.1%) or in conjunction with aortic root surgery in 43 (27.7%) patients.

Table 1 lists the details of primary open arch surgery for the study cohort at the time of AE.

Definitions and statistical analysis

The ethics committee of the Cardiovascular Clinic Bad Neustadt granted approval for this study. The principal investigators of each particular clinic (Supplementary Material, Table S1) confirmed the validation of their respective data set, especially that all consecutive patients who underwent arch surgery according to the study definition had been included.

The methodology of data acquisition for the initial study group has been reported previously [1]. In brief, the patient data were retrospectively reviewed in the absence of prospectively collected data (depending on the respective centre). Follow-up of patients who were not included in a routine institutional surveillance programme was conducted via a telephone interview with patients and/or their respective physicians. The following variables were updated or added to the existing data set with regard to AE (with or without REDO): date and location of AE, reoperation date and treated aortic segment as well as survival (early and late) and neurological morbidity (permanent) postoperatively. Follow-up time comprised the time interval between the primary aortic arch surgery and the last patient contact or death of all patients, independently of occurring AEs. Patient deaths were not excluded.

Table 1: Preoperative patient data ($n = 155$)

Patients with aortic event, *n* (%)	155 (100)
Age at event, median (IQR)	64.9 (53.8–70.4)
Male gender, *n* (%)	103 (66.5)
Indication for primary arch surgery, *n* (%)	
Aneurysm	92 (59.4)
Chronic dissection	54 (34.8)
False aneurysm	3 (1.9)
Infection/inflammation	4 (2.6)
Other	2 (1.3)
Primary arch surgery, *n* (%)	
Total arch replacement (3 supra-aortic anastomoses)	149 (96.1)
Conventional ET	41 (26.5)
FET	79 (51.0)
Subtotal arch replacement (2 supra-aortic anastomoses), *n* (%)	5 (3.2)
Partial arch replacement (1 supra-aortic anastomosis), *n* (%)	1 (0.6)
Supracoronary ascending aortic replacement, *n* (%)	87 (56.1)
Root surgery, *n* (%)	43 (27.7)
Bentall procedure, *n* (%)	24 (15.5)
Biological	12 (7.7)
Mechanical	12 (7.7)
David procedure,[a] *n* (%)	13 (8.4)
Yacoub procedure,[a] *n* (%)	5 (3.2)
Aortic valve replacement, *n* (%)	23 (14.8)
CABG, *n* (%)	15 (9.7)
Mitral valve repair, *n* (%)	2 (1.3)

[a]Including modifications.
CABG: coronary artery bypass graft; ET: elephant trunk; FET: frozen elephant trunk; IQR: interquartile range.

AEs were defined as any aortic complication and/or aortic reoperation/reintervention following primary aortic arch repair. Aortic diameter progression, as a continuous process, was defined as an AE at the time when a need for surgical or endovascular treatment was evident (as indicated by the treating surgeon). The data analysis was performed according to the statistical and data reporting guidelines of the *European Journal of Cardio-Thoracic Surgery* [10].

Categorical variables were reported using the number and percentage of occurrences. Continuous variables were expressed as median and IQR (25th–75th percentile) or mean ± standard deviation. The impact of the available variables on the in-hospital mortality was analysed using univariate and multivariate regression analyses. Binary logistic regression model was built using variables with a P-value of <0.1 from univariate analysis. A P-value of <0.05 was considered statistically significant. Actuarial survival was estimated by the Kaplan–Meier method. The statistical analysis was performed with the SPSS statistical software package (version 23.0; IBM, Ehningen, Germany).

RESULTS

The types of AE, their aortic localization and the treatment are presented in Table 2. The most frequent type of AE was aortic diameter progression in 97 (62.6%) patients after a median of 12.5 (IQR 5.5–42.5) months—including patients without ET, with conventional ET and FET in 14 (14.4%), 29 (29.9%) and 54 (55.7%) cases, respectively. Comparison of both ET techniques revealed a

Table 2: Aortic events: pathologies, localizations and treatments

	Ascending aorta/arch, *n* (%)	Descending aorta, *n* (%)	Abdominal aorta, *n* (%)	Unknown location, *n* (%)	Overall, *n* (%)
Aortic events					155 (100)
Aortic diameter progression[a]	2 (1.3)	83 (53.5)	12 (7.7)	0	97 (62.6)
Aortic rupture	2 (1.3)	17 (11.0)	3 (1.9)	2[b] (1.3)	24 (15.4)
Aortic dissection	2 (1.3)	3 (1.9)	0	0	5 (3.2)
False aneurysm	5 (3.2)	1 (0.6)	0	0	6 (3.8)
Endoleakage	0	17 (11.0)	0	0	17 (11.0)
Infection	2 (1.3)	2 (1.3)	0	0	4 (2.3)
Other events	1 (0.6)	0	1 (0.6)	0	2 (1.3)
REDO procedures					133 (100)
Open surgery	9 (6.8)	42 (31.6)	7 (5.3)	0	58 (43.6)
Endovascular surgery	0	70 (52.6)	5 (3.8)	0	75 (56.4)
Aortic events without REDO	1 (4.5)	13 (59.1)	3 (13.6)	2 (9.1)	22 (100)

[a]Progression to an aneurysmatic aortic diameter requiring endovascular or surgical treatment.
[b]Death occurred in different peripheral hospitals; no information other than 'aortic rupture' could be obtained retrospectively.
REDO: reoperation.

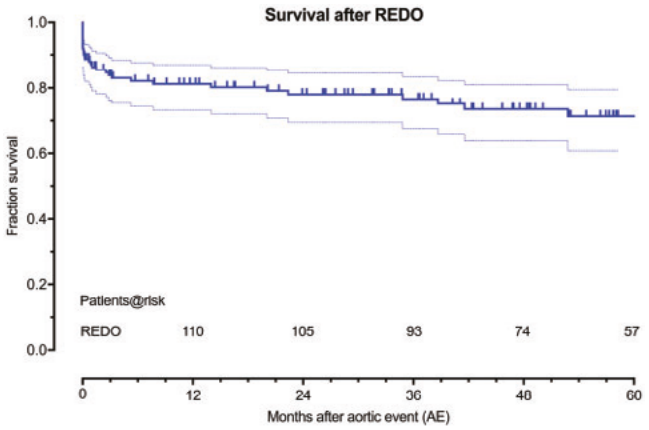

Figure 1: Actuarial survival estimation (Kaplan–Meier method) with 95% confidence interval after aortic REDO. Survival was calculated starting with the procedure. AE: aortic event; REDO: reoperation.

Table 3: Outcome after REDO (*n* = 133)

	Ascending/arch REDO, *n* (%)	Descending REDO, *n* (%)	Abdominal REDO, *n* (%)	Overall, *n* (%)
REDO procedures	9 (6.8)	112 (84.2)	12 (9.0)	133 (100)
Mortality				
In-hospital	2 (1.5)	18 (13.5)	3 (2.3)	23 (17.3)
During follow-up	0	11 (8.3)	0	11 (8.3)
Overall	2 (1.5)	29 (21.8)	3 (2.3)	34 (25.6)
Neurological complications				
Paraplegia	0	7 (5.3)	1 (0.8)	8 (6.0)
Stroke	1 (0.8)	1 (0.8)	0	2 (1.5)

REDO: reoperation.

significantly higher incidence of aortic diameter progression in patients with primary FET than conventional ET (35.2% vs 17.0%; $P = 0.0001$). The occurrence of a false aneurysm was less frequent ($n = 6$; 3.8%) with a late onset after arch surgery (median 41 months, IQR 37.0–80.0). In comparison, infection ($n = 4$; 3%) was found to be the earliest complication of the cohort with a median time-to-occurrence of 5.3 (IQR 1.1–12.4) months. Endoleak ($n = 17$; 11%) occurred at a median time frame of 6.8 (IQR 2.9–34.6) months. Acute life-threatening AE by means of 'rupture' and 'dissection', including 2 Type A and 3 Type B aortic dissections, occurred after a median time interval of 18.4 (IQR 6.5–31.5) and 48.6 (IQR 0–78.9) months, respectively. The median time interval between primary aortic arch surgery and occurrence of any AE was 11.3 (IQR 4.2–38.4) months.

The recorded AEs were distributed in the following locations: ascending aorta/arch, descending and abdominal aorta in 9.0% ($n = 14$), 79.4% ($n = 123$) and 10.3% ($n = 16$), respectively. Two (1.3%) patients had died in different peripheral hospitals due to acute aortic rupture. However, no further information, other than the plain cause of death (aortic rupture), regarding the exact aortic location could be obtained retrospectively.

In 133 patients suffering an AE, either an open or an endovascular REDO was performed, whereas 22 (14.1%) patients were either deemed inoperable or died prior to any intervention (Table 2).

Of note, 9 of the 133 patients required repeated treatment during follow-up time by means of 2 ($n = 8$, 6%) or 3 ($n = 1$, 0.8%) REDO procedures.

Surgical strategies

Open REDO was performed in 58 (43.6%) patients. The median interval between elective arch repair and open REDO was 13.9 (IQR 5.9–35.9) months. Proximal open repair of the ascending aorta or aortic arch was required in only 9 (6.8%) patients, whereas 49 (36.8%) patients underwent open surgical repair of the distal aorta, including the descending and abdominal aorta in 42 (31.6%) and 7 (5.3%) cases, respectively. Endovascular REDO of the thoracic or abdominal aorta was performed after a median time period of 9.2 (IQR 3.8–41.4) months. TEVAR was the primarily performed technique in 70 (52.6%) patients, whereas an abdominal endografting was performed in only 5 (3.2%)

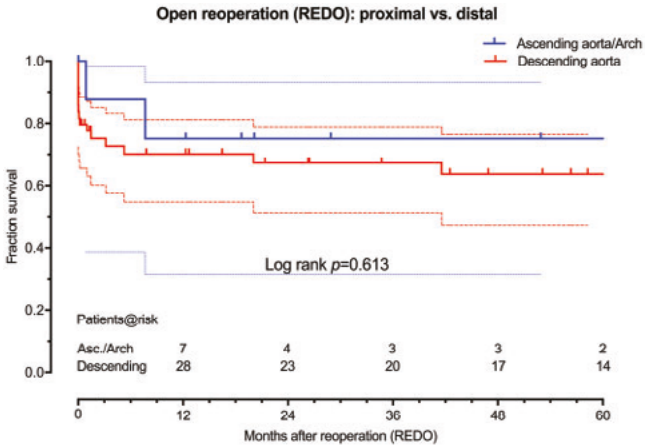

Figure 2: Actuarial survival estimation (Kaplan–Meier method) with 95% confidence interval after open REDO: proximal versus distal. Survival was calculated starting with the procedure. Asc.: ascending; REDO: reoperation.

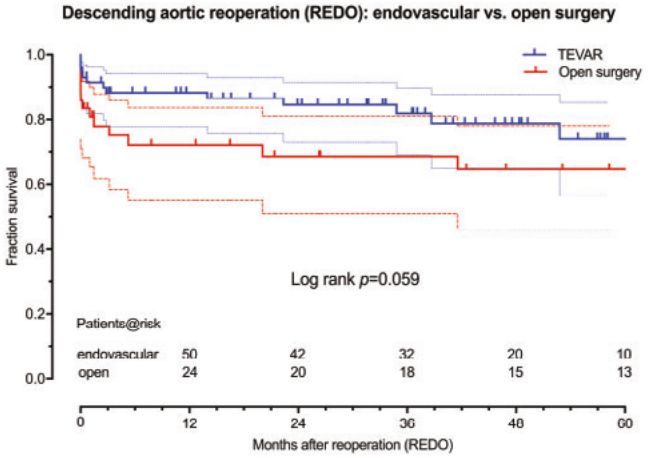

Figure 3: Actuarial survival estimation (Kaplan–Meier method) with 95% confidence interval after REDO of the descending aorta: open versus endovascular surgery. Survival was calculated starting with the procedure. TEVAR: thoracic endovascular aortic repair; REDO: reoperation.

patients for diameter progression of abdominal aortic aneurysms (Table 2).

Outcomes after reoperation

Median follow-up times for the entire AE cohort ($n = 155$) and for the REDO subcohort ($n = 133$) were 48.7 (IQR 23.7–81.9) months and 51.8 (IQR 29.8–83.9) months, respectively.

The intraoperative mortality in the REDO subcohort was 7.5% ($n = 10$) with 6 (4.5%) intraoperative deaths during open surgery and 4 (3.0%) fatal endovascular reinterventions ($P = 0.3309$). Overall in-hospital mortality (including 10 intraoperative deaths) was 17.3% ($n = 23$). New (permanent) postoperative neurological complications comprised paraplegia ($n = 8$; 6.0%) and stroke ($n = 2$; 1.5%). Paraplegia was more frequent after open ($n = 5$) than after endovascular ($n = 3$) procedures (8.6% vs 4.0%; $P = 0.2951$) with an incidence after descending ($n = 7$) and abdominal ($n = 1$) aortic REDO of 6.2% and 12.5% ($P = 0.4341$), respectively. The respective 1-, 3- and 5-year survival rates after REDO were 81.2%, 79.0% and 76.7% (Fig. 1, Table 3).

Table 4: Significant parameters associated with in-hospital mortality as identified by univariate and multivariate analyses

Univariate analysis				*P*-value
Primary arch surgery				
No ET				0.029
FET				0.021
Aortic event				
Diameter progression				0.006
Rupture				0.001
Age at REDO				0.002
Multivariate analysis	OR	95% CI		*P*-value
		Low	High	
Age at REDO	1.087	1.005	1.176	0.008

CI: confidence interval; ET: elephant trunk; FET: frozen elephant trunk; OR: odds ratio; REDO: reoperation.

Comparison of the survivals after open surgery of the proximal aorta (ascending aorta/arch) and descending aorta showed no significant differences (log rank, $P = 0.613$) (Fig. 2). However, comparison of REDO for descending aortic pathology showed a trend toward better survival at 5 years after TEVAR versus open surgery: 77.2% vs 69.1% (log rank, $P = 0.059$) (Fig. 3).

Univariate analysis identified the AE rupture ($P < 0.001$) and AE diameter progression ($P = 0.006$), older age at REDO (mean 61.3 ± 12.3 vs 70.1 ± 6.6 years; $P = 0.002$) and the primary surgical strategies 'FET' ($P = 0.021$) and 'no elephant trunk' ($P = 0.029$) as predictors of increased in-hospital mortality. However, multivariate analysis identified older age at REDO ($P = 0.008$) as the only independent risk factor for in-hospital mortality (Table 4; Supplementary Material, Table S2).

Causes of death for the entire study cohort ($n = 155$) were noted as aortic (18.6%), cardiac (3.8%), non-cardiac (5.1%), neurological (0.6%), sudden/unknown (2.6%) and other (0.6%) (Supplementary Material, Table S3). However, aortic-related deaths occurred in 14 (63.6%) of the 22 non-REDO patients.

DISCUSSION

Open surgery is still considered the gold standard for definite treatment of aortic arch pathologies with well-documented postoperative results worldwide [1, 3, 11, 12]. However, little is known about AEs after elective arch replacements and subsequent therapeutic strategies. As shown in the current analysis, most indications for REDO typically arise from the descending thoracic aorta rather than from the aortic arch or the ascending aorta. Despite being less frequently present and not directly related to proximal aortic arch repair in the study group, abdominal AEs can also develop over time and, if not diagnosed in time, may result in fatal outcomes (e.g. aortic rupture). This stresses the need for routine surveillance programmes after proximal aortic surgery—using advanced imaging techniques and interdisciplinary teams—to detect indications for REDO of the non-treated aortic segments at an early stage [13].

Of the 1232 electively operated aortic arch repairs between 2003 and 2013 [1], 155 (12.6%) patients experienced an AE during the median follow-up period of 48.7 months. Reoperation of the

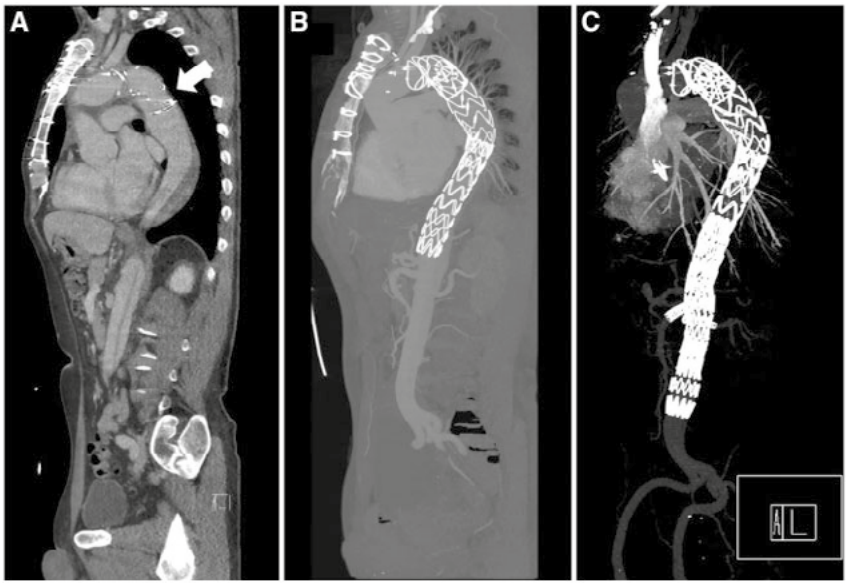

Figure 4: Endovascular extension of the frozen elephant trunk prosthesis (white arrow) (**A**) at the descending aortic level by thoracic endovascular repair (**B**) and at the abdominal level by 4-branched endovascular repair (**C**).

proximal aorta by means of ascending aortic REDO was very low and occurred in only 0.7% of the initial study cohort. This result confirms that elective open surgery of the arch, accompanied by surgical treatment of aortic valve and/or root, provides a very durable result for the proximal part of the aorta. In contrast, postoperative AEs frequently involve the distal aortic arch and the adjacent descending aorta, and often need to be resolved by several reinterventions.

At the descending aortic level, 112 (84.2%) of 133 REDO patients underwent either open ($n = 42$, 31.6%) or endovascular ($n = 70$, 52.6%) surgery due to an AE. The most frequent AE in the study group ($n = 155$) was aneurysmal diameter progression in the descending aortic segment ($n = 83$, 54.2%), representing 6.7% of the original study cohort ($n = 1232$). Distal aneurysmal diameter progression occurred more frequently after conventional ET or FET procedures ($n = 74$) than in patients without ET ($n = 9$) (6.0% vs 0.7%), suggesting that extensive aortic disease or some mild descending aortic dilatation most likely had been present at the primary operation of patients treated by ET or FET. However, the significantly higher incidence of diameter progression in FET compared with conventional ET patients was rather unexpected due to the recent theory of positive aortic remodelling [14, 15].

In the literature, the true incidence of aneurysmal dilatation of the distal aorta after proximal aortic arch surgery is not well defined but has been reported to vary from 5% to 35% of patients with Marfan syndrome, depending upon the extent of previous surgery and the quality of follow-up [16]. The increased wall tension and the pressure rise in the residual aorta after prosthetic replacement of the ascending aorta, as observed by Scharfschwerdt *et al.* [17] in an *in vitro* model, may additionally increase the risk of distal aortic dilatation and subsequent surgery. This also seems to apply for the risk of aortic rupture and dissection, both of which occurred most frequently in the descending aortic segment (Table 2).

In the absence of a proximal LZ, an open extensive aortic REDO may be the only treatment option. However, primary surgery including ET and FET procedures may prevent open REDO in the downstream aorta by facilitating subsequent endovascular repair [8, 13, 18, 19] (Fig. 4). As an alternative to ET/FET procedures, a proximal move of supra-aortic arteries to the ascending aorta can, during conventional arch surgery, sufficiently create an appropriate LZ [12, 20]. This strategy of creating a sufficient LZ during primary arch surgery is also supported by the finding that TEVAR showed a trend towards better survival rates when compared with open REDO of the descending aorta. However, if the respective aortic pathology (e.g. descending aortic aneurysm) extends to the distal level of the descending aorta, the stent graft of the FET prosthesis usually cannot be properly anchored. In such cases, the use of longer hybrid prostheses or TEVAR extension in the same session may be required; however, there is an increased risk of paraplegia [13, 21].

In the univariate analysis, primary arch replacement with FET was identified as a predictor of increased operative mortality. It remains unclear, however, whether FET is most frequently used in high-risk patients with extensive arch and descending pathology, especially because in some centres, this technique seems to be used preferably or even exclusively in all patients [1]. On the other hand, it is a fact that the use of the FET technique is associated with a longer circulatory arrest time that, undoubtedly, can impact surgical outcome. Nevertheless, a lack of proximal LZ after arch replacement can hinder a later use of TEVAR and can make a more risky and extended open surgery necessary. Therefore, the approach to the primary arch replacement should definitely consider the preparation of a sufficient LZ for potential reinterventions.

Older age at REDO was found to be the only independent risk factor for operative mortality by multivariate analysis. As a matter of fact, surgery in the elderly is often compromised by associated comorbidities, resulting in higher mortality rates [22]. Shortly after primary surgery, the disease process as such may have already strained the body's resources and, as found in the study group, early REDO may be required emergently due to lethal events, such as aortic infection or rupture.

The most evident neurological complication after open and endovascular REDO was paraplegia with an overall occurrence of 6%. These observations stress the need for further measures to

completely eliminate paraplegia as the most devastating complication of thoracic and thoraco-abdominal aortic surgery. As there is still no consensus as to whether to reimplant or sacrifice the aortic segmental arteries during open thoracic surgery and thoraco-abdominal surgery. In TEVAR segmental artery preservation is not possible at all, new concepts such as spinal cord collateral network preconditioning by segmental artery occlusion prior to either open or endovascular aortic repair should be considered in the future [23]. However, this new strategy of spinal cord precondition requires further experimental and clinical evaluation [24, 25].

Limitations

Due to the retrospective nature of the study and the heterogeneity of the study cohort, as regards the different participating centres and the primary surgical indications and techniques of total arch repair performed, the underlying results and their implications may be limited. However, to our knowledge, this retrospective clinical multicentre analysis currently comprises the largest cohort of patients suffering from AEs after primary elective total aortic arch replacement and may therefore offer valuable information to the cardiovascular community.

CONCLUSIONS

In summary, the presented data reveal that the rate of AEs and REDO after elective surgery is not irrelevant and mainly involves the descending aorta. Open and endovascular reoperations have acceptable outcome. However, TEVAR seems beneficial for survival at the descending level, and, consequently, preparation of an adequate proximal LZ at the time of primary arch surgery is advisable. Moreover, routine follow-up and institutional surveillance programmes are necessary after aortic arch surgery for early recognition of pathological sequelae and consequently, the need for reoperation.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *EJCTS* online.

Conflict of interest: none declared.

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6.3 Extra-anatomic revascularization for preoperative cerebral malperfusion due to distal carotid artery occlusion in acute type A aortic dissection

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Extra-anatomic revascularization for preoperative cerebral malperfusion due to distal carotid artery occlusion in acute type A aortic dissection†

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Abstract

OBJECTIVES: Management of patients with acute aortic dissection type A (AADA) and cerebral malperfusion secondary to occlusion or stenosis of the left common carotid artery (LCCA) or right common carotid artery (RCCA) is a significant challenge. The aim of this study is to present our institutional strategy and postoperative results for this high-risk patient cohort.

METHODS: Between November 2005 and July 2013, 23 of 354 consecutively operated AADA patients [median age: 66.3; interquartile range (IQR): 55.2–69.9] suffered from cerebral malperfusion due to bilateral ($n = 1$) or unilateral occlusion of the LCCA/RCCA ($n = 22$). AADA repair comprised hemi- ($n = 14$) or total ($n = 9$) arch replacement in combination with aortic valve repair ($n = 7$) or replacement ($n = 11$), root replacement ($n = 15$) and coronary bypass ($n = 3$). Extra-anatomic aorto-carotid bypass was performed in all patients. Aorto-carotid bypass was performed at the beginning of the procedure to allow for unilateral selective cerebral perfusion ($n = 17$; 73.9%) or during the procedure if persisting malperfusion was suspected by near-infrared spectroscopy ($n = 6$; 26.1%).

RESULTS: The median follow-up was 15.2 months (IQR: 4.8–34.1) and 100% complete. Median hospital stay and ICU stay were 16.0 (IQR: 12.5–26.0) and 13.7 (IQR: 2.0–16.5) days, respectively. Rethoracotomy for haemorrhage or cardiac tamponade was performed in 6 (26.1%) patients. Other postoperative complications comprised low cardiac output with extracorporeal membrane oxygenation ($n = 2$; 8.7%), sepsis ($n = 4$; 17.4%), respiratory insufficiency ($n = 10$; 43.5%), renal failure with temporary dialysis ($n = 7$; 30.4%) and visceral malperfusion ($n = 2$; 8.7%) requiring stent grafting ($n = 1$) or laparotomy with intestinal resection ($n = 1$). New stroke with or without permanent sensory or motor deficit was diagnosed in 8 (34.8%) patients. Temporary neurological deficits were seen in 9 (39.1%) individuals. Hospital and 1-year mortality rates were 13.0 and 30.4%, respectively. Overall survival after 36 months of the 23 patients (Group I = Extra-anatomic bypass) versus the remaining 331 AADA patients without distal RCCA/LCCA occlusion (Group II = no extra-anatomic bypass) was 69.6% ($n = 16$) in Group I vs 72.5% ($n = 240$) in Group II ($P = 0.90$).

CONCLUSION: Extra-anatomic bypass for LCCA or RCCA occlusion allows for early selective cerebral perfusion during AADA repair, and may reduce the risk of neurological complications in patients with preoperative cerebral malperfusion.

Keywords: Type A aortic dissection • Cerebral malperfusion • Distal carotid artery occlusion • Carotid cannulation • Selective cerebral perfusion • Stroke • Neurological complications

INTRODUCTION

Involvement of aortic arch branches in patients suffering from acute aortic dissection type A (AADA) occurs with varying frequency, ranging from 5 to 43% [1]. Secondary cerebral malperfusion may occur in such patients, significantly influencing long-term outcome due to increased mortality and perioperative stroke rate [2]. Immediate restoration of cerebral perfusion is a goal of aortic repair in such patients, but is very unlikely if occlusion of the distal left (LCCA) or right (RCCA) common carotid arteries is present. Such occlusion may occur secondary to complete collapse of the true lumen with or without thrombus formation. Extra-anatomic aorto-carotid bypass has been suggested to restore cerebral perfusion in

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these high-risk patients [3– 5]. However, no clinical series with regard to postoperative outcome have been published thus far for this surgical strategy.

The purpose of this study was to therefore present our institutional surgical strategy and outcomes after extra-anatomic bypass for AADA patients with preoperative cerebral malperfusion due to common carotid artery occlusion.

PATIENTS AND METHODS

A total of 354 patients suffering from AADA were operated on at our centre between November 2005 and July 2013. We identified a subgroup of 23 patients with cerebral malperfusion due to occlusion or severe stenosis of the RCCA ($n = 12$), the LCCA ($n = 10$) or both arteries ($n = 1$). The median patient age was 66.3 years [interquartile range (IQR): 55.2–69.9] and 18 (78.3%) were males. The operative reports and clinical charts of the operated patients were retrospectively reviewed. The local ethics committee did not require individual patient consent.

The patients' characteristics and preoperative data are summarized in Table 1.

Definition of malperfusion

Cerebral malperfusion was diagnosed if AADA patients had neurological symptoms and signs with radiographic evidence of dissection of the corresponding aortic branch vessel(s). In those patients who were already sedated and intubated upon presentation to our hospital, neurological symptoms were noted as recorded by the emergency physician or referring hospital. Patients with cerebral malperfusion and complete occlusion of the RCCA and/or LCCA formed the focus of the current study. Patients with a dissection membrane in aortic branch vessels without carotid artery occlusion or severe stenosis were not included.

The proportions of patients with coronary, mesenteric, spinal and limb malperfusion, as previously described [2], are displayed in Table 1.

Table 1: Preoperative data

Patient characteristics ($n = 23$)	
Age (years), median (IQR)	66.3 (55.2–69.9)
Male gender, *n* (%)	18 (78.3)
Left ventricular ejection fraction (mean ± SD)	54.5 ± 7.1
Hypertension, *n* (%)	15 (65.2)
Hyperlipidaemia, *n* (%)	6 (26.1)
Diabetes mellitus [*n* (%)]	5 (21.7)
Chronic obstructive pulmonary disease [*n* (%)]	1 (4.3)
Renal insufficiency [*n* (%)]	2 (8.7)
With permanent dialysis	1 (4.3)
Obesity [*n* (%)]	2 (8.7)
Clinical presentation and neurological symptoms	
ASA score [median (IQR)]	4.0 (IQR 4.0–4.5)
Intubated [*n* (%)]	5 (21.7)
Cardiogenic shock [*n* (%)]	3 (13.0)
Pericardial tamponade [*n* (%)]	3 (13.0)
Anicosoria [*n* (%)]	4 (17.4)
Previous syncope [*n* (%)]	7 (30.4)
Previous seizure [*n* (%)]	1 (4.3)
Vertigo [*n* (%)]	5 (21.7)
Photopsia [*n* (%)]	1 (4.3)
Confusion [*n* (%)]	7 (30.4)
Malperfusion syndromes	
Cerebral [*n* (%)]	23 (100)
Coronary [*n* (%)]	3 (13.0)
Mesenteric [*n* (%)]	0 (0)
Spinal [*n* (%)]	0 (0)
Lower limb [*n* (%)]	2 (8.7)

IQR: interquartile range; SD: standard deviation; ASA: American Society of Anesthesiologists.

Clinical presentation

All patients were admitted to our institution emergently within 7.0 h (median; IQR: 4.9–12.1) after AADA occurrence. Preoperative patient data are given in Table 1.

Diagnosis of AADA was made via computed tomography (CT) of the thorax in all cases (Fig. 1). Additional cranial CT examinations were performed because of significant neurological deficits in 8 patients, revealing a large cerebral infarct in 3. Aortic dissection with unilateral or bilateral carotid occlusion or severe stenosis was diagnosed in all 23 patients (Fig. 2). Other supra-aortic vessels that were dissected (but not occluded or severely stenosed) included the brachiocephalic trunk, the left subclavian artery and the left vertebral artery in 91, 65 and 9% of patients, respectively. Four patients presented with monoplegia of the left ($n = 3$) or plegia of both upper extremities ($n = 1$). Dissection of the aortic root was detected in 15 cases (65%)—including 3 patients with coronary malperfusion. Dissection of the descending/throaco-abdominal aorta was observed in 16 patients (70%) with dissection of the coeliac trunk in 7 patients, the superior mesenteric artery in 1 patient, the left renal artery in 5 patients, the right renal artery in 1 patient, the inferior mesenteric artery in 3 patients and the common iliac arteries in 14 patients.

Surgical procedures

We have previously published details of our institutional surgical strategy to address AADA in the presence of malperfusion syndromes [2]. In brief, surgical access was achieved via a full sternotomy in all patients. In 17 patients (74%), the occluded RCCA ($n = 10$) or LCCA ($n = 7$) was exposed at the beginning of the procedure, usually at the level of the carotid bifurcation. The vessel was then cannulated either directly ($n = 5$) or via anastomosis of a 6 or 8 mm prosthetic graft ($n = 12$) above the level of occlusion to allow for early selective cerebral perfusion via an extra line (Fig. 3). Subsequently, venous drainage as well as additional arterial cannulation was performed to allow for cardiopulmonary bypass (CPB). After reaching the target cooling temperature, the aortic arch was opened and an additional perfusion cannula was inserted into either the proximal LCCA ($n = 10$) or the brachiocephalic trunk ($n = 2$) to allow for bilateral selective cerebral perfusion (SCP) ($10\ \text{ml} \times \text{kg}^{-1} \times \text{min}^{-1}$). In 5 patients with unilateral perfusion via the LCCA, bilateral SCP was achieved via additional axillary artery cannulation (Fig. 4). In the single patient who presented with occlusion of both the LCCA and RCCA, bilateral SCP was performed via prosthetic grafts anastomosed to both of these vessels at the level of the carotid bifurcation. Additional cannulation sites and operative details are given in Table 2.

Systemic cooling was carried out down to an oesophageal temperature of 26.0 ± 3.3°C with a maximal CPB temperature gradient of 6°C. Distal aortic perfusion (25–32°C; 3 l/min) was performed

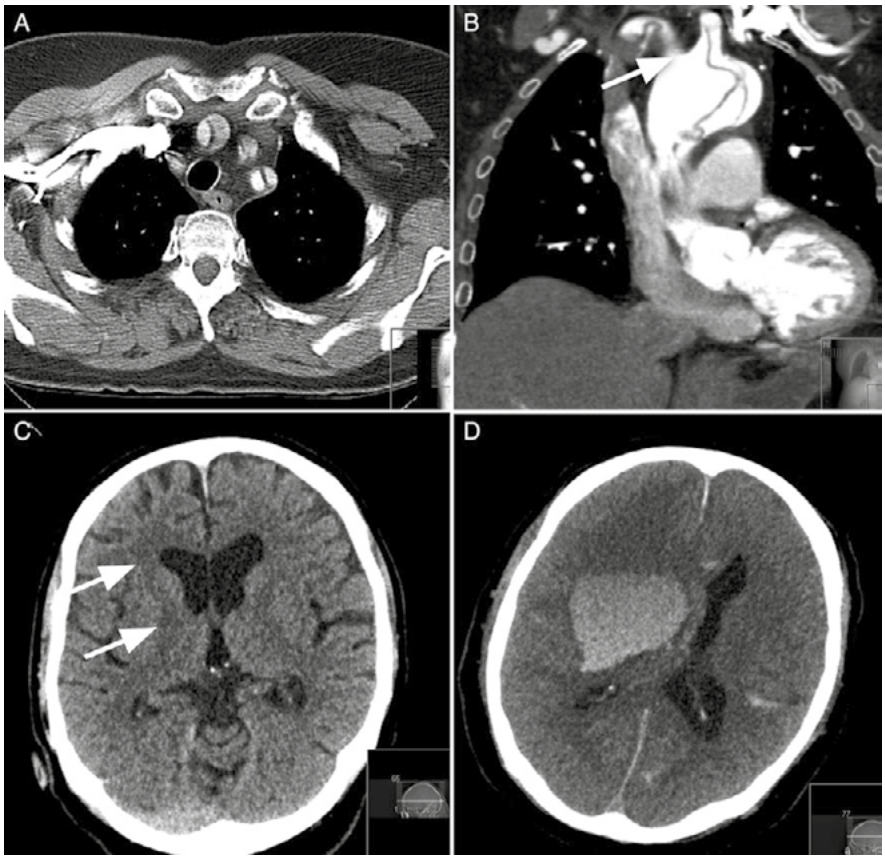

Figure 1: Computed tomography (CT) scan showing involvement of all supra-aortic branches in a patient with acute aortic dissection type A (**A**). Acute dissection of the aortic arch with malperfusion of the brachiocephalic trunk and a dissection membrane within the left common carotid artery (**B**). Preoperative cranial CT revealing subacute cerebral ischaemia indicating preoperative stroke (**C**). Postoperative cranial CT of the same patient showing left-sited cerebral haemorrhage originating from the area of preoperative cerebral infarction (**D**).

retrogradely via the femoral artery or antegradely via a side-graft after the distal aortic anastomosis for adequate visceral and spinal cord protection if a prolonged duration of lower body circulatory arrest was expected ($n = 2$).

Aortic root repair with or without aortic valve repair ($n = 7$) or replacement ($n = 11$) was performed in routine fashion during the cooling phase. Concomitant coronary bypass was performed in the 3 patients with coronary malperfusion. During SCP and lower body circulatory arrest, proximal hemiarch ($n = 14$) or total arch replacement with an elephant trunk ($n = 9$) was performed as previously described [6]. Additional extra-anatomic reconstruction of supra-aortic branches was performed in 34.8% of patients.

During rewarming, a prosthetic graft was anastomosed to the affected RCCA/LCCA (if not performed at the beginning of the procedure) and tunnelled below the sternocleidomastoid muscle and anastomosed as an extra-anatomic bypass to the ascending aortic graft.

Near-infrared spectroscopy (NIRS) was routinely used for cerebral oxygenation monitoring of the frontal cortex to detect potential cerebral malperfusion in all patients. In 6 patients without initiation of SCP via the RCCA/LCCA at the beginning of the procedure, extra-anatomic aorto-carotid bypass was performed during or at the end of the procedure if persisting malperfusion was suspected by NIRS/Doppler sonography ($n = 6$; 26.1%).

Follow-up

The follow-up was 100% complete (median: 15.2; IQR: 4.8–34.1), and included a telephone interview with the patient or patient's family members, as well as a written questionnaire was sent to the patient's general practitioners.

Study variables and definitions

Intraoperative death or death within the first 24 h postoperatively was defined as intraoperative death. New stroke was defined either by new (postoperative) permanent neurological impairment or signs of new CT infarct/haemorrhage. Stroke was sub-classified into three subgroups: (i) no/minimal symptoms, (ii) persistent stroke with symptoms and (iii) deteriorating stroke with fatal outcome. Postoperative temporary or permanent (TND/PND) neurological deficits were defined as neurological deficits/complications noted for the first time after the operation. Neurological deficits that resolved during the clinical course were defined as TND, while PND was defined as persisting significant cognitive, sensory or motor deficits.

Renal failure was defined as an increase in serum creatinine >1.5 mg/dl, temporary (resolved by the time of discharge) or

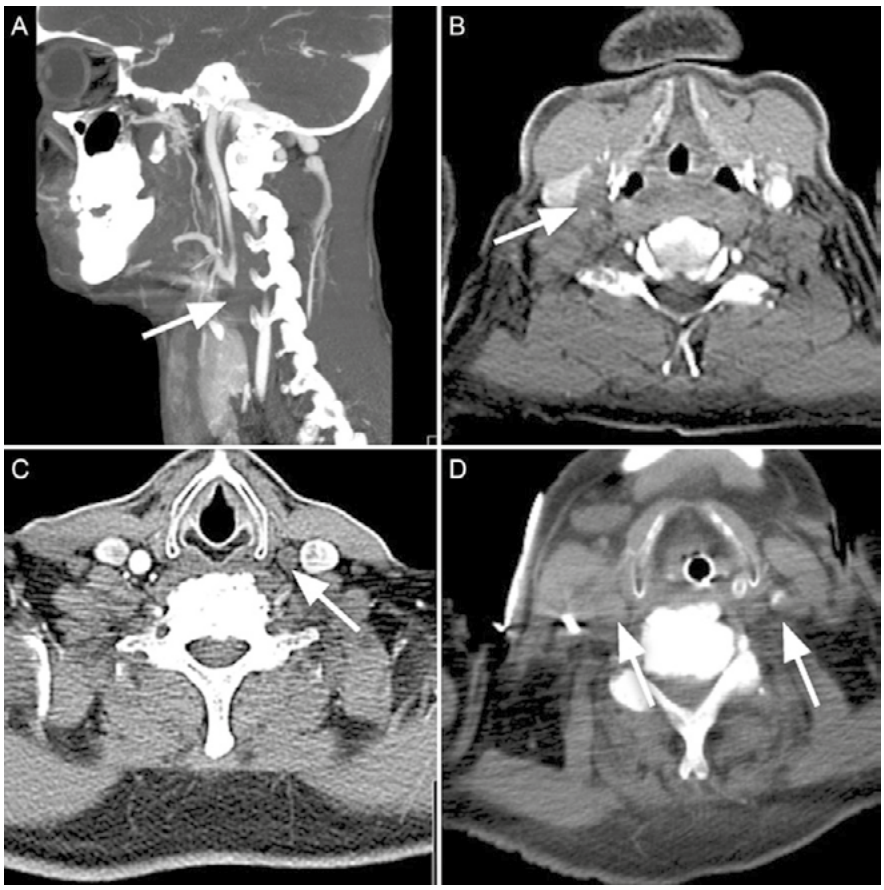

Figure 2: Computed tomography scan of a patient with right common carotid artery occlusion at the level of the carotid bifurcation with retrograde filling (**A**). Examples of complete true lumen collapse due to unilateral (**B** and **C**) and bilateral common carotid artery occlusion/stenosis (**D**).

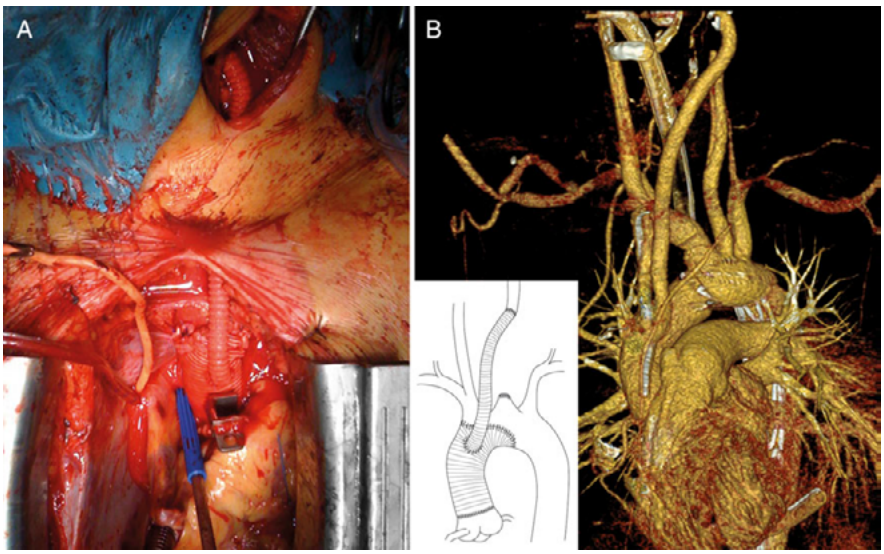

Figure 3: Intraoperative view showing extra-anatomic aorto-carotid bypass (**A**). Schematic figure of the procedure and 3D reconstruction by computed tomography (**B**).

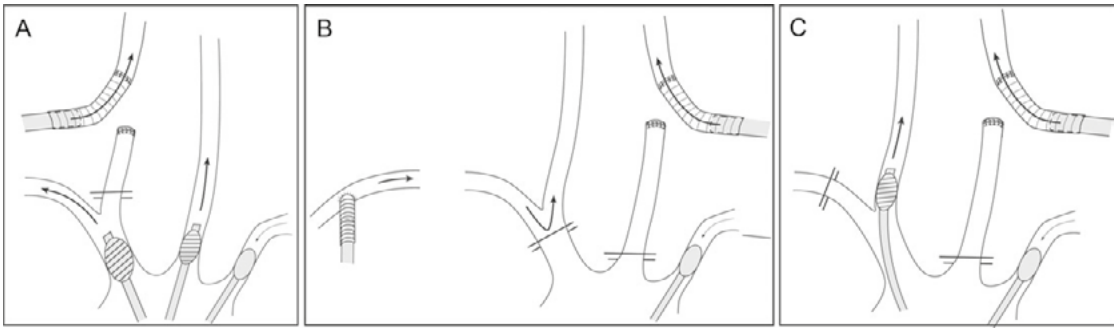

Figure 4: Cannulation sites for bilateral selective cerebral perfusion: perfusion of the RCCA (via prosthetic graft) in combination with direct LCCA cannulation (**A**); LCCA perfusion (via prosthetic graft) in combination with additional axillary artery (**B**) or direct RCCA cannulation (**C**).

Table 2: Operative data

Operative procedures	
Extra-anatomic bypass [*n* (%)]	23 (100)
RCCA	12 (52.2)
LCCA	10 (43.5)
RCCA & LCCA	1 (4.3)
Additional repair	8 (34.8)
Brachiocephalic trunk	2 (8.7)
Proximal left carotid artery	5 (21.7)
Left subclavian artery	3 (17.4)
Right subclavian artery	4 (13.4)
Aortic valve repair [*n* (%)]	7 (30.4)
Aortic valve replacement [*n* (%)]	11 (47.8)
Aortic root replacement [*n* (%)]	15 (65.2)
Supracoronary ascending aortic replacement [*n* (%)]	8 (34.8)
Hemiarch repair [*n* (%)]	14 (60.9)
Total arch repair [*n* (%)]	9 (39.1)
With conventional elephant trunk	4 (17.4)
CABG [*n* (%)]	3 (13.0)
Additional cannulation sites	
Axillary artery [*n* (%)]	15 (65.2)
Femoral artery [*n* (%)]	7 (30.4)
Brachiocephalic trunk [*n* (%)]	1 (4.3)
Ascending aorta [*n* (%)]	1 (4.3)
Cardiac apex [*n* (%)]	1 (4.3)
Venous drainage sites	
Right atrium [*n* (%)]	17 (73.9)
Femoral vein [*n* (%)]	6 (26.1)
Perfusion data	
SCP time (min), mean ± SD	33.4 ± 14.2
LBCA time (min), mean ± SD	33.5 ± 14.4
Lowest oesophageal temperature (°C), mean ± SD	26.1 ± 3.3
CPB time (min), mean ± SD	198.2 ± 53.6
Cross-clamp time (min), mean ± SD	111.4 ± 36.2
Reperfusion time (min), mean ± SD	49.2 ± 21.8

SD: standard deviation; RCCA/ LCCA: right/left common carotid artery; CABG: coronary artery bypass graft; SCP: selective cerebral perfusion; LBCA: lower body circulatory arrest; CPB: cardiopulmonary bypass.

permanent need for haemodialysis. Respiratory insufficiency was defined as weaning failure from mechanical ventilation by means of mechanical ventilation (>7 days), required reintubation or tracheostomy. Hospital mortality was defined according to current guidelines as death in hospital prior to discharge or within 30 days after surgery (regardless of location).

The American Society of Anesthesiologists (ASAs) physical status classification system was used in all 23 patients on admission to evaluate the patient and estimate the urgency of surgery.

Statistical methods

Standard definitions were used for patient variables and outcomes. Categorical data are reported as frequencies (percentages) and continuous variables as median (IQR) or mean (±standard deviation), respectively. Statistical analyses were performed with the GraphPad Prism 6 software (GraphPad, Inc., La Jolla, CA, USA). Survival analysis was performed according to the methods of Kaplan and Meier, and statistical differences were analysed by the log-rank test. Values of $P < 0.05$ were considered to be significant. Patients that died intraoperatively or within the first 24 h were excluded from the survival analysis by the methods of Kaplan and Meier. At 36 months postoperatively, the number of patients at risk in Group I was considered to be too low to allow for further comparison (>36 months).

RESULTS

Hospital and follow-up mortality

The respective in-hospital and 1-year mortality rates were 13.0% ($n = 3$) and 30.4% ($n = 7$). After a median time period of 15.2 months (IQR: 4.8–34.1), 16 (69.6%) patients were still alive (Table 3).

Of the 3 perioperative deaths, 2 patients were intubated because of a large stroke confirmed by preoperative CT (including the single patient with bilateral common carotid artery occlusion). Postoperatively, both patients suffered from cerebral haemorrhage in the area of infarction, and never regained consciousness (Fig. 1C and D). The third patient developed postcardiotomy low cardiac output syndrome, requiring extracorporeal membrane oxygenation (ECMO) therapy. He subsequently died of sepsis with resulting multiorgan failure.

We also compared survival of the 23 patients with cerebral malperfusion secondary to RCCA/LCCA occlusion (Group I) with that of the remaining 331 AADA patients without RCCA/LCCA occlusion (Group II). The follow-up information was available for all discharged patients, and was of comparable duration between both groups. After a median follow-up of 33.7 months (IQR: 11.9–55.9), 223 (67.4%) patients of Group II were still alive. The overall survival after 36 months was 69.6% ($n = 16$) in Group I versus 72.5% ($n = 240$) in Group II ($P = 0.90$) (Fig. 5).

Postoperative complications

Complications leading to resternotomy occurred in 6 (26.1%) patients due to postoperative haemorrhage ($n = 2$; 8.7%) and

Table 3: Postoperative data

Mortality, *n* (%)	
In-hospital	3 (13.0)
1-year	4 (30.4)
Hospital stay (days), median (range; IQR)	16 (12.5–26.0)
Intensive care unit stay (days), median (range; IQR)	7 (2.0–16.5)
Postoperative interventions and complications	
Resternotomy, *n* (%)	6 (26.1)
Haemorrhage	2 (8.7)
Pericardial tamponade	4 (17.4)
Drainage for pericardial effusion [*n* (%)]	3 (13.0%)
Mesenteric malperfusion, treated by	2 (8.7)
TEVAR	1 (4.3)
Laparotomy (with duodenojejunal resection)	1 (4.3)
Postoperative ECMO therapy	2 (8.7)
Sepsis [*n* (%)]	4 (17.4)
Respiratory insufficiency [*n* (%)]	10 (43.5)
Percutaneous tracheostomy	6 (26.0)
Reintubation	6 (26.0)
Postoperative pneumonia	2 (8.7)
Renal failure with temporary dialysis	7 (30.4)
Postoperative neurological complications	
New neurological deficits [*n* (%)]	14 (60.9)
Stroke [*n* (%)]	8 (34.8)
No/minimal symptoms	4 (17.0)
Persisting stroke	3 (13.0)
Deteriorating stroke	1 (4.3)
Permanent neurological deficits [*n* (%)]	3 (13.0)
Hemiparesis	2 (8.7)
Hemiplegia	1 (4.3)
Temporary neurological deficits [*n* (%)]	9 (39.1)
Tetraparesis	1 (4.3)
Hemiparesis	5 (21.7)
Hemiplegia	1 (4.3)
Seizure	2 (8.7)
Cerebral oedema without stroke	2 (8.7)

IQR: interquartile range; SD: standard deviation; TEVAR: thoracic endovascular aortic repair; ECMO: extracorporeal membrane oxygenation.

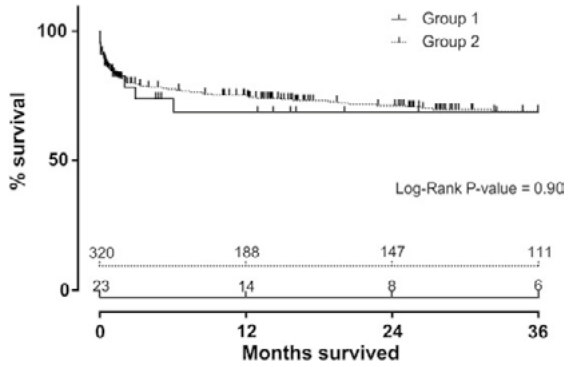

Figure 5: Postoperative survival of patients with common carotid artery occlusion with cerebral malperfusion (Group 1) versus all other patients with acute aortic dissection type A (Group 2); intra-operative deaths excluded from analysis.

pericardial tamponade (*n* = 4; 17.4%). Three other patients (13%) developed pericardial effusion during their clinical course requiring elective pericardial drainage. Postoperatively, 2 of 16 patients with aortic dissection extending into the thoraco-abdominal aorta showed signs of mesenteric malperfusion, and were treated by either thoracic endovascular aortic repair (*n* = 1) or laparotomy with duodenojejunal resection (*n* = 1). Two patients required ECMO therapy due to low cardiac output syndrome (Table 3).

Ten patients (43.5%) developed respiratory insufficiency and percutaneous tracheostomy was required in 6 cases. Acute renal failure requiring temporary dialysis occurred in 7 (30.4%) patients.

New postoperative neurological deficits corresponding to perioperative cerebral malperfusion were noted in 14 (60.9%) of the 23 patients (Table 3). Stroke rate was 34.8% (*n* = 8)—excluding the 3 patients with preoperative CT confirmation of stroke—with 4 patients showing no/minimal symptoms, 3 patients affected by persisting stroke with symptoms and 1 patient suffering from deteriorating stroke. In addition, postoperative cranial CT revealed cerebral haemorrhage (*n* = 3) and/or oedema (*n* = 3) in 6 cases. Permanent neurological deficits (PNDs) due to persisting stroke comprised permanent hemiparesis (*n* = 2) and hemiplegia (*n* = 1). Temporary neurological deficits (TNDs) occurred in 9 patients, and included temporary tetraparesis (*n* = 1), temporary hemiparesis (*n* = 5)/hemiplegia (*n* = 1) and postoperative seizure (*n* = 2). Of note, 6 (26.1%) patients recovered from surgery without any neurological complications, whereas 4 other patients (17.4%) experienced an episode of delirium as the only postoperative complication. All postoperative complications are listed in Table 3.

Overall median time to hospital discharge was 16.0 days (IQR: 12.5–26.0) with a median intensive care unit stay of 7.0 days (IQR: 2.0–16.5).

DISCUSSION

End-organ malperfusion syndromes have been reported to occur in approximately one-third of AADA patients [7], and are associated with an increased in-hospital mortality ranging between 14.6 and 30.5% [2, 8, 9].

One of the main principles of AADA management is the immediate restoration of blood flow into the true aortic lumen by emergency open surgery [10]. We previously analysed 279 AADA patients—including 92 (33.4%) patients with end-organ ischaemia—and identified preoperative malperfusion syndrome as a significant risk factor for long-term mortality after AADA repair (HR, 1.7; 95% confidence intervals, 1.2–3.1) [2]. The Kobe group identified prolonged time-to-surgery of more than 9.1 h to significantly predict poor survival and lack of neurological recovery in patients with central nervous malperfusion [9]. However, restoration of cerebral blood flow by conventional AADA repair may be very difficult if severe stenosis or occlusion of the common carotid arteries is present. Such lesions are usually the result of true lumen collapse and thrombus formation within the false lumen, and may prohibit sufficient perfusion by SCP via the axillary artery, brachiocephalic trunk or proximal left carotid artery.

Direct carotid cannulation [11] and extra-anatomic distal aorto-carotid bypass have been suggested to successfully restore cerebral perfusion in AADA patients with preoperative cerebral malperfusion, either prior to [3], during [4] or following central aortic repair [5]. We feel that immediate aortic repair in combination with extra-anatomic revascularization offers the best treatment option in this high-risk subgroup of AADA patients. Treatment of the 23 patients by extra-anatomic distal aorto-carotid bypass was performed in 6.5% of all operated AADA patients at our institution between November 2005 and July 2013. Despite the high-risk nature of such patients, our observed in-hospital mortality of 13.0% and 3-year survival of 69.6% did not significantly differ from

the 331 operated AADA patients without carotid artery occlusion (Fig. 5). We would hypothesize from this observation that our treatment strategy may have prevented fatal perioperative stroke in these high-risk patients.

Severe preoperative neurological complications such as stroke and/or coma have been considered as major contraindications for emergency aortic repair by some investigators [12]. Estrera *et al.* [13] reported on the surgical outcome of 14 of 151 consecutive AADA patients with preoperative stroke, and found that the neurological status improved or completely recovered in 8 cases, while neurological deficits remained the same in the remaining 6. The authors concluded that, since no worsening of neurological symptoms occurred postoperatively, immediate surgical repair is warranted even if AADA is complicated by stroke. In 2006, Pocar *et al.* published their results on 5 comatose AADA patients due to cerebral malperfusion of which 4 completely recovered and only a single patient suffered from left hemiparesis and cognitive impairment. These authors concluded that coma (with stroke) may not represent an absolute contraindication for emergency surgery [14]. In our reported series, 2 of the 3 patients diagnosed with stroke on preoperative CT developed cerebral haemorrhage, and never regained consciousness, while the third patient recovered completely without clinically relevant neurological symptoms. Since cranial CT imaging was performed in only 8 patients, the actual preoperative stroke rate was probably much higher in our patient population. Despite the fact that all 23 patients on admission either showed clinical signs or had a recent history of significant cerebral malperfusion, 9 (39.1%) patients recovered completely without relevant neurological deficits during their postoperative course. New neurological complications were noted in the remaining 14 (60.9%) patients, however, with 8 completely resolving during their hospital course. In summary, only 6 (26.1%) out of 23 patients with significant preoperative central nervous malperfusion developed PND with significant neurological compromise. Therefore, we also recommend emergency surgery in AADA patients, even if complicated by preoperative stroke.

Extra-anatomic revascularization may be a valuable option in high-risk AADA patients presenting with cerebral malperfusion due to distal common carotid artery occlusion. We now routinely initiate unilateral SCP via the respective carotid artery at the beginning of the procedure, and perform additional perfusion of the contralateral side (i.e. bilateral SCP) after opening the aortic arch (Fig. 4), followed by distal aorto-carotid bypass after central aortic repair in such patients.

CONCLUSIONS

Patients with preoperative cerebral malperfusion due to distal common carotid artery occlusion or stenosis represent a very high-risk subgroup of AADA patients. Extra-anatomic distal aorto-carotid bypass allows for early initiation of SCP, and is associated with acceptable postoperative morbidity and mortality. Such a strategy may result in decreased mortality in these high-risk patients.

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APPENDIX. CONFERENCE DISCUSSION

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Dr G. Weiss (Vienna, Austria): During the study period more than 350 patients were operated for aortic dissections, and out of those, 23 patients were identified who had undergone an extra-anatomic carotid bypass. Did all patients in your centre receive a bypass to the carotid artery if the CT scan revealed a malperfusion?

The more standardized surgical strategy is to exclude the primary entry tear and limit the operation to a conventional repair of the aortic arch in expectation that the restored blood flow in the true lumen leads to adequate reperfusion of the dissected carotid artery. Since stroke rate was rather elevated at 35%, it would have been interesting to know how high the stroke rate was in the patient group not undergoing extra-anatomic bypass surgery.

My second question is about timing and imaging. You mentioned that every patient received a cranial CT scan before surgery. It is well known that the diagnosis of stroke cannot be definitely confirmed by CT scan within the first six hours after the initial event. However, in three patients, a stroke was diagnosed before surgery, and these patients received an extra-anatomic bypass to a carotid artery. There is also evidence that revascularization of cerebral areas with a recent stroke might be harmful in terms of intracranial bleeding. What was the purpose of performing a bypass to the carotid artery in a patient with a verified stroke?

My third question, what would be your surgical strategy if you observe a dissected carotid artery by CT without any clinical symptoms? Would you still perform an extra-anatomic bypass?

My last question, in rare occasions the dissection does not end in the common carotid artery but extends into the internal carotid artery or even at an intracranial level. Would you still perform a bypass in these cases?

Dr Luehr: I would like to answer your first question regarding the patients with cerebral malperfusion and if all of those patients receive an extra-anatomic bypass. So what we did in our series was to retrospectively identify all patients with distal carotid occlusion treated by extra-anatomic bypass, which turned out to be a little difficult. However, I cannot exclude that there might have been one or two with distal carotid occlusion but without carotid-to-aortic bypass that I didn't identify.

In our previous series on the outcome of patients with type A dissection related malperfusion syndromes, we had 14% of patients with preoperative cerebral malperfusion, and 41% of those 39 patients had a stroke. Unexpectedly, in this series the incidence of stroke is even lower, which actually underlines our surgical strategy.

With regard to the second question, there is no clear consensus regarding the treatment of patients with preoperative stroke. We did not have a CT scan of the cranium in every patient of the series. Most of those patients were emergently admitted to our centre, often with an externally performed chest CT clearly showing type A aortic dissection and were taken to the OR right away.

Only patients that were already intubated or showed neurological impairment had an additional cranial CT scan. It was eight patients in the series, and three of those had a preoperative stroke.

Postoperatively, all patients that showed neurological impairment, had CT of the cranium just to make sure and we found eight strokes in those patients. As I showed you before, four had no or only minor symptoms which were not clinically relevant while four patients had a severe stroke, including two patients with cerebral haemorrhage, and they obviously did not do very well. But in total it was only six patients that suffered from significant neurological deficits postoperatively.

I guess it was your third question regarding a situation in which a patient has a unilateral right distal carotid dissection but has no clinical symptoms? We would, as it is our institutional routine approach or strategy for type A aortic dissection, cannulate the axillary artery, and aim for bilateral selective cerebral perfusion after aortotomy via the left carotid artery. But we would always look at the NIRS monitoring, which we do routinely as well. And once there is some evidence of malperfusion to the brain, we would always try to get to the carotids and make sure that the brain is perfused, of course.

The last question, if I remember correctly, was what to do if the dissection extends above the carotid bifurcation. Well, it's difficult in those patients. Fortunately, we didn't see such cases in our series. However, once you have a dissection extending into the internal carotid artery or even higher, there is not a lot you can do.

So I guess our strategy would be to dissect the carotid artery at the bifurcation, identify the true lumen, glue the layers, perfuse the brain and do the extra-anatomic bypass after central aortic repair.

Dr B. Rylski *(Freiburg, Germany):* My question is on the follow-up CT.

Could you please tell us if you observed any kind of remodelling of the carotid artery? Did the dissection disappear after anastomosing it to the bypass?

Dr Luehr: We had five patients with a thrombus in the false lumen, so there was some evidence for a false lumen which was expanding. But I did not find any patient who had postoperatively a false lumen that was somehow in the remodelling process.

So once the carotids were revascularized, we could see nicely that the carotids were perfused, but we did not identify or see any remodeling of the false lumen.

Dr S. Soliman *(Cairo, Egypt):* My question is about the patients who need total arch replacement and those with dissected carotids. Do you also do extra-anatomical bypass for them or just you do the total arch bypass?

Dr Luehr: We had nine patients with a total arch replacement due to dissection involving the whole arch and the supra-aortic branches. Therefore, we performed complete revascularization of the dissected supra-aortic vessels in those cases.

However, in those patients that had a distal carotid occlusion with resulting true lumen collapse, we performed an extra-anatomic bypass to the respective vessel additionally because we could not ensure that, even though we might have connected the respective true lumen to the prosthetic arch graft, sufficient bilateral cerebral perfusion was achieved afterwards.

6.4 Incidence of neurological complications following overstenting of the left subclavian artery

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Incidence of neurological complications following overstenting of the left subclavian artery☆

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Abstract

Objective: Aortic endovascular stent-graft implantation is associated with low morbidity and mortality rates. Overstenting of the left subclavian artery may be necessary to create a satisfactory proximal 'landing zone' for the stent-graft. Few cases have been published reporting adverse neurological events after overstenting of the left subclavian artery. We thus evaluated whether this procedure is associated with a higher rate of neurological complications by focusing on the management of the supra-aortic vessels. **Methods:** Twenty patients suffering from aortic arch aneurysms ($n = 3$), descending aortic aneurysms ($n = 7$), acute ($n = 6$) and chronic ($n = 4$) type-B aortic dissections underwent stent-graft repair with complete ($n = 14$) or partial ($n = 6$) overstenting of the left subclavian artery. Three patients underwent overstenting of the entire aortic arch with ascending aortic-bi-carotid bypass grafting. One patient with right carotid and vertebral artery occlusion underwent initial carotid-to-subclavian bypass. All patients subsequently underwent neurological examination and Doppler ultrasound for detection of neurological and peripheral vascular complications. **Results:** Aortic stent-graft repair was successful in all patients without acute neurologic complications. Two patients developed late central adverse neurological events: right-sided vertebral artery occlusion with brainstem infarction ($n = 1$) and impaired binocular vision combined with dizziness ($n = 1$), necessitating secondary subclavian transposition in one patient. Peripheral symptoms related to occlusion of the left subclavian artery were observed in five patients as sensory and motoric deficits of the left hand and arm. **Conclusions:** Overstenting of the left subclavian artery as treatment of aortic pathologies in high-risk patients is feasible but associated with the risk of neurological complications and peripheral symptoms. Side effects were mild or transient in most of our patients. Detailed preoperative exploration of vascular anatomy and pathology via Doppler ultrasound, CT- or MRI scan is mandatory to avoid adverse neurological events. Prior surgical revascularization of the left subclavian artery is essential in patients with high-grade stenoses, occlusions, or anatomic variants of the supra-aortic branches. Delayed surgical revascularization is necessary only in patients with relevant subclavian steal syndrome or severe peripheral vascular symptoms.

Keywords: Endovascular stent-graft; Supra-aortic vessels; Aortic aneurysm; Aortic dissection; Neurological complication; Subclavian artery overstenting

1. Introduction

Endovascular stent-graft implantation (ESI) is a less invasive treatment of aortic pathologies, associated with lower morbidity and mortality rates than conventional open aortic repair [1—4]. Open surgical treatment of aortic diseases necessitates aortic cross-clamping and occasionally hypothermic circulatory arrest. In contrast to open repair, ESI requires suitable proximal and distal 'landing zones' for stent-graft fixation. Thus, 2 cm of normal aortic wall is needed for adequate sealing [5,6]. Thoracic aortic pathologies such as aneurysms or dissections often involve the origin of the supra-aortic branches. If the distal aortic arch is affected, overstenting of the left subclavian artery (LSA) can be performed to elongate the proximal 'landing zone' [7,8]. However, this strategy has been associated with delayed onset of vertebrobasilary insufficiency and arm ischemia [9]. Surgical transposition of the LSA to the left common carotid artery (LCCA) or LCCA-to-LSA bypass prior to ESI is sometimes necessary to preserve the blood

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flow and avoid adverse events resulting from LSA overstenting [10].

After preoperative evaluation of the supra-aortic vessels we applied a tailored approach with overstenting of the LSA without revascularization in the absence of supra-aortic vascular disease and performed selective subclavian revascularization only in patients with supra-aortic vascular pathology. There are a few cases reporting adverse events after overstenting of the LSA, and no consensus exists on how best to manage and treat patients requiring overstenting of the LSA [6]. We thus evaluated whether overstenting of the LSA is associated with a higher rate of neurological complications and peripheral symptoms by focusing on management of supra-aortic vessels.

2. Materials and methods

Since 1996, we have considered ESI of aortic diseases as an alternative to open surgical aortic repair in 265 high-risk patients. Between December 2000 and March 2006, 20 of these patients (10 female and 10 male) with a mean age of 64.3 ± 12.23 years (range 39–79 years) were suffering from thoracic or thoracoabdominal aortic diseases close to or involving the supra-aortic arteries requiring complete overstenting or partial covering of one or more supra-aortic vessels with endovascular stent-grafts.

The patients' preoperative risk factors and comorbidities are found in Table 1. Due to the high perioperative risk these particular patients presented, conventional surgical repair was not deemed appropriate. Preoperative Doppler ultrasound of the supra-aortic branches was performed in 15 patients and was not feasible due to time constraints in five emergent or urgent cases. In 3 of the 20 patients (15%), preoperative Doppler ultrasound detected mild supra-aortic vessel pathologies (wall thickening of the right and LCCA ($n = 3$) and atherosclerotic plaques in the internal and external carotid arteries ($n = 2$)). Two patients had severe supra-aortic vessel pathologies with complete occlusion of the right internal carotid and vertebral artery ($n = 1$) and occlusion of the LSA based on a type-B aortic dissection with incomplete subclavian steal syndrome ($n = 1$) (Table 2).

Additionally, evaluation for elective and urgent patients was done by angiography, computed tomography (CT), or magnetic resonance imaging (MRI) to exclude stenoses, occlusion, or anatomical variants of the supra-aortic branches and aortoiliac axis (Fig. 1). The supra-aortic branches were examined to determine whether an adequate 'landing zone' would be available.

Pathologies included aneurysms of the aortic arch ($n = 3$) and descending aorta ($n = 7$), and acute ($n = 6$) and chronic ($n = 4$) type-B aortic dissections. Two of the chronic dissections involved a secondary aneurysm. Two patients (10%) had a preoperative history of stroke and five patients had undergone aortic surgery due to aortic type-A dissection ($n = 3$) and aortic coarctation ($n = 2$). Seven of the 20 patients (35%) required emergency stent-grafting for treatment of contained rupture ($n = 2$) resulting from acute ($n = 1$) or chronic ($n = 1$) aortic dissections, malperfusion of the renal and visceral arteries ($n = 3$) or of the iliac and femoral arteries ($n = 2$). Indication for stent-grafting in 10 patients with aneurysms (50%) was rapid progression of aneurysm, aneurysm greater than 5 cm, or excentric aneurysms. Ten patients with acute or chronic type-B dissections (50%) were treated for associated complications such as contained rupture, visceral or renal malperfusion, limb ischemia, persistent pain despite medication, or secondary aneurysm associated with the dissection (Table 2).

Eleven patients with atherosclerotic aneurysms ($n = 6$) and aortic type-B dissections ($n = 5$) in whom the LSA origin revealed aneurysm involvement or proximity to the primary entry site of the dissection required partial or complete overstenting of LSA by ESI. Nine patients in whom the distance from the LSA to the beginning of the aneurysm ($n = 4$) or to the primary dissection entry site ($n = 5$) was under 1.5 cm also required partial or complete overstenting of the LSA (Table 3).

Table 1
Preoperative risk factors and co-morbidities

Pat	Stroke/TIA	Hypertension	Hyperlipidemia	COPD	Obesity	CAD	Atrial fibrillation	Renal insufficiency
1	–	–	–	–	–	–	–	–
2	–	Yes	–	–	–	Yes	Yes	Yes
3	–	Yes	–	–	–	–	–	–
4	–	Yes	Yes	–	–	–	–	–
5	–	Yes	Yes	–	–	–	–	–
6	–	Yes	–	–	–	–	–	–
7	–	Yes	–	–	–	–	–	–
8	–	Yes	–	–	–	–	–	–
9	–	Yes	–	Yes	–	–	Yes	–
10	Yes	Yes	Yes	–	Yes	Yes	–	–
11	–	Yes	Yes	–	–	–	–	–
12	–	Yes	–	–	–	Yes	–	–
13	–	Yes	Yes	–	Yes	Yes	–	–
14	–	Yes	–	Yes	–	–	–	–
15	–	Yes	Yes	–	–	Yes	–	–
16	–	Yes	–	–	–	–	–	–
17	–	–	–	–	–	–	–	–
18	Yes	Yes	Yes	–	–	–	–	Yes
19	–	Yes	–	–	Yes	Yes	–	–
20	–	Yes	–	–		Yes	–	Yes

COPD, chronic obstructive pulmonary disease; CAD, coronary artery disease; TIA = transient ischemic attack.

Table 2
Preoperative data

Pat	Age	Sex	Prior cardio-vascular surgery	Aortic pathology	Supra-aortic pathology	Urgency	Rupture	Malperfusion
1	40	M	Aortic coarctation	TAA (5.5 cm)	–	Elective	–	–
2	79	M	–	Chronic type-B dissection	–	Urgent	–	–
3	53	M	–	Chronic type-B dissection	Dissection involving the LSA causing proximal LSA occlusion and incomplete subclavian steal syndrome	Emergent	–	Iliac/femoral
4	60	F	–	Acute type-B dissection	–	Urgent	–	–
5	63	M	–	Acute type-B dissection	–	Emergent	–	Renal/visceral
6	39	F	Aortic coarctation	TAA (7.1 cm)	–	Elective	–	–
7	58	M	–	Acute type-B dissection	–	Emergent	–	Renal/visceral
8	44	F	–	Acute type-B dissection	–	Emergent	–	Iliac/femoral
9	79	F	–	TAA (7.6 cm)	Plaques of the ICAs and ECAs, thickened walls of the CCAs	Urgent	–	–
10	67	M	–	TAA (5.3 cm) + infrarenal aortic stenosis	Occlusion of the right ICA and the right VA	Urgent	–	–
11	67	F	–	Acute type-B dissection	Plaques of both ICAs, thickened walls of the CCAs	Emergent	Yes	–
12	73	M	–	TAA (6.0 cm)	–	Elective	–	–
13	73	F	Type-A dissection, CABG	AAA + TAA (5.5 cm)	–	Urgent	–	–
14	69	M	–	AAA + TAA (6.0 cm)	–	Urgent	–	–
15	67	F	Type-A dissection, CABG	AAA + TAA (6.5 cm)	Thickened walls of the CCAs	Urgent	–	–
16	78	M	–	TAA (5.5 cm)	–	Elective	–	–
17	72	F	–	Chronic type-B dissection	–	Elective	–	–
18	72	F	Type-A dissection	TAA (rapidly growing)	–	Emergent	Yes	–
19	72	F	–	TAA (5.5 cm)	–	Urgent	–	–
20	60	M	CABG	Chronic type-B dissection	–	Emergent	–	Renal/visceral

M, male; F, female; CABG, coronary artery bypass grafting; TAA, thoracic aortic aneurysm; AAA, aortic arch aneurysm; ICA, internal carotid artery; ECA, external carotid artery; LSA, left subclavian artery; CCA, common carotid artery; VA, vertebral artery.

In 14 patients, the LSA was completely overstented, preventing antegrade perfusion of the LSA. In 3 of these 14 patients, aortic-bi-carotid bypass without revascularization of the LSA was initially performed prior to overstenting of the entire aortic arch for aortic arch aneurysm. Simultaneous revascularization of the LSA by LCCA-to-LSA bypass was carried out in 1 of the 14 patients treated by complete overstenting of the LSA. That last patient presented with an occlusion of the right internal carotid artery and the right vertebral artery (VA) preoperatively, and a history of three strokes, ruling out any occlusion of the supra-aortic branches without additional revascularization. All initial bypass procedures were performed during the same operation prior to ESI. Details of the surgical revascularizations of the supra-aortic branches are shown in Table 3. Coverage of the LCCA with the bare metal tip of the endovascular stent-graft was necessary in four further patients in that group, which still allowed sufficient antegrade perfusion of the LCCA.

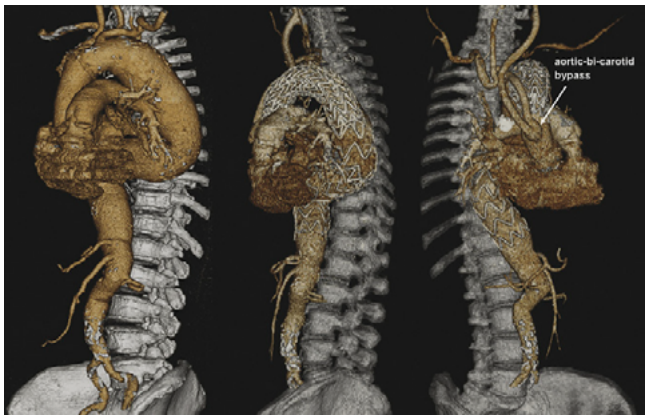

Fig. 1. Preoperative 3D-MRI with aortic arch and thoracoabdominal aneurysm (Crawford type I) involving the supra-aortic great arteries (left); postoperative 3D-MRI after endovascular stent-graft implantation with three stent-grafts covering the entire aortic arch to the celiac axis (middle), and aortic-bi-carotid bypass using woven prosthesis (right).

In six patients, the LSA was not completely covered by the endovascular stent-graft, thus permitting antegrade LSA perfusion. In four of those patients, the LSA was only covered by the bare metal tip, and in two of them the proximal coated portion of the stent-graft did not completely occlude the LSA orifice (Table 3).

2.1. Intraoperative neurophysiological monitoring

Cerebral perfusion was controlled in each patient by an arterial line placed in the right radial artery. Intraoperative neurophysiological monitoring with transcranial motor-evoked potentials (tcMEP) and somatosensory-evoked potentials (SSEP), as well as cerebrospinal fluid (CSF) pressure monitoring was applied in 17 (elective = 5, urgent = 7, emergent = 5) patients as a control mechanism to identify spinal cord ischemia during ESI (Table 3). This technique has been described in detail previously [11,12]. Whenever CSF pressure exceeded 15 mmHg, CSF drainage was carried out. In three patients who underwent emergency surgery, intraoperative neurophysiological monitoring was not applied.

Table 3
Intraoperative data

Pat	Endovascular stent-grafts	Access	Surgical revascularization	Degree of supra-aortic overstenting	Neuromonitoring (tcMEP, SSEP, CSFP)
1	1× Valiant/Medtronic (28 × 150 mm)	FA	–	LSA completely	Yes
2	1× Zenith TX 1/Cook (42 × 166 mm)	FA	–	LSA partially w/coated part	Yes
3	1× EXCLUDER/GORE (40 × 200 mm)	FA	–	LSA completely	Yes
4	2× Talent/Medtronic (44 × 113 mm/ 44 × 111 mm)	FA	–	LSA partially w/coated part	Yes
5	1× Talent/Medtronic (38 × 114 mm)	FA	–	LSA partially w/uncoated part	Yes
6	1× Zenith TX 1/Cook (22 × 100 mm)	FA	–	LSA completely	Yes
7	1× Zenith TX 1/Cook (34 × 140 mm)	FA	–	LSA completely	Yes
8	1× Talent/Medtronic (38 × 100 mm) 1× Zenith TX 1/Cook (40 × 100 mm)	FA	–	LSA completely	Yes
9	2× Talent/Medtronic (34 × 100 mm/ 38 × 100 mm)	IA	–	LSA partially w/uncoated part	No
10	1× Talent/Medtronic (42 × 111 mm) 1× Palmaz/Cordis (23 ×150 mm)	FA	Initial carotid-to-subclavian bypass	LSA completely	Yes
11	1× Talent/Medtronic (36 × 114 mm)	FA	–	LSA completely	No
12	4× Valiant/Medtronic (1× 44 × 200 mm, 1× 46 × 200 mm, 1× 46 × 100 mm, 1× 42 × 100 mm)	FA	Secondary LSA transposition	LSA completely	Yes
13	1× TAG/GORE (40 × 200 mm), 1× Talent/Medtronic (42 × 111 mm) 1× Valiant/Medtronic (40 × 200 mm)	AAo	Initial ascending aortic-bi-carotid bypass	Aortic arch completely	Yes
14	1× TAG/GORE (24 × 200 mm)	AAo	Initial ascending aortic-bi-carotid bypass	Aortic arch completely	Yes
15	1× TAG/GORE (40 × 200 mm) 2× Talent/Medtronic (46 × 112 mm)	FA	Initial ascending aortic-bi-carotid bypass, secondary carotid subclavian bypass	Aortic arch completely	Yes
16	2× Talent/Medtronic (36 × 114 mm/ 38 × 114 mm)	FA	–	LSA completely	Yes
17	2× Talent/Medtronic (42 × 113 mm)	FA	–	LSA partially w/uncoated part	Yes
18	1× Talent/Medtronic (42 × 115 mm)	IA	–	LSA completely	No
19	1× Talent/Medtronic (40 × 160 mm)	FA	–	LSA completely	Yes
20	1× EXCLUDER/GORE (40 × 150 mm)	FA	–	LSA partially w/uncoated part	Yes

FA, femoral artery; AAo, ascending aorta; IA, iliac artery; LSA, left subclavian artery; tcMEP, transcranial motor evoked potentials; SSEP, somatosensory-evoked potentials; CSFP, cerebrospinal fluid pressure.

2.2. Ascending aortic-bi-carotid bypass

Following upper L-shaped hemisternotomy, the ascending aorta was exposed in usual fashion. The brachiocepahlic trunk and LCCA were circumferentially dissected. After systemical heparinization with 100 IU/kg bodyweight, the ascending aorta was tangentially clamped and a longitudinal arteriotomy performed. An end-to-side anastomosis between the proximal portion of a bifurcated Dacron prosthesis (Gelweave®, Vascutek, Scotland, UK) and the ascending aorta took place with reinforcement of Teflon felt strips with a 4-0 Prolene running suture (Ethicon Inc., Somerville, NJ, USA). The cross-clamp was gently released, and the air within the graft removed. The supra-aortic vessels were then exposed. First, the brachiocephalic trunk, and then the LCCA were cross-clamped. Following longitudinal arteriotomy, each branch of the bifurcated prosthesis was side-to-end anastomosed to the right and LCCA. Blood flow was restored after complete deaeration in usual fashion (Fig. 1).

2.3. Endovascular stent-graft implantation

We used four types of commercial endovascular stent-graft devices in our study. The selection of the stent-graft devices was based on availability, length, required diameter, and anatomical findings. Stent-graft diameter was calculated from the largest proximal or distal neck diameter and an over-sizing factor of 10%. The EXCLUDER/TAG (W. L. GORE & Associates, Flagstaff, AZ, USA), the Talent/Valiant (Medtronic, Santa Rosa, CA, USA), the Zenith TX 1 (Cook, Bloomington, IN, USA), and the Palmaz (Cordis Endovascular, New York, NY, USA) stent-graft devices were implanted in the operating room under general anesthesia (Table 3). For optimal visualization, the patient was positioned with the left shoulder elevated in order to maximize the distance between the supra-aortic branches' origins. The common femoral artery access was chosen in 16 patients. Due to severe calcification, significant stenoses or occlusion of the femoral arteries, or significant thoracoabdominal kinking, an alternative stent-graft access was chosen in four patients: one common iliac artery, one infrarenal aorta, and in two cases the ascending aorta (Table 3). Intraoperative angiography was performed using 'breath-hold' technique using a mobile C-arm intensifier (Siemens, Munich, Germany). The stent-grafts were advanced under fluoroscopic guidance and deployed during mild systemic hypotension. We used latex balloons (Reliant balloon, Medtronic, Sunrise, Fl) to improve expansion for modeling the stent-grafts to the aortic wall.

Aortography documented adequate aneurysm exclusion, sealing of the proximal entries in cases of aortic dissection, and occurrence of endoleaks. We defined successful ESI as deployment in the correct aortic passage with satisfactory blood flow proximal and distal of the stent-graft.

2.4. Follow-up

Follow-up CT- or MRI scans were performed before hospital discharge and after 3, 6, and 12 months, and annually thereafter (Fig. 1). Mean follow-up was 19.7 ± 17.3 months (range 2–60 months). All pre- and postoperative clinical examinations, as well as those during follow-up included bilateral blood pressure measurements, multislice CT- or MRI scans, and Doppler ultrasound of the supra-aortic vessels.

2.5. Neurological evaluation and examination

All surviving 18 patients underwent neurological follow-up performed by an experienced neurologist. A careful medical history was taken to detect transient or persistent neurological deficits prior to or after ESI. Furthermore, we took thorough patient histories, enquiring in particular about transient or persistent central neurological deficits (i.e., brainstem ischemia becoming manifest in vertigo, dizziness, acute deficits in motoric function or sensibility, dysarthria, dysphagia, or ocular movement disorders) or peripheral symptoms (i.e., arm claudication, numbness, or weakness) at rest or following exercise of the ipsilateral upper limb.

Neurological examination was performed to detect cranial nerve lesions with special attention paid to the existence of left-sided Horner syndrome. Furthermore, the motor-sensory system was examined with special regard to central or peripheral origin of paresis or sensory disorders of the left upper extremity, and to cerebellar or gait disorders. Subclavian steal syndrome was defined as presence of subclavian steal effect as diagnosed by ultrasound and the presence of clinical symptoms [13].

2.6. Ultrasound examination

Ultrasound measurements were taken by two experienced sonographers assessing the carotid arteries using Doppler ultrasound scanning. A 2 MHz probe was used for transnuchal scanning of the vertebrobasilar vascular territory; 4 MHz linear and 8 MHz curved array scanners were employed for examination of extracranial arteries (HDI 5000; ATL Bothell, USA). With the patient in a supine position, a careful search was made for transverse and sagittal planes of all supra-aortic vessels (i.e., the proximal and distal subclavian artery, the VAs from the origin to intracranial course including the basilary artery, and the common, external, and internal carotid arteries on both sides). Associated graft interponents (e.g., aortic-bi-carotid bypass) were carefully analyzed for superimposed thrombi or stenoses defined as circumscribed luminal narrowing in B-mode and significant flow acceleration in Doppler ultrasound.

We classified the degree of subclavian steal effect (i.e., the extend of hemodynamic changes in the vertebral arteries in ultrasound measurement regardless of clinical symptoms), varying from (I): systolic flow deceleration, to (II): alternating flow profile, to (III): completely reversed flow. LSA occlusion or high-grade stenoses were assumed in cases of completely reversed flow in the ipsilateral VA and upon detection of vertebro-vertebral, carotido-vertebral, or externo-vertebral collateral flow. Diagnosis of subclavian steal effect was confirmed using functional tests based on reactive hyperemia following compression of the upper left extremity, which resulted in an increase in the reverse component of the VA blood flow. Furthermore, a difference in blood pressure in the radial arteries or a difference in blood pressure between both arms ≥30 mmHg confirmed the diagnosis.

2.7. Data collection

In accordance with current legislative recommendations, all interventions were performed with approval of our institutional review board. All patients were informed in detail about ESI and additional revascularization procedures. All patients provided written consent. Data were maintained in a database of this Department of Cardiovascular Surgery. The collected data were reviewed according to the guidelines indicated by our institutional review board.

3. Results

Aortic stent-graft repair was successful in each patient in this series. All aneurysms were excluded without intraoperative complications. Closure of the entry tear and expansion of the true lumen with reperfusion of visceral, renal, or iliac arteries was achieved in all patients suffering from chronic or acute aortic dissections. The mean number of stent-grafts in all 20 patients was 1.65 (range 1–4) with a mean overstented aortic portion of 22 cm in length. Mean duration of all procedures was 189 min (30–550 min). The median hospital stay was 12 days.

3.1. Intraoperative neurophysiological monitoring

No patient suffered from complications related to spinal cord ischemia, even though we observed alterations in tcMEP (i. e., extended latency or shortened amplitude) in three cases after stent-graft deployment. When alterations of evoked potentials occurred, we initiated spinal-cord protection efforts. These protection methods have been described in detail [11,12]. In all other 14 patients measured, tcMEP potentials were consistent at the end of the operation. SSEP potentials were consistent in all measured patients.

3.2. Follow-up

Our follow-up was 100%. Two patients in our series died of unrelated causes, yielding no mortality related to ESI. One developed necrotic pancreatitis with peritonitis resulting in multiorgan failure 72 days after the ESI procedure. In that case, the LSA had only been covered with the bare metal tip of the stent-graft device, allowing antegrade perfusion of the LSA. The other patient had a complete overstented LSA and died 3 years after the initial operation.

Table 4
Postoperative data

Pat	Situation of flow direction in the vertebrobasilar system (degree of subclavian steal effect I–III)	Central neurological symptoms related to LSA occlusion	Peripheral symptoms related to LSA occlusion	Neurological complications not related to ESI and LSA occlusion	Mortality
1	SSE III	–	–	–	–
2	–	–	–	Intracerebral bleeding unrelated to prior surgery	–
3	SSE II	–	–	–	–
4	–	–	–	–	–
5	–	–	–	Dysesthesia due to a lesion of a cutaneous branch of the right femoral nerve	–
6	SSE III	Impaired binocular vision, dizziness	Disturbed fine motor skills of the left hand, temporary weakness of the left arm	–	–
7	–	–	–	–	–
8	SSE III	–	Weakness of the left arm, numbness of the left hand	–	–
9	–	–	–	–	Unrelated to prior surgery
10	SSE I	–	–	–	–
11	SSE III	–	Disturbed fine motor skills of the left hand, numbness of the left arm	–	–
12	SSE II	Brainstem (pontine) infarction	–	–	–
13	SSE III	–	–	–	–
14	SSE III	–	Numbness of the left arm and hand	Recurrent laryngeal nerve irritation	–
15	SSE III	–	Numbness and weakness of the left arm, numbness and disturbed fine motor skills of the left hand	–	–
16	–	–	–	–	–
17	–	–	–	–	–
18	–	–	–	–	Unrelated to prior surgery
19	–	–	–	–	–
20	–	–	–	–	–

LSA, left subclavian artery; ESI, endovascular stent-graft implantation; SSE, subclavian steal effect (degree I = systolic deceleration, degree II = alternating flow profile, degree III = completely reversed).

3.3. Hemodynamics and peripheral symptoms related to LSA occlusion

Occlusion of the LSA was followed by a differential in blood pressure between the right and the left arm. A lower ($n = 5$) or complete loss ($n = 5$) of blood pressure of the left arm occurred postoperatively in 50% of the patients. During follow-up, four patients with completely overstented LSA still had left arm pulses that could be measured noninvasively.

Pathological blood flows in the supra-aortic branches were detected in 10 of the 14 patients (71%) who had undergone complete LSA occlusion. Doppler ultrasound showed development of subclavian ($n = 2$), vertebro-vertebral ($n = 2$), vertebro-basilar ($n = 2$), combined vertebro-vertebral, and carotid-vertebral ($n = 2$) steal effects, as well as crossflow in the deep neck arteries ($n = 1$). The following degrees of subclavian steal effects (SSE) were observed: (I) systolic deceleration ($n = 1$); (II) alternating flow profile ($n = 2$); and (III) completely reversed flow ($n = 7$). The relationship between flow patterns and vascular peripheral symptoms is shown in detail in Table 4. Of the 14 patients with complete overstenting of the LSA, 5 patients (36%), developed associated peripheral symptoms. All had pathological blood flow degree III. These five patients suffered from ischemic-related peripheral arm deficits such as exercise-induced, sensory ($n = 3$), and motoric ($n = 3$) deficits of the left hand, temporary ($n = 1$) and persisting ($n = 2$) weakness of the left arm, and sensory deficits (numbness) of the left arm ($n = 3$). The symptoms were mild and improved over time in four of them, not necessitating subclavian revascularization. One of them presented 4 months after the initial operation with a combination of several neurological symptoms such as numbness of the left arm and hand, weakness of the left arm, and disturbed fine motor skills of the left hand. The patient was successfully treated surgically with delayed LCCA-to-LSA bypass and proximal LSA ligation leading to improvement of symptoms. In the remaining five patients with pathological blood flow (I = 1, II = 2, III = 2), no peripheral symptoms were observed (Table 4).

In the group of patients ($n = 6$) in whom complete overstenting of the LSA was avoidable, we identified no pathological changes in supra-aortic blood flow.

3.4. Neurological outcome

All patients recovered from surgery without any initial signs of significant neurological complications during their hospital stay. In the follow-up period, none of the 14 patients with complete overstenting of the LSA developed reversible

exercise-induced signs of central vertebrobasilar insufficiency, including the 10 patients who had a subclavian steal effect detected on Doppler examination. Five of 20 patients (25%) presented with adverse neurological events during follow-up (Table 4). In two (10%) of them, neurological events were associated with complete LSA occlusion. These two patients suffered from late central neurological events such as right-sided brainstem infarction ($n = 1$) and transient ischemic attack manifested by impaired binocular vision combined with dizziness ($n = 1$). The acute right-sided pontine brainstem infarction, confirmed by cerebral MRI, occurred 2 months after ESI due to an acute occlusion of the right hypoplastic VA causing left-sided facial paresis, dysarthria, severe hemiparesis, and hemihypesthesia (initial NIH stroke scale = 14). The patient underwent LSA transposition to the LCCA to prevent further brainstem infarction due to the impaired perfusion of the vertebro-basilary arteries.

Other neurological complications not related to the occlusion of supra-aortic vessels occurred in three patients. One suffered from dysesthesia due to a lesion of a cutaneous branch of the right femoral nerve (stent-graft access), another patient was hoarse as a result of recurrent laryngeal nerve irritation following aortic-bi-carotid bypass, and the third patient suffered from intracerebral bleeding unrelated to previous surgery due to a hypertensive crisis while under anticoagulation therapy (Table 4).

3.5. Endoleaks and other stent-graft related problems

We identified postoperative problems with the implanted stent-grafts via CT scans during follow-up. No type II endoleak due to overstenting of the LSA was observed in our cohort. In one patient (5%), an incomplete seal in the proximal attachment zone (type Ia endoleak) occurred, and two patients (10%) showed an incomplete seal between the stent-graft segments (type III endoleak). All three patients were successfully treated with additional stent-grafts, in a mean time of 133 days (range 10–400 days). The initial implanted stent-graft in another patient collapsed 1 year after implantation due to material failure. This patient was also successfully treated with an additional stent-graft.

4. Discussion

Open surgical repair of the aortic arch, the descending and the thoracoabdominal aorta are invasive procedures with high morbidity and mortality rates [4,14]. ESI is a less invasive and effective treatment for high-risk patients showing a low complication rate [11,12]. One of the most difficult aspects of stent-graft application is the absence of an adequate proximal 'landing zone', because the LSA is often involved in or too close to aortic pathologies.

For optimal stent-graft fixation, the 'landing zones' should be over 2 cm long. Patients with a proximal 'landing zone' of at least 1.5 cm can undergo ESI with the intention to preserve antegrade flow in the LSA. Complete coverage of the LSA ostium must take place occasionally to expand the application of stent-graft devices for aortic pathologies beside the LSA [15]. The carotid arteries limit the use of stent-grafts in pathologies located in the aortic arch.

Patients with atherosclerotic subclavian artery stenoses or occlusions are often asymptomatic, as the slow disease progression promotes collateral vessel development [16]. The LSA is not usually transposed, because LSA overstenting without revascularization is a well-tolerated procedure in patients with normal supra-aortic branches [17,18]. In contrast, acute LSA occlusion by overstenting of the LSA in the absence of collateral vessels might lead to problems induced by ischemia.

In the study of Görich et al. [17] of incomplete LSA overstenting in 4 and complete occlusion of the LSA in 19 patients, three patients (13.6%) reported ischemic arm symptoms but none of them showed persistent signs of vertebrobasilary insufficiency. In the series of Tiesenhausen et al. [9], three of eight patients (37.5%) with partial or complete occlusion of LSA had vertebrobasilar symptoms. In the study of Schoder et al. [2], six of eight patients (75%) with complete occlusion of the LSA presented symptoms. Secondary transposition of LSA was necessary in two of those patients, in one patient to treat critical arm ischemia and in the other to treat an endoleak. Paraparesis and paraplegia occurred in 5.1% of their patients. One of them underwent overstenting of the LSA.

Surgical revascularization of the supra-aortic vessels may present a potential strategy for expanding the applicability of thoracic aortic ESI. Some patients require revascularization of the LSA, such as CABG patients with patent left internal mammary arteries, because LSA occlusion in such cases may cause myocardial ischemia [19]. Anatomic variants, such as origin of the left VA at the arch, or the absence of fusion of the VAs to the basilary artery, or an otherwise functionally-compromised circle of Willis, do not permit LSA occlusion without previous revascularization [2]. As reported in the literature, occlusion of one VA caused vertebrobasilary ischemia resulting in cerebellar infarction in 2.7% [20]. Bilateral VA occlusion (by overstenting of the LSA and an additional pathological right VA) caused persistent neurological deficits in 23% of the patients [2]. Carotid or vertebral artery stenosis as well as aberrant subclavian arteries (lusoria) require revascularization of the LSA, as overstenting of the lusorian artery carries the increased risk of consecutive cerebellar infarction [15,19].

Another indication for transposing the LSA, or for LCCA-to-LSA bypass surgery with proximal ligation, is to avoid retrograde perfusion of the aneurysm sac or the false lumen in dissections [9]. With coverage of the LSA, retrograde perfusion from the LSA may prevent thrombosis in the aneurysmal sac and can cause type-II endoleaks. Interestingly, we observed no type-II endoleaks after complete overstenting of the LSA in our series. If type-II endoleaks occur, coil embolization or surgical ligation of the LSA may become necessary [14]. The rate of primary endoleaks after thoracic aortic ESI was reported to be 11–25% [2,7,10].

In case of aortic arch involvement, other surgical revascularization techniques to maintain cerebral perfusion have been developed to make ESI in the aortic arch possible [21–23]. Czerny et al. [24] carried out reconstructions of the supra-aortic branches in patients with aortic arch aneurysms or type-B aortic dissections. Treatment was by sequential transposition of the LCCA into the brachiocephalic trunk and of the LSA into the already-transposed LCCA.

However, surgical revascularization of the LSA has a 1—5% mortality rate [15]. Surgical complications after LSA transposition in Schoder et al.'s [2] series were Horner syndrome and hoarseness in 7.1% of the patients. An 11% rate of recurrent nerve paralysis was described in another series [6]. Therefore, we question the need for prophylactic LSA transposition or LCCA-to-LSA bypass due to the fact that most patients with subclavian steal syndrome are asymptomatic. Flow inversion from a normal right VA to the left VA seems adequate to compensate after LSA occlusion in patients with normal supra-aortic vessels. These revascularization techniques should thus be reserved only for those patients developing ischemic symptoms or presenting a potentionally compromised collateral blood supply.

To summarize, our results clearly demonstrate the difficulty and complexity of endovascular stent-graft repair of the aortic arch and descending aortic pathologies with overstenting of the supra-aortic branches. In the absence of supra-aortic vascular pathologies, intentional LSA occlusion may be justified when a proximal 'landing zone' for ESI is required without subclavian revascularization. Hemodynamically relevant stenoses, occlusions, or anatomic variants of the supra-aortic branches are preoperative risk factors that can lead to a higher rate of neurological complications after LSA overstenting. Preoperative exploration of the supra-aortic branches by Doppler ultrasound, CT- or MRI scan is therefore mandatory. Surgical supra-aortic revascularization techniques managing aortic arch vessels can expand the applicability of ESI even in patients presenting with stenoses, occlusions, or anatomical variants of the supra-aortic branches. Should overstenting of the LSA become necessary in patients with insufficient collateral pathways and a thus significantly increased risk of brain ischemia or peripheral ischemic events, we recommend revascularization of the supra-aortic branches in advance rather than as a secondary procedure. In the absence of supra-aortic vessel pathologies, prophylactic transposition of the LSA or LCCA-to-LSA bypass is not required prior to intentional stent-graft occlusion of the LSA, but surgical revascularizations may be designated as an elective measure after ESI when ischemic symptoms do occur.

In conclusion, overstenting of the LSA resulted in ischemic disorders and neurological events in a number of our patients. However, coverage of the LSA and other supra-aortic vessels — to make ESI possible in the aortic arch and in the presence of descending aortic pathologies with additional supra-aortic revascularization — is an effective treatment for high-risk patients with an overall lower rate of morbidity and mortality compared to open surgery.

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Appendix A. Conference discussion

Dr M. Turina (*Zurich, Switzerland*): Thank you very much for this report, which raises many questions really. Would you consider monitoring the blood pressure in the left radial artery as sufficient during overstenting or do you rely simultaneously on the ultrasound measurements in the operating room?

Dr Weigang: We monitored the blood pressure on both arms pre-, intra- and postoperatively. Surprisingly, we found a blood pressure signal on the left arm as well in some of our patients undergoing overstenting of the left subclavian artery. We do not take ultrasound measurements during these procedures.

Dr G. Ziemer (*Tuebingen, Germany*): When you checked your supra-aortic flow after implantation of the graft you said you had two subclavian steal syndromes but you didn't treat them. So I think you did not mean subclavian steal syndromes as this would imply neurologic symptoms. You meant just flow reversal in the vertebral artery without symptoms, which is not subclavian steal syndrome. So was there reverse of the flow in the left vertebral artery without symptoms?

Dr Weigang: Yes, that's right. Most of these patients had no severe neurological symptoms.

An independent neurologist performed the follow-up examinations of our patients after the overstenting of the left subclavian artery. He observed two subclavian steal syndromes and other collateral pathways such as vertebro-vertebral, vertebro-basilar, combined vertebro-vertebral, and carotid-vertebral steal effects as well as crossflow in the deep neck arteries.

Dr Turina: The comment is totally right, because speaking of a syndrome denotes symptomatic or subclavian reduction or reversal of the flow. The title of your slide is correct but the terminology is not.

Dr Weigang: Some of the patients had subclavian steal syndrome.

Dr Ziemer: Flow reversal in the left vertebral artery, which does not lead to symptoms and therefore it is not a syndrome. This should be easily distinguished.

Dr Weigang: But they had symptoms, as I showed here.

In the group with complete overstenting of the left subclavian artery we observed two central neurological complications. One patient had brainstem infarction with hemiparesis and the other patient suffered from impaired vision and dizziness due to transient ischemic attack.

Additionally we observed peripheral symptoms in five patients in the same group, including numbness of the left arm or hand, disturbed fine motor skills of the left hand, weakness of the left arm due to arm claudication.

Dr Ziemer: Then the syndromes, namely symptomatic patients have to be in the clinical findings list or slide.

Dr Weigang: They had symptoms.

Five of our patients had peripheral and two had central neurological symptoms. Another three patients presented with neurological symptoms which were not related to overstenting of the left subclavian artery.

Dr Ziemer: Semantics possibly. Vertebral artery flow reversal without symptoms is no syndrome.

Dr Weigang: That is a question of definition.

Dr Turina: So you mean eight of the 14 had symptoms and that had a subclavian steal syndrome?

Dr Weigang: Yes.

Dr Turina: Six did not.

Dr P. Ghosn (*Montreal, Canada*): I have two questions. The first one is how do you explain the right-sided infarction in your series? And the second one, in view of the high percentage of symptoms after the subclavian exclusion, did you consider doing a bypass to the subclavian artery prior to putting your stent graft into the aorta?

Dr Weigang: To answer your first question, this was a patient who suffered from a right-sided brainstem infarction two months after the initial operation. At that time that patient had developed a new occlusion of the right vertebral artery. To prevent another brainstem infarction we performed a left subclavian transposition in him.

Can you repeat your second comment, please?

Dr Ghosn: About bypassing the left subclavian artery before inserting your stent graft, like a carotid subclavian bypass or carotid subclavian transposition to keep the flow going into the subclavian artery before inserting your stent graft in the aorta.

Dr Turina: The question is why don't you consider putting the graft first and then overstenting.

Dr Weigang: The literature describes many complications with such revascularization techniques. The mortality rate is 1–5% for subclavian transposition and bypass grafting of the supra-aortic branches. Therefore, we carry out those examinations in advance of the stent-graft implantation. If a proximal landing zone with overstenting of the left subclavian artery is necessary, we perform subclavian transposition or carotid-to-subclavian bypass only when anatomic variants, stenoses or occlusion of the supra-aortic branches have been detected in the preoperative examinations.

Dr Turina: And blood pressure reduction in the radial artery would not be considered an indication?

Dr Weigang: No. We had patients with no blood pressure signal in the left arm without symptoms. On the other hand, we had patients with complete overstenting of the left subclavian artery with neurological symptoms and a blood pressure signal around 70 mmHg in the left arm.

Dr M. Krasoń (*Zabrze, Poland*): I would like to ask you one question regarding your antihypertensive regimen postoperatively, because if you have to rely on collateral flow that is reversible in vertebral artery flow, you would expect to have some higher pressure, because it is not regular flow, and having that, probably some deficits could not happen. This is one remark.

And second, we have had several patients with complete overstenting of the left subclavian artery, and in these patients there was no pulsatile flow at the left radial artery. And probably, in my opinion, if you have pulsatile flow and pressure as high as 70 mmHg, it is not complete covering.

Dr Weigang: To address your second question first: after the procedure, we routinely perform CT scans in all of our patients. Fourteen of our patients underwent complete covering of the left subclavian artery without type-II endoleaks.

And regarding your first remark: if you have good intracranial cross flow and collateral flow, the patients don't have such symptoms. However, neurological complications after endovascular stent-graft repair in the aortic arch and the descending aortic position are underreported in the literature, because most of these problems do not occur until after a couple of months. And I am quite sure that if you are sending your own patients to an independent neurologist, they will find also some of the problems you never expected.

Dr Krason: What was the mean age of the group with left subclavian artery overstented, because it is also an issue? If you have pretty young patients you have a safer approach, if you have older patients, the risk is much higher. The mean age in the group?

Dr Weigang: The mean age of our patients with overstenting of the left subclavian artery was 64 years.

6.5 Outcomes after thoracic endovascular aortic repair with overstenting of the left subclavian artery

Outcomes After Thoracic Endovascular Aortic Repair With Overstenting of the Left Subclavian Artery

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Background. **Our study aim was to evaluate the impact of left subclavian artery (LSA) flow preservation during thoracic endovascular aortic repair (TEVAR) on outcome.**

Methods. **Between August 2001 and October 2016, 176 patients (mean age, 61.3 ± 15.8 years) underwent TEVAR with complete LSA coverage. Fifty-five of those patients (31.3%) also underwent LSA revascularization, whereas 121 patients (68.7%) did not. Perioperative data were acquired retrospectively for statistical analysis at the three study institutions.**

Results. **Overall in-hospital and follow-up mortality was 8.5% (n = 15) and 9.1% (n = 16), respectively, including 88 urgent and emergent cases (50%). Stroke (independent of location) and permanent paraplegia rates were 6.8% and 6.3%, respectively, for the entire cohort. Isolated upper-left extremity malperfusion exclusively occurred in 12 (9.9%) of the 121 patients without LSA revascularization. Left-hemispheric stroke was observed four times more often in patients without LSA revascularization and left arm malperfusion (16.7% versus 3.7%, $p = 0.095$). Multivariate analysis identified no LSA revascularization (odds ratio [OR] 3.779, 95% confidence interval [CI]: 1.096 to 13.029, $p = 0.035$), two or more endografts (OR 3.814, 95% CI: 1.557 to 9.343, $p = 0.003$), and coronary artery disease (OR 3.276, 95% CI: 1.262 to 8.507, $p = 0.015$) as independent risk factors for procedure-related adverse events (left-hemispheric stroke, left arm malperfusion, and permanent paraplegia) after TEVAR with complete LSA overstenting.**

Conclusions. **Every 10th patient with LSA overstenting and no revascularization experienced left arm malperfusion. No LSA revascularization, extensive aortic coverage with two or more endografts, and coronary artery disease increased the risk of permanent paraplegia, left-hemispheric stroke, and left arm malperfusion. Patients should undergo LSA revascularization to prevent left vertebral artery-associated central neurologic complications and to maintain upper-left extremity perfusion.**

(Ann Thorac Surg 2019;■:■–■)

Extending thoracic endovascular aortic repair (TEVAR) to the level of the aortic arch requires strategies to preserve supraaortic perfusion by rerouting procedures in cases of overstenting of supraaortic vessels to prevent posterior cerebellar malperfusion, symptomatic spinal cord injury (SCI), and, finally, the blood supply to the upper-left extremity [1–4]. In emergency situations when the acute thoracic aortic pathologic process determines the pace and the time for primary revascularization strategies, sophisticated imaging to reconfirm sufficient collateralization is a viable alternative. The only data currently available addressing this issue have mainly been from single centers [5].

Aim of this multicenter study was to compare the outcome of patients undergoing TEVAR and overstenting of the left subclavian artery (LSA) with and without a primary revascularization strategy.

Patients and Methods

Perioperative data on 176 consecutive patients (128 men, 72.7%) undergoing TEVAR with complete overstenting of the LSA for acute and chronic thoracic aortic disease at the Leipzig Heart Center, the Heart Center Freiburg

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University, and the Ludwig Maximilian University Munich were retrospectively analyzed between August 2001 and October 2016. Two study groups were defined for statistical analysis with regard to LSA revascularization before TEVAR: LSA revascularization versus no LSA revascularization.

Table 1 illustrates our preoperative patient data and details on previous surgical procedures.

TEVAR

The TEVAR technique was performed at the three participating centers as previously reported [6–8]. In general, TEVAR procedures were performed in a (hybrid) operating room equipped with a C-arm and carbon fiber operating table. All procedures were performed in patients under general anesthesia. Rapid pacing took place to support exact endograft positioning. Vascular access was obtained by an inguinal incision downward or by percutaneous preclosure technique—according to the individual clinical scenario—of the common femoral artery for retrograde delivery of the stent graft. The following commercially available devices were implanted: Talent/Valiant or Valiant Captivia (Medtronic Vascular, Santa Rosa, CA), TAG/C—TAG (W. L. Gore and Associates, Flagstaff, AZ), Endofit (Endomed Inc, Phoenix, AZ), and Relay NBS plus (Bolton Medical, Inc, Sunrise, FL). Endograft sizing was routinely based on preoperative computed tomography (CT) angiography.

Table 1. Preoperative Patient Data

Variable	All Patients (N = 176)	LSA Revascularization (n = 55)	No LSA Revascularization (n = 121)	*p* Value
Age at TEVAR, years	61.3 ± 15.8	63.4 ± 11.5	60.4 ± 17.8	0.170
Male sex	128 (72.7)	39 (70.9)	89 (73.6)	0.718
Connective tissue disease	3 (1.7)	…	3 (2.5)	0.553
COPD	30 (17.0)	7 (12.7)	23 (19.0)	0.389
History of smoking	50 (28.4)	21 (38.2)	29 (24.0)	0.071
Coronary artery disease	41 (23.3)	16 (29.1)	25 (20.7)	0.250
Hypertension	137 (77.8)	47 (45.5)	90 (74.4)	0.119
Diabetes	24 (13.6)	8 (14.5)	19 (15.7)	0.816
Obesity	55 (31.3)	15 (27.3)	40 (33.1)	0.487
Renal insufficiency	47 (26.7)	6 (10.9)	41 (33.9)	0.002[a]
Preop ventilation	22 (12.5)	1 (1.8)	21 (17.4)	0.003[a]
Preop neurologic deficit				
Temporary	5 (2.8)	…	5 (4.1)	0.327
Permanent	2 (1.1)	…	2 (1.7)	1.000
Aortic pathologic process				
Aneurysm	60 (34.1)	26 (47.3)	34 (28.1)	0.016[a]
Acute TBAD	58 (33.0)	15 (27.3)	43 (35.5)	0.304
Chronic TBAD	31 (17.6)	8 (14.5)	23 (19.0)	0.529
Traumatic injury	5 (8.5)	3 (5.5)	12 (9.9)	0.397
Other	12 (6.8)	3 (5.5)	9 (7.4)	0.756
Aortic diameter, mm	47.9 ± 16.3	53.6 ± 14.2	45.3 ± 16.5	0.001[a]
Aneurysm	61.0 ± 13.8	61.0 ± 13.1	61.0 ± 14.6	1.000
Other pathologic process	41.0 ± 13.0	47.0 ± 11.4	39.0 ± 13.1	0.001[a]
Previous surgery				
Open cardiac	12 (6.8)	5 (9.1)	7 (5.8)	0.520
Open aortic	24 (13.6)	11 (20.0)	13 (10.7)	0.104
Ascending	14 (8.0)	6 (10.9)	8 (6.6)	0.372
Proximal arch	7 (4.0)	3 (5.5)	4 (3.3)	0.679
Descending	9 (5.1)	4 (7.3)	5 (4.1)	0.463
Abdominal	1 (0.6)	…	1 (0.8)	1.000
TEVAR/EVAR	10 (5.7)	5 (9.1)	5 (4.1)	0.463
Descending	4 (2.3)	1 (1.8)	3 (2.5)	1.000
Abdominal	4 (2.3)	2 (3.6)	2 (1.7)	0.590
Iliac axis	2 (1.1)	2 (3.6)	…	0.096

[a] Statistically significant.

Values are expressed as mean ± SD or n (%).

COPD = chronic obstructive pulmonary disease; EVAR = endovascular aortic repair; LSA = left subclavian artery; Preop = preoperative; TBAD = type B aortic dissection; TEVAR = thoracic endovascular aortic repair.

Details on the TEVAR procedures are given in Table 2.

LSA Revascularization

Of 176 TEVAR patients with LSA overstenting, LSA revascularization was performed in 55 patients (31.3%)—to create an adequate landing zone (LZ) or to minimize the risk of stroke, SCI, and left arm malperfusion—whereas the LSA was not revascularized in the remaining 121 patients (68.7%). In 41 patients (74.5%), the LSA was revascularized concurrently with TEVAR (before endograft deployment), whereas 14 patients (25.5%) underwent LSA revascularization in another operation before TEVAR. These revascularization procedures comprised left common carotid-to-LSA bypass grafting (n = 47, 85.5%) or transposition (n = 8, 14.5%). Just 1 patient underwent an additional right-to-left common carotid bypass (1.8%) (Table 2).

The decision—whether to prophylactically revascularize the LSA—was made by an interdisciplinary team at each respective study center (including cardiac and vascular surgeons, endovascular specialists, radiologists, and anesthesiologists).

Neuroprotection of the Spinal Cord

Neuroprotective strategies during TEVAR to avoid SCI varied among study centers. In general, cerebrospinal fluid drainage was applied as recommended in all centers—routinely for all patients in only one center—if an increased risk of SCI was expected preoperatively (eg, extensive aortic coverage) or if clinical symptoms occurred perioperatively [9]. In addition, the mean arterial pressure (MAP) was maintained supranormal (>80 mm Hg) intraoperatively and postoperatively on the intensive care unit for at least 48 hours at all participating centers. Furthermore, two centers routinely applied somatosensory/motor evoked potentials [10] or near infrared spectroscopy (NIRS) of the lumbar paraspinal musculature [11] to detect potential SCI perioperatively. However, lumbar NIRS as a neuromonitoring strategy was not routinely used until 2012 [12].

Definitions and Statistical Analysis

The ethics committees at the participating centers granted approval for this study. The principal investigators at each clinic confirmed the validation of their data sets according to the study definition.

Data were acquired retrospectively at the three study institutions. Only patients with endograft deployment in LZ 2 with complete LSA overstenting were included. Exclusion criteria were LZ 0, 1, and 3, as well as partial coverage of the LSA orifice in LZ 2. Follow-up of patients not included in a routine institutional surveillance program was conducted by a telephone interview with patients or their respective physicians. Follow-up time comprised the time interval between TEVAR and last patient contact or death of all patients. No expired patient was excluded.

In-hospital mortality was defined as death before hospital discharge after TEVAR. Reoperations were defined as any open or endovascular operation related to TEVAR or post-TEVAR complications. Pulmonary insufficiency was defined as single or combined need for reintubation,

Table 2. TEVAR Procedural Details

Variable	All Patients (N = 176)	LSA Revascularization (n = 55)	No LSA Revascularization (n = 121)	*p* Value
TEVAR duration, minutes	128.7 ± 84.6	201.2 ± 106.9	95.5 ± 41.1	<0.001[a]
Priority				
Elective	88 (50.0)	32 (58.2)	56 (46.3)	0.193
Urgent	59 (33.5)	13 (22.0)	46 (38.0)	0.084
Emergent	29 (16.5)	10 (18.2)	19 (15.7)	0.667
Urgent/emergent	88 (50)	23 (41.8)	65 (53.7)	0.193
Endografts (total)	248	78	170	…
Endografts per patient	1.4 ± 0.6	1.4 ± 0.7	1.4 ± 0.6	0.900
1	115 (65.3)	36 (65.5)	79 (65.3)	1.000
2	53 (30.1)	16 (29.1)	37 (30.6)	1.000
3 or more	11 (6.3)	4 (7.3)	7 (5.8)	0.706
Endograft length,[b] mm	224.9 ± 126.5	224.9 ± 117.0	224.9 ± 130.7	0.999
LSA revascularization				
Before TEVAR	14 (8.0)	14 (25.5)	…	…
In conjunction with TEVAR	41 (23.3)	41 (74.5)	…	…
LSA revascularization procedures				
Bypass	47 (26.7)	47 (85.5)	…	…
Transposition	8 (4.5)	8 (14.5)	…	…

[a] Statistically significant. [b] Cumulative length of endograft devices.

Values are expressed as mean ± SD or n (%).

LSA = left subclavian artery; TEVAR = thoracic endovascular aortic repair.

prolonged ventilation (>5 days), or tracheostomy. Paraplegia was defined either as temporary or permanent with regard to complete recovery during that individual's hospital stay. Postoperative stroke was defined as any new cerebral infarction after the TEVAR procedure diagnosed and verified by a clinical neurologist or computed brain tomography. Only symptomatic patients with clinically relevant subclavian steal syndrome (vertebrobasilar territory neurologic symptoms) or left arm claudication with a difference in blood pressure between both arms of greater than 15% mm Hg were defined as left arm malperfusion. A specific procedure-related adverse event after LSA overstenting, as the study's primary end point, was defined as single or combined occurrence of left-hemispheric stroke, permanent paraplegia, left arm malperfusion, or a combination.

Categorical variables were reported by using the number and percentage of occurrences. Continuous variables were expressed as mean ± SD or (if the SD exceeded the mean value) as median with interquartile range (IQR; 25th to 75th percentile). The impact of patient baseline characteristics, comorbidities, previous treatments (open/endovascular surgery), prophylactic LSA revascularization, and intraoperative data of the TEVAR procedure (Tables 1 and 2) on the incidence of procedure-related adverse events was investigated by univariate and multivariate regression analysis. A binary logistic regression model was built by using the variables with p value less than 0.1 from univariate analysis: no LSA revascularization ($p = 0.069$), aortic coverage with two or more endografts ($p = 0.011$), coronary artery disease ($p = 0.011$), and preoperative renal insufficiency ($p = 0.095$). For the univariate and multivariate regression analyses a p value of less than 0.05 was considered statistically significant. Actuarial survival was estimated by the Kaplan-Meier method with the log-rank (Mantle-Cox) test for group comparison. Statistics were analyzed with SPSS statistical software package (version 25.0; IBM, Ehningen, Germany).

Results

TEVAR indications in our study cohort were aortic aneurysm (n = 60, 34.1%), acute (n = 58, 33.0%) and chronic (n = 31, 17.6%) type B aortic dissection, traumatic aortic injury (n = 15, 8.5%), and other aortic pathologic processes (n = 12, 6.8%). The maximum mean aortic diameter at the time of TEVAR was 61.0 ± 13.8 mm for aneurysms and 41.0 ± 13.0 mm for other aortic pathologic processes. Previous cardiac, open or endovascular aortic surgery had been performed in 12 patients (6.8%), 24 patients (13.6%), and 10 patients (5.7%), respectively (Table 1). In total, 248 aortic endografts (mean: 1.4 ± 0.6 aortic endografts per patient) were administered in the 176 consecutive patients in an elective (n = 88, 50.0%), urgent (n = 58, 33.0%), or emergent (n = 30, 17.0%) setting (Table 2).

The entire study cohort's median follow-up time was 16.8 months (interquartile range [IQR]: 1.3 to 48.7 months). Median intensive care unit and hospital stay were 2 days (IQR: 1.0 to 5.0 days) and 12 days (IQR: 7.0 to 19.5 days), respectively. Overall in-hospital and follow-up mortality rates did not differ significantly between patients with or without LSA revascularization and amounted to 8.5% (n = 15) and 9.1% (n = 16) ($p = 0.291$) (Table 3). Of note, 11 of the 15 patients who died in hospital were treated on an urgent or emergent basis, resulting in an in-hospital mortality for elective versus urgent/emergent cases of 4.5% versus 12.5% ($p = 0.102$). Actuarial survival estimation of patients with or without LSA revascularization revealed no significant differences (log rank $p = 0.570$); the respective 1-, 3-, and 5-year survival rates for both groups (LSA revascularization versus no LSA revascularization) were 91.8% ± 5.0% versus 84.7% ± 5.7%, 88.0% ± 7.1% versus 81.7% ± 6.4%, and 80.0% ± 12.1% versus 76.0% ± 8.1% (Fig 1).

Reoperations

The overall endovascular reintervention rate for TEVAR-related complications was 10.8%, whereas open LSA revascularization was required in 5.8%. Open surgery for secondary LSA revascularization was performed in 10 of the 121 patients (8.3%) without prior LSA revascularization—compared with 0% of LSA revascularization patients ($p = 0.032$). The indication for secondary LSA revascularization was clinically relevant left arm malperfusion in all 10 patients after a median time interval of 4.5 days (IQR: 2.0 to 18.0 days). Furthermore, open surgery during follow-up because of aortic dissection and aortoesophageal fistula was required in 6 patients (5.0%) without LSA revascularization after a median of 54.5 ± 44.8 days, whereas open reoperations by sternotomy were not required in the 55 patients with previous LSA revascularization ($p = 0.100$). Endovascular reoperations were substantially more often required in patients with LSA revascularization than without (21.8% versus 5.8%). TEVAR extension (re-TEVAR) was the most frequent procedure in the study group (n = 12, 6.8%), whereas other required endovascular procedures comprised reballooning (n = 2, 1.1%) and LSA coil embolization (n = 5, 2.1%) (Table 3). Freedom from aortic reintervention for LSA revascularization versus no LSA revascularization is shown in Figure 2 (log rank $p = 0.072$).

Postoperative Complications

Postoperative complications are listed in Table 3. Left arm malperfusion occurred in 12 patients (9.9%) after TEVAR without LSA revascularization versus 0% in the previously revascularized group ($p = 0.018$). New postoperative neurologic complications were stroke (6.8%, n = 12) and spinal cord ischemia (7.4%; n = 13). The stroke occurrence did not significantly differ between groups (5.5% versus 7.4%, $p = 0.756$). Similarly, we observed no difference in the incidence of left-hemispheric stroke between patients with and without LSA revascularization (3.6% versus 5.0%, $p = 1$). However, left-hemispheric stroke was observed four times more frequently in patients without LSA revascularization and resulting left arm malperfusion compared with patients without left arm malperfusion (16.7% versus 3.7%, $p = 0.095$).

Table 3. Postoperative Outcome

Outcome	All Patients (N = 176)	LSA Revascularization (n = 55)	No LSA Revascularization (n = 121)	*p* Value
ICU stay, days	5.8 ± 9.5	3.7 ± 5.2	6.8 ± 10.7	0.011[a]
Hospital stay, days	14.9 ± 12.0	15.1 ± 10.4	14.7 ± 12.7	0.400
Open LSA revascularization	10 (5.7)	…	10 (8.3)	0.032[a]
Bypass	6 (3.4)	…	6 (5.0)	0.179
Transposition	4 (2.3)	…	4 (3.3)	0.311
Endovascular reinterventions	19 (10.8)	12 (21.8)	7 (5.8)	0.003[a]
Re-TEVAR	12 (6.8)	6 (11.0)	6 (5.0)	0.196
Re-ballooning	2 (1.1)	1 (1.8)	1 (0.8)	0.529
LSA coil embolization	5 (2.8)	5 (9.1)	…	0.003[a]
Open surgery (during follow-up)	6 (3.4)	…	6 (5.0)	0.100
Postoperative complications				
Hemorrhage	1 (0.6)	…	1 (0.8)	1.000
Endoleak	32 (18.2)	10 (18.2)	22 (18.2)	1.000
Ia	14 (8.0)	4 (7.3)	10 (8.3)	1.000
Ib	10 (5.7)	3 (5.5)	7 (5.8)	1.000
II	6 (3.4)	2 (3.6)	4 (3.3)	1.000
III	2 (1.1)	1 (1.8)	1 (0.8)	0.529
Pulmonary insufficiency	35 (19.9)	5 (9.1)	30 (24.8)	0.015[a]
Re-intubation	6 (3.4)	3 (5.5)	3 (2.8)	0.378
Prolonged ventilation	13 (7.4)	…	13 (10.7)	0.010[a]
Tracheostomy	16 (9.1)	2 (3.6)	14 (11.6)	0.154
Renal insufficiency (dialysis)	9 (5.1)	2 (3.6)	7 (5.8)	0.722
Left arm malperfusion	12 (6.8)	…	12 (9.9)	0.018[a]
Aortic dissection type A	4 (2.3)	1 (1.8)	3 (2.8)	1.000
Classic	3 (1.7)	…	3 (2.8)	0.553
Retrograde	1 (0.6)	1 (1.8)	-	0.314
Aorto-esophageal fistula	2 (1.1)	…	2 (1.7)	1.000
Paraplegia				
Temporary	2 (1.1)	1 (1.8)	1 (0.8)	0.529
Permanent	11 (6.3)	3 (5.5)	8 (6.6)	1.000
Stroke	12 (6.8)	3 (5.5)	9 (7.4)	0.756
Left hemisphere	8 (4.5)	2 (3.6)	6 (5.0)	1.000
Right hemisphere	9 (5.1)	2 (3.6)	7 (5.8)	0.722
Sepsis	2 (1.1)	…	2 (1.7)	1.000
Multi-organ failure	7 (4.0)	2 (3.6)	5 (4.1)	1.000
Mortality	31 (17.6)	7 (12.7)	24 (19.8)	0.291
In-hospital	15 (8.5)	4 (7.3)	11 (9.1)	0.779
During follow-up	16 (9.1)	3 (5.5)	13 (10.7)	0.396

[a] Statistically significant.

Values are expressed as mean ± SD or n (%).

ICU = intensive care unit; LSA = left subclavian artery; TEVAR = thoracic endovascular aortic repair.

As a result of spinal cord ischemia, temporary and permanent paraplegia occurred in 2 patients (1.1%) and 11 patients (6.3%); however, their incidence did not differ significantly between study groups (LSA revascularization versus no LSA revascularization): 1.8% versus 0.8% ($p = 0.529$) and 5.5% versus 6.6% ($p = 1$), respectively (Table 3). The incidence of permanent paraplegia after elective or urgent/emergent TEVAR was 6.8% (n = 6) and 5.6% (n = 5), respectively ($p = 1$).

Risk Factor Analysis for LSA Overstenting-Related Adverse Events

A single or combined occurrence of left-hemispheric stroke, permanent paraplegia, or left arm malperfusion after complete LSA overstenting was noted in 14.8% (n = 26) of the 176 patients. Univariate analysis of our entire study cohort (n = 176) revealed that no LSA revascularization ($p = 0.069$), two or more endografts ($p = 0.011$), and coronary artery disease ($p = 0.011$) were

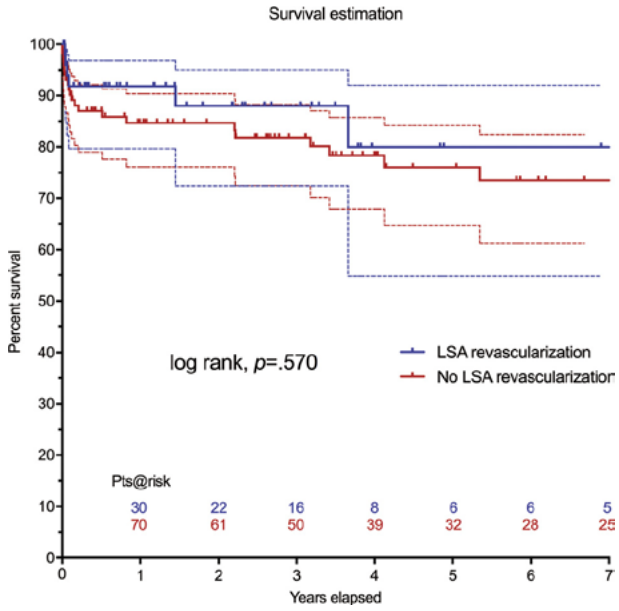

Fig 1. Actuarial survival estimation (Kaplan-Meier) after thoracic endovascular aortic repair (TEVAR) with complete Left Subclavian Artery (LSA) overstenting (LSA revascularization versus no LSA revascularization). (Pts = patients.)

associated with a higher risk of procedure-related adverse events. Multivariate analysis showed that no LSA revascularization (odds ratio [OR] 3.779, $p = 0.035$), two or more endografts (OR 3.814, $p = 0.003$), and coronary artery disease (OR 3.276, $p = 0.015$) were independent risk factors for procedure-related adverse events after TEVAR with complete LSA overstenting (Table 4).

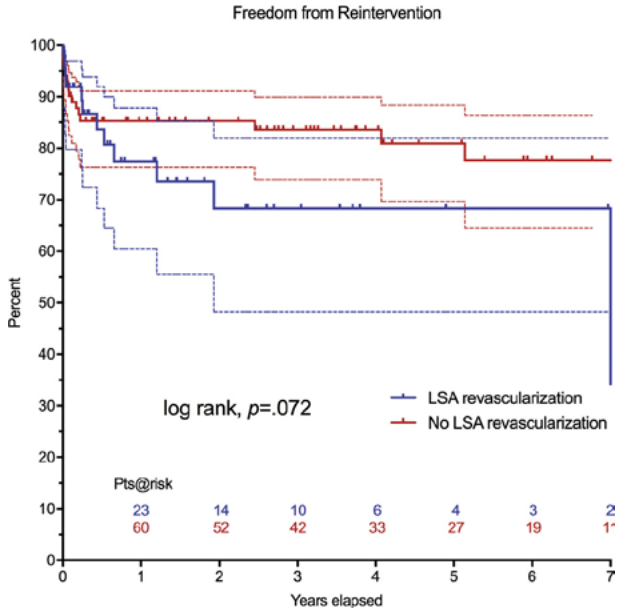

Fig 2. Freedom from aortic reintervention (Kaplan-Meier estimation) after thoracic endovascular aortic repair (TEVAR) with complete left subclavian artery (LSA) overstenting (LSA revascularization versus no LSA revascularization). (Pts = patients.)

Comment

The treatment of aortic pathologic processes that involve the descending aorta has changed in recent years thanks to TEVAR's clinical implementation and technical improvements [2, 13]. TEVAR has now become the treatment of choice for patients with a traumatic aortic injury or complicated acute type B aortic dissection [2, 14]. Acute and chronic pathologic processes of the proximal descending aorta often involve the aortic arch or at least require a suitable proximal LZ of at least 2 cm in the distal arch to enable successful endovascular repair with positive aortic remodeling, but the LSA's intentional coverage by TEVAR is not without risk and may raise the risk of perioperative cerebrovascular accidents and SCI [3, 9, 15, 16]. However, prophylactic open LSA revascularization may exacerbate the risk of minor (eg, seroma, nerve damage, lymph leak) and major (neurologic) perioperative complications, and it is known to be associated with operative mortality, ranging from 1.2% to 5% [17–19]. Some investigators, therefore, suggest performing prophylactic revascularization of the LSA only when an increased risk of neurologic complications, especially stroke or SCI, is likely [20, 21].

The present results are in line with other reports on endovascular aortic treatment [3, 22], thereby confirming TEVAR as a valuable treatment strategy in our armamentarium for descending aortic disease that extends into the aortic arch. Because 50% of our study patients underwent operation on an urgent or emergent basis, their overall in-hospital mortality was only 8.5%—with a low in-hospital mortality rate of 4.5% for the elective cases. Note that postoperative pulmonary complications occurred in almost 20% of patients, potentially coinciding with their high incidence of chronic obstructive pulmonary disease and need for preoperative ventilation, which were both higher in the previously non-revascularized patient group. Open reoperations by sternotomy for rare TEVAR complications, namely (retrograde) aortic dissection (2.3%) and aortoesophageal fistula (1.1%), were limited to patients without previous LSA revascularization and occurred with a similar incidence as that reported in the literature [23, 24].

Table 4. Independent Risk Factors for Procedure-Related Adverse Events After Complete LSA Overstenting

		95% Confidence Interval		
Risk Factors	Odds Ratio	Low	High	*p* Value
No LSA revascularization	3.779	1.096	13.029	0.035
Two or more endografts	3.814	1.557	9.343	0.003
Coronary artery disease	3.276	1.262	8.507	0.015

LSA = left subclavian artery.

Endovascular procedures within the aortic arch carry the risk of devastating neurologic complications such as perioperative cerebrovascular accidents and SCI, especially when complete LSA occlusion becomes necessary to achieve an adequate LZ for TEVAR [3]. These complications may be caused or aggravated by the occurrence of left subclavian steal syndrome, especially in the presence of anatomic variations such as an incomplete circle of Willis or a hypoplastic right vertebral artery [3, 25, 26]. Therefore, the primary end point of our underlying study—to evaluate the impact of LSA flow preservation during TEVAR—was defined as the occurrence of a single or combined procedure-related adverse event, namely left arm malperfusion, left-hemispheric stroke, or permanent paraplegia.

In general, minor, otherwise nonsymptomatic upper-left extremity symptoms because of arm malperfusion, such as blood pressure differences or activity-dependent subclavian steal syndrome, may be easily overlooked clinically but have been reported to occur in up to 21% of patients after complete LSA overstenting [3]. In our study cohort, symptomatic left arm malperfusion (eg, because of left arm claudication or subclavian steal with resulting vertebrobasilar territory neurologic symptoms) occurred exclusively in 12 previously non-revascularized patients (9.9%), ultimately requiring early secondary open LSA revascularization in 10 patients after a median of 4.5 days. Patients with left arm malperfusion experienced a left-hemispheric stroke four times more often.

Neurologic complications after TEVAR with LSA overstenting are known to vary between 2% and 14.3% for stroke [2, 14, 19, 21] and 0% and 5% for SCI [19, 27–29], but there is little data on the latter. The overall incidence of postoperative stroke (independent of location) in the present study was 6.8% (n = 12), including 8 patients (4.5%) with left-hemispheric stroke. Despite a substantially higher incidence of atherosclerotic aneurysms in the LSA revascularization group (47.3% versus 28.1%, $p = 0.016$), no statistically significant differences were found. Temporary and permanent paraplegia rates in the study cohort were 1.1% and 6.3%, respectively (Table 2).

Patients with coronary artery disease as an independent risk factor (23.3% of the study cohort) were found to be at a 3.3-fold increased risk to develop adverse events related to complete LSA overstenting. It may well be that patients with coronary artery disease also had cerebrovascular disease and aortic calcification, especially because the incidence of (atherosclerotic) aortic aneurysms was as high as 46.3%. Unfortunately, the degree of aortic calcification—as a potential risk factor for stroke—could not be determined retrospectively for this study cohort. Cardiac catheterization before TEVAR seems to be a valuable diagnostic tool not only to assess the coronary arteries' status but also to pre-estimate the degree of aortic calcification.

The arterial spinal cord collateral network is fed by three major inflow sources comprising the subclavian (vertebral), aortic segmental (thoracic and lumbar), and internal iliac (hypogastric) arteries [30]. The risk of permanent paraplegia rises especially if two arterial inflow sources of spinal cord blood flow are compromised simultaneously [31]—without enough time to enable the collateral network to adapt [30]. The deployment of two (or more) endografts usually results in a longer aortic coverage and requires more endovascular manipulation within the aortic arch, a factor likely to increase the risk of cerebrovascular accidents and SCI in these patients. The deployment of at least two endografts was identified as an independent risk factor (with a relative risk of 3.8) for adverse events after LSA overstenting through multivariate analysis. In our series, the cumulative device length of 1 versus 2 or more endografts—as the above-mentioned independent risk factor—was 149.8 ± 34.7 mm versus 360.3 ± 118.1 mm ($p < 0.001$). This result is in line with previous clinical reports of hybrid (eg, frozen elephant trunk) and TEVAR techniques that showed an increased incidence of paraplegia in conjunction with extended descending aortic endograft coverage [9, 20, 31]. Especially in elderly patients presenting with atherosclerotic aneurysms or chronic aortic disease, the spinal cord's arterial blood supply may already be compromised because of acquired vascular stenosis or thrombosis (with subtotal or total occlusion), which in combination with extended endograft coverage will most likely affect spinal blood supply.

Because aortic segmental artery preservation—as a measure to prevent SCI in open aortic surgery—is impossible during extended TEVAR with LSA coverage, new concepts such as spinal cord collateral network preconditioning—by minimally invasive segmental artery coil embolization—may be considered before TEVAR to reduce the risk of paraplegia in certain patients [32].

Study Limitations

The preoperative CT scan protocols for TEVAR patients (with LSA overstenting) varied at the three participating centers over time or were limited to an aortic angiography with imaging of the proximal supraaortic branches (especially in urgent/emergent situations). Therefore, important anatomic variations, such as dominance of the left or right vertebral artery or completeness of the circle of Willis, could not be fully obtained for statistical analysis retrospectively. Perioperative stroke may occur silently and often remains undetected if no clinical symptoms are present and postoperative brain imaging is clinically not indicated. Postoperative neurologic evaluation and CT of the brain were not routinely performed in asymptomatic patients in this series. Paraplegia—as the most dreaded complication after TEVAR—may occur delayed and for various reasons. The respective data of applied perioperative neuroprotective strategies—such as the amounts of drained cerebrospinal fluid, drops below the lumbar NIRS baseline and relevant changes of somatosensory/motor evoked potentials—to avoid potential spinal cord ischemia could not be fully obtained retrospectively. Therefore, the interpretation of our results with regard to SCI may be limited.

Conclusion

Every 10th patient who underwent LSA overstenting but no revascularization experienced left arm malperfusion. Patients without LSA revascularization and resultant left arm malperfusion experienced left-hemispheric stroke more frequently. We found that no LSA revascularization, extensive aortic coverage with two or more endografts, and coronary heart disease increased the risk of permanent paraplegia, left-hemispheric stroke, and left arm malperfusion. LSA revascularization should be performed to prevent left vertebral artery-associated central neurologic complications and to maintain upper-left extremity perfusion.

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6.6 Outcomes of secondary procedures after primary thoracic endovascular aortic repair

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Outcomes of secondary procedures after primary thoracic endovascular aortic repair[†]

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Abstract

OBJECTIVES: The purpose of this study is to retrospectively evaluate, with an 'all-comers' approach, the survival and outcome of patients following secondary surgical or interventional procedures after thoracic endovascular aortic repair (TEVAR).

METHODS: Between October 2002 and December 2013, 371 patients with different aortic pathologies underwent primary TEVAR at our institution. Fifty-six out of the 371 patients (15.1%, 18 females, mean age 62.3 ± 13.7 years) required secondary procedures, either interventionally (*N* = 31; 55.4%) or surgically (*N* = 25; 44.6%), due to stent graft-related complications. After TEVAR complications comprised endoleaks (*N* = 28; 7.5%), organ malperfusion (*N* = 9; 2.4%), aorto-oesophageal/-bronchial fistulae (*N* = 9; 2.4%), stent graft infections (*N* = 4; 1.1%), aneurysm progression (*N* = 3; 0.8%), retrograde type A aortic dissection (*N* = 2; 0.5%) and aortic regurgitation (*N* = 1; 0.3%).

RESULTS: The overall in-hospital mortality rate was 10.7% (*N* = 5): open surgery (*N* = 1; 4%) versus reintervention (*N* = 5; 16%; *P* = 0.14). The cumulative survival rates after secondary procedures at 6 months, 1 year and 3 years were 80.4, 73.5 and 69.3%, respectively. Postoperative complications either for open surgery or reintervention comprised stroke (8 vs 9.6%; *P* = 0.82), paraplegia (4 vs 6.4%; *P* = 0.68), renal failure (16 vs 3.2%; *P* = 0.09), respiratory failure (12 vs 0%; *P* = 0.04), sepsis (16 vs 3.2%; *P* = 0.87), organ malperfusion (4 vs 3.2%; *P* = 0.87) and need for a tertiary procedure (8 vs 6.4%; *P* = 0.82).

CONCLUSIONS: Stent graft complications after primary TEVAR were not infrequent and often required secondary procedures for definite treatment. Endoleaks (type Ia), organ malperfusion, stent graft infections, fistula formation and expanding aneurysm occurred predominantly during early and mid-term follow-up. Despite the high-risk nature of the complications, secondary open surgical or interventional procedures may be successfully performed with an acceptable outcome.

Keywords: Thoracic endovascular repair • Aortic aneurysm • Chronic aortic dissection • Stent graft complications • Reoperation • Reintervention

INTRODUCTION

Thoracic endovascular aortic repair (TEVAR) has become an established alternative to open surgery for a variety of thoracic aortic diseases (i.e. aneurysm and type B dissection), particularly in patients with a high operative risk and unclear overall life expectancy, or in the acutely unstable patient to achieve rapid aortic stabilization. Growing experience with endovascular interventions and continued technological advancements have resulted in a wide spectrum of indications for TEVAR and a progressively increasing utilization of new advanced technologies for more complex aortic anatomy and pathologies, e.g. thoraco-abdominal aortic aneurysms [1, 2]. However, the more liberal use of TEVAR carries the risk of serious complications that may require secondary procedures, such as endovascular reinterventions and/or open surgical repair. Experience with secondary procedures for failed or complicated primary TEVAR is limited and the outcome after reinterventions/operations is only infrequently reported.

The purpose of the current report was to retrospectively evaluate, with an 'all-comers' approach, the survival and the outcome of patients following secondary procedures after TEVAR.

PATIENTS AND METHODS

From October 2002 to December 2013, 371 patients underwent primary TEVAR, including 126 (33.9%) patients with intentional

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Table 1: Preoperative baseline characteristics of all 371 patients treated by primary TEVAR

Baseline characteristics	All patients	No. of second procedures	Secondary procedure	*P*-value
Age, years (median; IQR)	69 (57–75)	69 (59–76)	64 (53–72)	0.10
Female sex, *n* (%)	108 (29.1)	90 (28.6)	18 (32.1)	0.58
Hypertension, *n* (%)	299 (80.6)	249 (79.0)	50 (89.3)	0.07
CHD, *n* (%)	74 (19.9)	59 (18.7)	15 (26.8)	0.16
Marfan's syndrome, *n* (%)	3 (0.8)	3 (1.0)	–	0.46
Smoking, *n* (%)	95 (25.6)	79 (25.1)	16 (28.6)	0.58
COPD, *n* (%)	61 (16.4)	49 (15.6)	12 (21.4)	0.27
IDDM, *n* (%)	58 (15.6)	48 (15.2)	10 (17.9)	0.61
Obesity (BMI ≥30), *n* (%)	99 (26.7)	81 (25.7)	18 (32.1)	0.31
Renal insufficiency, *n* (%)	103 (27.8)	89 (28.3)	14 (25.0)	0.61
Previous neurological dysfunction, *n* (%)	45 (12.1)	39 (12.4)	6 (10.7)	0.46
Preoperative paraplegia, *n* (%)	4 (1.1)	4 (1.3)	–	–
Stroke, *n* (%)	31 (8.4)	27 (8.5)	4 (7.1)	–
Other, *n* (%)	9 (2.4)	7 (2.2)	2 (3.6)	–
Previous cardiac surgery, *n* (%)	88 (23.7)	72 (22.8)	16 (28.6)	0.35
Aortic pathology				
Dissection, *n* (%)	129 (35)	106 (34)	23 (41)	0.28
Aneurysm, *n* (%)	113 (30)	96 (30)	17 (30)	0.90
Covered rupture, *n* (%)	82 (22)	70 (22)	12 (21)	0.80
Acute rupture, *n* (%)	20 (5.5)	17 (5.5)	3 (6)	0.70
Fistula, *n* (%)	4 (1)	4 (1.5)	–	0.48
Other, *n* (%)	23 (6.5)	22 (7)	1 (2)	0.10
Total, *n* (%)	371 (100)	315 (100)	56 (100)	–

IQR: interquartile range; CHD: coronary heart disease; COPD: chronic obstructive pulmonary disease; IDDM: insulin-dependent diabetes mellitus; BMI: body mass index; TEVAR: thoracic endovascular aortic repair.

overstenting of the left subclavian artery (LSA), for different thoracic aortic pathologies at our institution. The respective indications for primary TEVAR as well as detailed patient baseline characteristics are summarized in Table 1.

Secondary procedures after thoracic endovascular aortic repair

Fifty-six (15.1%; 18 females, mean age 62.3 ± 13.7 years) of the 371 patients underwent secondary procedures due to stent graft-related complications. Following elective TEVAR, reinterventions or operations were performed in 30 patients (54%) with chronic type B aortic dissection (TBAD; *N* = 13), thoracic aortic aneurysm (*N* = 16) or penetrating atherosclerotic ulcer (*N* = 1). In comparison, secondary procedures after rescue/emergency TEVAR were required in 26 patients (46%) suffering from acute (*N* = 3) or impending aortic rupture (*N* = 12), complicated TBAD (*N* = 10) and pseudoaneurysm (*N* = 1). The respective indications for secondary procedures following elective and emergency TEVAR are summarized in Table 2.

Reinterventions were performed in 55.4% (31/56), while 44.6% (25/56) of patients required open surgical repair as a secondary treatment. The decision on 'how to treat' was made on an individual basis and was based on the clinical status and the underlying stent graft complication. In any case of stent graft infection [including aorto-oesophageal/-bronchial fistulae (AOF/ABF), *N* = 13] and occurrence of retrograde type A aortic dissection (*N* = 2), urgent/emergency open surgery was chosen as the only treatment option. Otherwise, complications such as endoleaks (*N* = 23), aneurysm progression (*N* = 3), malperfusion syndrome (*N* = 9) or other causes (*N* = 1) were only treated by open surgery if (endovascular) interventional procedures were unfeasible or contraindicated, e.g. in the absence of an adequate aortic landing zone (minimal length 20 mm) or rapid aneurysm progression.

The respective complications after primary TEVAR with regard to the performed secondary procedures are listed in Table 3.

Open surgical repair

Secondary open surgery was performed in 25 (44.6%) of the 56 patients. The details of our institutional surgical technique to address stent graft complications after TEVAR have been described previously [3, 4]. In brief, surgical access was achieved via a left-sided posterolateral thoracotomy (*n* = 14), full sternotomy (*n* = 10) or both (*N* = 1). Arterial cannulation for cardiopulmonary bypass (CPB; *N* = 22) was performed via the femoral artery (*N* = 12), the axillary artery (*N* = 4) or both (*N* = 3). In 3 cases, the brachiocephalic trunk was used as the arterial cannulation site. Three patients were operated without CBP via left-sided thoracotomy. Antegrade bilateral selective cerebral perfusion (ASCP) was used as an adjunct to hypothermic circulatory arrest (HCA) in 10 patients via the right axillary artery (*N* = 4) or directly after aortotomy by using balloon perfusion catheters in the brachiocephalic trunk (*N* = 6) and left carotid artery (*N* = 10) with a flow sufficient to maintain a pressure of 50–60 mmHg at moderate hypothermia of 21–28°C. Additional perfusion of the LSA was performed in 2 cases for additional spinal cord protection. Intraoperative duration times (median) for HCA, CPB, ASCP and aortic cross-clamping were 46 min (range 20–59), 175 min (range 55–264), 54 min (range 20–62) and 80 min (range 22–152), respectively. Perioperative cerebrospinal fluid (CSF) drainage as an additional measure to minimize the risk of paraplegia was used up to 72 h postoperatively in 9 cases.

Aortic repair comprised total or distal aortic arch replacement (*N* = 10), isolated descending aortic (*N* = 9) and/or

Table 2: Indications for primary and secondary procedures

Primary indication for TEVAR	Indication for secondary procedure									
	Type of endoleak				Aneurysm progression	Malperfusion syndrome	Retrograde type A dissection	AOF/ ABF	Stent graft infection	Aortic regurgitation
	Ia	Ib	II	III						
Elective										
Aneurysm (n = 16)	2	2	2	1	–	2	1	4	2	–
TBAD (n = 13)	6	1	1	–	1	3	1	–	–	–
PAU (n = 1)	–	–	–	–	–	–	–	1	–	–
Rescue/emergency										
Rupture/fistulae (n = 3)	–	–		1	–	1	–	–	1	–
TBAD (n = 10)	7	–		–	2	1	–	–	–	–
Covered rupture (n = 12)	–	3		2	–	2	–	4	1	–
Pseudoaneurysm (n = 1)	–	–		–	–	–	–	–	–	1
Total (n = 56)	15	6	3	4	3	9	2	9	4	1

TEVAR: thoracic endovascular aortic repair; AOF/ABF: aorto-oesophageal/aorto-bronchial fistula; TBAD: type B aortic dissection; PAU: penetrating atherosclerotic ulcer.

Table 3: Stent graft complications and treatment strategies

Stent graft complication	Secondary procedures		
	Open surgery (N = 25)	Reintervention (N = 31):	
		Re-TEVAR (N = 17)	Others (N = 14)
Type of endoleak			
Ia	8	7	–
Ib	–	3	3 (1× ES; 2× BA)
II	–	1	2 (2× EC)
III	–	4	–
Aneurysm progression	1	2	–
Malperfusion syndrome	–	–	9 (6 × CSB/T; 3 × ST)
Retrograde type A	2	–	–
AOF/ABF	9	–	–
Stent graft infection	4	–	–
Aortic regurgitation	1	–	–

TEVAR: thoracic endovascular aortic repair; ES: endostapler; BA: ballooning; CSB/T: carotid–subclavian bypass/transposition; ST: stenting; EC: endovascular coiling; AOF/ABF: aorto-oesophageal/ aorto-bronchial fistula.

thoraco-abdominal aortic repair (N = 4). Additional aortic valve reconstruction due to aortic valve regurgitation—most likely caused by wire perforation during the primary TEVAR procedure—was performed in 1 patient. Complete stent graft removal was performed in 11 cases due to stent graft infection (N = 4), AOF (N = 5) or ABF (N = 2). A single AOF patient—presenting with severe mediastinitis and several oesophageal abscesses—underwent oesophagectomy with cervical oesophagostomy via a right-sided posterolateral thoracotomy prior to scheduled aortic surgery with stent graft removal.

Interventional procedures

Secondary interventions were performed in 31 (55.4%) patients. Endovascular repair included various catheter techniques such as re-TEVAR, re-ballooning of the implanted stent graft, endovascular coiling of aortic branches, stenting of stenosed aortic branches and endostapling. Other reinterventions included carotid-to-subclavian bypass/transposition (Table 3).

Repeated TEVAR, which was the preferred reintervention following primary TEVAR, was performed due to endoleaks (N = 15) and aneurysm progression (N = 2) in 17 (54.8%) of the 31 patients of the reintervention group under general anaesthesia. Re-ballooning was used to reattach the implanted stent graft to the aortic wall in 2 patients presenting with type Ib endoleak. A single patient—initially treated for a large thoraco-abdominal aneurysm with intentional LSA coverage—suffered from persistent type Ib endoleak despite a repeated re-ballooning procedure. To avoid open surgery, the Aptus EndoStapling System (Aptus Endosystems, Sunnyvale, CA, USA) was used to provide fixation and sealing of the previously implanted stent graft to the aortic wall, finally resulting in complete resolution of the type Ib endoleak (Fig. 1).

Two patients with type II endoleak originating from the LSA with relevant progression of aortic diameter during early follow-up underwent endovascular coil embolization of the LSA, 66 and 88 days after TEVAR, via percutaneous brachial artery access.

Delayed end-organ malperfusion as the indication for reintervention was observed in 9 cases. In 3 patients with visceral malperfusion syndrome, stenting of the respective aortic side branches (coeliac trunk: N = 1 and superior mesenteric artery: N = 2) was performed under local anaesthesia via a percutaneous access. In the remaining 6 patients, intentional LSA coverage had resulted in left vertebrobasilar insufficiency (N = 1) or left upper limb ischaemia (N = 5) and subsequently were treated by carotid-to-subclavian transposition (N = 2) or carotid-to-subclavian bypass using a prosthetic graft (N = 4).

Statistical analysis

All continuous variables are expressed as the mean ± standard deviation, or as median with interquartile range (IQR). The categorical variables are reported as counts and percentages. Categorical variables were compared using the χ^2test or Fisher's exact test and independent continuous variables were compared by unpaired Student's t-test or the Kruskal–Wallis test as appropriate. Survival

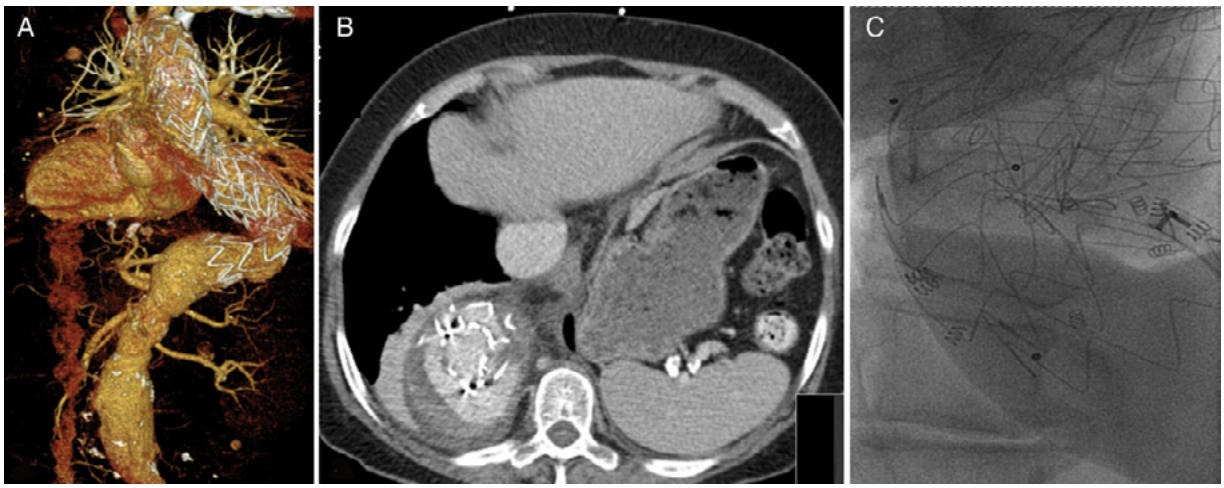

Figure 1: Three-dimensional reconstructed computed tomographic (CT) scan (**A**) after thoracic endovascular aortic repair (TEVAR) with two Valiant stent grafts (Medtronic). The CT scan revealed (**B**) an endoleak type Ib, despite a repeated ballooning procedure to enable the stent grafts to adapt to the aortic wall. Aortogram (**C**) showing the deployment of an endostapling device (HeliFx EndoAnchors, Aptus Endosystems), which was placed circumferentially around the stent graft.

and freedom from secondary procedure survival estimates were generated using the Kaplan–Meier analysis. The threshold of significance was set at $P < 0.05$. All statistical analyses were performed with SPSS® V. 20 software package (IBM®, Armonk, New York, NY, USA).

Postoperative follow-up comprised clinical surveillance [computed tomography (CT), endoscopy, clinical examinations, etc.] at 3, 6 and 12 months (and annually thereafter) amended by routine annual telephone questionnaire of the patient, and their respective general physicians. The clinical charts of all patients were retrospectively reviewed.

Secondary procedure was defined as any endovascular, open surgical or hybrid procedure related to aortic disease during follow-up, including early and late conversion, except for planned staged procedures. Secondary open surgery was defined as any operation requiring reopening of the chest with or without aortic replacement. All endovascular procedures were defined as interventions. Carotid–subclavian artery bypass or transposition—without the need for reopening the chest, CPB and circulatory arrest—was defined as an interventional procedure. Endoleaks were categorized as described by Grabenwöger *et al.* [5].

In-hospital mortality was defined according to the STS guidelines as death in hospital prior to discharge or within 30 days after surgery (regardless of location). Stroke was defined as new-onset neurological deficit and/or evident brain injury visualized by CT scan. Paraplegia was defined as either permanent or temporary bilateral motor deficit of the lower extremities: early (immediately after the procedure) and delayed (after a period of intact motor function during the postoperative course). Renal failure was defined as an increase in serum creatinine >1.5 mg/dl, temporary—resolved by the time of discharge—or permanent need for haemodialysis. Respiratory insufficiency was defined as weaning failure from mechanical ventilation requiring mechanical ventilation (>7 days), reintubation or a tracheostomy.

The following stent grafts have been used in the study for primary intervention: the TAG and the newer-generation C-TAG devices (W.L. Gore and Associates, Flagstaff, AZ, USA); Talent/Valiant/Captivia (Medtronic, Minneapolis, MN, USA); Zenith (Cook, Inc., Bloomington, IN, USA); and Endofit (LeMaitre Vascular, Burlington, MA, USA). Stent graft selection was at the discretion of the endovascular surgeon.

RESULTS

Fifty-six (15.1%) out of 371 patients treated by TEVAR for various thoracic aortic pathologies required a secondary procedure due to stent graft-related complications. Secondary procedures were performed either interventionally or surgically in 55.4% (31/56) and 44.6% (25/56) of patients, respectively (Table 3). In total, 60 after TEVAR procedures were performed in the 56 patients, including 4 patients undergoing two procedures. The overall median follow-up after primary stent graft implantation was 21.4 months (IQR 6.5–51.4; $N = 371$). The median follow-up for the 56 patients who underwent a secondary procedure following primary TEVAR was 10.5 months (IQR 1.7–39.1).

Preoperative baseline characteristics of all 371 patients were not statistically different between patients with or without a secondary procedure (Table 1).

The overall median interval after primary TEVAR to secondary procedure was 2.98 months (IQR: 0.32–16.60 months) in the study group. However, the respective intervals (time to the secondary procedure) varied between the respective after TEVAR complications: endoleaks (median: 3.7 months; IQR: 1.4–17.9), malperfusion syndrome (median: 0.16 months; IQR: 0.05–0.85), AOF/ABF (median: 3.0 months; IQR: 1.0–27.0), stent graft infection (median: 2.7 months; IQR: 0.9–6.2), retrograde type A aortic dissection (median: 0.38 months), aneurysm progression (median: 20.1 months; IQR: 17.0–30.0) and aortic regurgitation (median: 0.1 months). Table 4 summarizes the different time intervals until treatment for early and mid-term complications after primary TEVAR.

The overall in-hospital mortality rate after secondary surgical or interventional treatment after primary TEVAR was 10.7% ($N = 6$): open surgery (4%; $N = 1$) versus reintervention (16.1%; $N = 5$; $P = 0.41$). The cumulative survival rates at 6 months, 1 year and 3 years were 80.4, 73.5 and 69.3%, respectively. Survival was not significantly different between both groups (log-rank test: $P = 0.60$). Figure 2 shows the survival curves estimated by the Kaplan–Meier method, stratified by secondary management strategy after TEVAR.

Neurological complications, by means of stroke and paraplegia, occurred in both groups. The overall incidence rate of stroke was 8.9% ($N = 5$). The group-specific incidence rate of stroke was 8.0% ($N = 2$) in the open surgical group and 9.6% ($N = 3$) in the

Table 4: Time to secondary procedure

Treatment	Time-to-secondary treatment (months)
Secondary procedure (overall), median (IQR)	2.98 (0.32–16.60)
Open surgery, median (IQR)	3.83 (1.00–14.40)
Reintervention, median (IQR)	1.57 (0.14–17.00)
Stent graft complications	
Endoleak (*N* = 28), median (IQR)	3.7 (1.4–17.9)
Aneurysm progression (*N* = 3), median (IQR)	20.1 (17.0–30.0)
Malperfusion syndrome (*N* = 9), median (IQR)	0.16 (0.05–0.85)
Retrograde type A (*N* = 2), median	0.38
AOF/ABF (*N* = 9), median (IQR)	3.0 (1.0–27.0)
Stent graft infection (*N* = 4), median (IQR)	2.7 (0.9–6.2)
Aortic regurgitation (*N* = 1), months	0.1

IQR: interquartile range; AOF/ABF: aorto-oesophageal/aorto-bronchial fistula.

Table 5: Early outcome and post-procedural complications stratified by the secondary management strategy

Complication	Open surgery (*N* = 25)	Reintervention (*N* = 31)	*P*-value
In-hospital mortality, *n* (%)	1 (4)	5 (16)	0.14
Paraplegia, *n* (%)	1 (4.0)	2 (6.4)	0.68
Stroke, *n* (%)	2 (8.0)	3 (9.6)	0.82
Renal failure, *n* (%)	4 (16.0)	1 (3.2)	0.09
Sepsis, *n* (%)	4 (16.0)	1 (3.2)	0.09
Malperfusion, *n* (%)	1 (4.0)	1 (3.2)	0.87
Respiratory failure, *n* (%)	3 (12.0)	0	0.04[a]
Tertiary procedure (interventional or surgical), *n* (%)	2 (8.0)	2 (6.4)	0.82

[a]Significantly different.

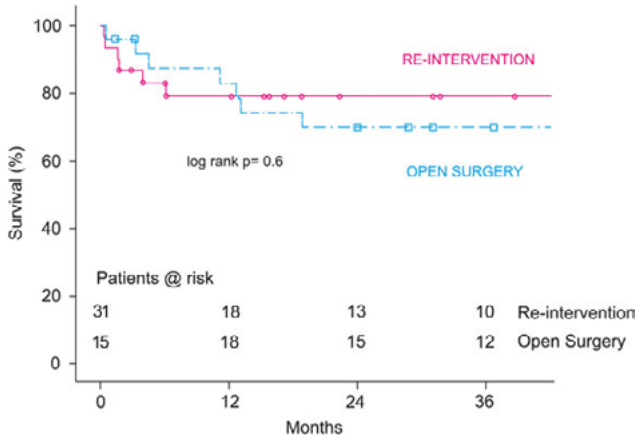

Figure 2: Kaplan–Meier survival curve stratified by the two groups that underwent secondary procedures (open surgery versus reintervention) due to complications after primary thoracic endovascular aortic repair (TEVAR). No significant difference with regard to survival was found (log-rank test, *P* = 0.6) after 36 months.

reinterventional group (*P* = 0.82). Paraplegia occurred less frequently (*N* = 3; 5.6%) with only 1 (4.0%) case following open surgical treatment and 2 (6.4%) cases after re-TEVAR (*P* = 0.82).

Renal failure (*N* = 5; 8.9%) occurred more often in the open surgery group than in the reinterventional group (16 vs 3.2%); however, no statistical difference was found between groups (*P* = 0.09). Postoperative sepsis (*N* = 5; 8.9%) showed a similar distribution between groups (16 vs 3.2%; *P* = 0.09). Malperfusion syndrome following secondary procedures occurred in 1 patient of both groups (*N* = 2; 3.6%). Respiratory failure was found to only occur in the open surgery group (*N* = 3; 12%) and reached statistical significance (*P* = 0.04). Tertiary procedures, by means of reoperations or reinterventions, occurred in 4 (7.1%) patients: open surgery (*N* = 2; 8.0%) versus reintervention (*N* = 2; 6.4%).

Post-TEVAR complications are listed in Table 5.

DISCUSSION

In the past decade, TEVAR was primarily reserved for emergency treatment of high-risk patients with unclear overall life expectancy or as a 'bridge-to-surgery' in case of acute aortic rupture. However, increasing experience with high procedural success rates has resulted in a progressive use in aortic surgery, which is now being proposed as an alternative for most aortic pathologies affecting the descending aorta, and in individual cases even for extensive thoracoabdominal pathologies [6]. As the number of TEVAR survivors grows, reports of complications are on the increase [7, 8], with an incidence rate of open repair after TEVAR approaching 2.2–7.2% in experienced centres. It seems likely that the incidence of severe stent graft-related complications or even TEVAR failure is currently under-reported in the medical literature, and therefore the associated morbidity and mortality may be significantly higher than in primary open repair [3, 9, 10].

In the current study, 371 patients treated by TEVAR at our institution were retrospectively screened for secondary procedures due to stent graft complications within a time period of more than 10 years. Overall, 56 patients (15.1%) underwent a secondary procedure after TEVAR with a median time interval to secondary treatment of 2.98 months. Twenty-five (6.7%) out of 371 patients required open surgical repair, which is in line with recently published clinical reports [11]. Recent publications on elective TEVAR report endovascular reinterventions to occur with an incidence rate between 0 and 32.3% [12], while the incidence rate of vertebrobasilar ischaemia and subclavian steal syndrome after complete LSA overstenting may be as high as 24 and 20%, respectively [13]. In comparison, 25 (6.7%) patients of the current study required an endovascular reintervention after primary TEVAR, whereas 6 out of 126 (4.8%) patients after intentional LSA coverage required a revascularization procedure due to vertebrobasilar insufficiency or left upper limb ischaemia.

The time to secondary procedure after TEVAR differed between the respective complications—with aortic regurgitation and retrograde aortic dissection being the fastest and aneurysm progression being the slowest complications to occur (Table 4). Interestingly, patients with stent graft infections and AOF/ABF formation presented rather early during follow-up at 2.7 months (median) and 3.0 months (median), respectively. However, time to secondary procedure for the reintervention group (median: 1.57 months; IQR 0.14–17.00) was shorter in comparison with the open surgery group (median: 3.83 months; IQR 1.00–14.40).

In-hospital mortality was not significantly different between the treatment groups (*P* = 0.14). The higher trend for in-hospital

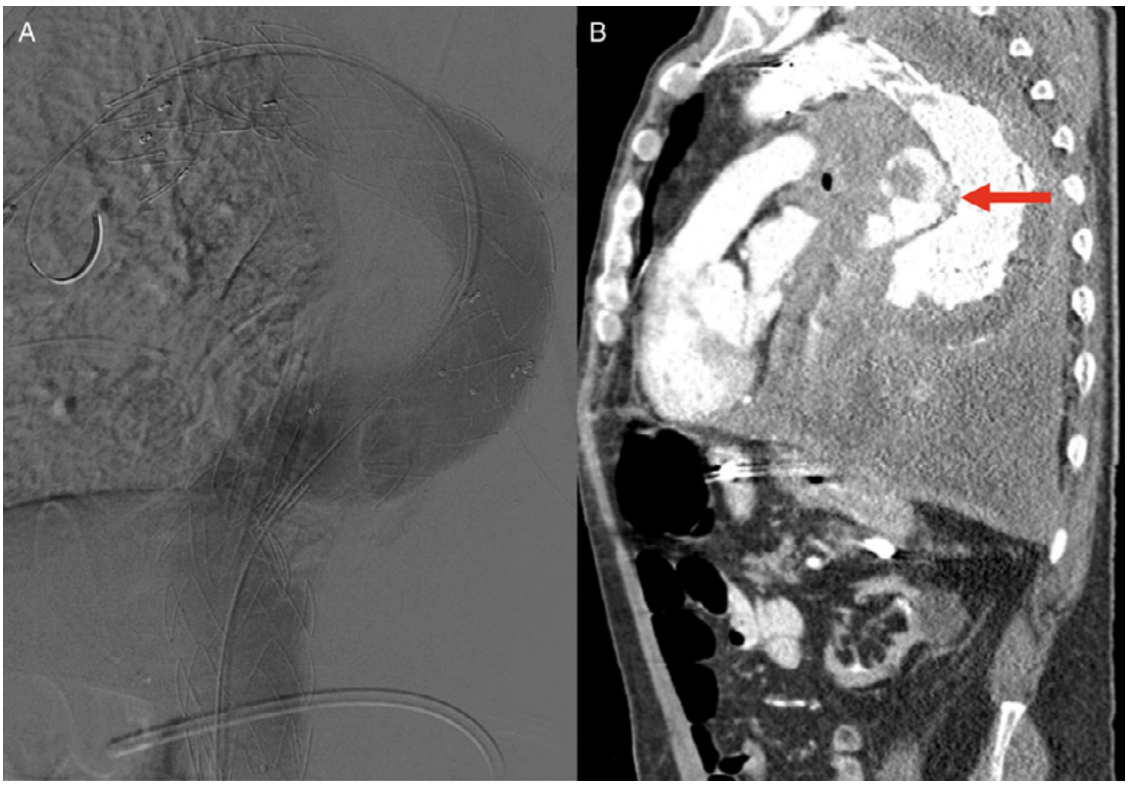

Figure 3: (**A**) Aortogram after thoracic endovascular aortic repair (TEVAR) using two Valiant stent grafts (Medtronic) for aneurysm exclusion due to chronic type B aortic dissection. (**B**) Computed tomography scan on POD#1 after TEVAR showed an acute rupture at the level of the overlapping zone (endoleak type II) of both stent prostheses (red arrow).

mortality of the reintervention group (16%)—even though not statistically different—could be explained by a high rate of emergency cases (acute or impending aortic rupture) of the descending aorta with re-TEVAR performed as a rescue therapy (Fig. 3).

Ten late deaths occurred during follow-up of the secondary procedure cohort ($N = 56$), including 1 aorta-related death due to a new aortic rupture distally to the stent graft. In the other 9 cases, causes of death included respiratory failure ($N = 3$), heart failure ($N = 4$), pancreatitis ($N = 2$) and cancer ($N = 1$). The cumulative survival rates of both groups at 6 months, 1 year and 3 years were 80.4, 73.5 and 69.3%, which are in line with other clinical series of endovascular aortic centres. Roselli *et al*. [14] reported similar survival rates of 83, 75, and 67% at 6 months, 1 year and 3 years, respectively. In comparison, the observed in-hospital and mid-term mortality rates were similar in both groups (log-rank test $P = 0.06$; Fig. 2).

The currently reported incidence rate of endoleaks following TEVAR ranges from 1 to 29% [15, 16]. In our series, the overall incidence rate of endoleaks was 7.5% ($N = 28$; out of 371 patients) with type Ia endoleak being the most frequent indication for a secondary procedure (26.8%; $N = 15$; out of 56 patients). Of note, 12 of these patients were initially treated for chronic TBAD, which tended to have shorter-than-recommended landing zones and larger aortic diameters.

Currently, no expert consensus regarding the indications for secondary endovascular or open surgical repair in patients with type I endoleaks after TEVAR exists. An adequate landing zone in Zone 3 or 4 according to Ishimaru's classification usually allows for re-TEVAR, which is commonly accepted as the primary choice of reintervention. However, in case of steep angulation, short length of the proximal landing zone or progressive aortic lesions adjacent to or even involving the distal aortic arch conversion to open surgical repair is often required [17]. Open surgical repair of proximal type Ia endoleak ($N = 8$) was performed due to progression of the disease involving the aortic arch if secondary TEVAR was technically impossible. In most of these cases ($N = 6$), replacement of the ascending aorta and aortic arch was performed by the 'reverse' frozen elephant technique, as described by Coselli *et al*. [18]. These patients showed superior outcome with no in-hospital mortality or stroke, but with resulting permanent paraplegia in a single case. Alternatively, if a type I endoleak persists despite repeated procedures—similar to the case in the series—endostapling may be considered [19].

Common risk factors for the development of any type of endoleaks are the LSA coverage, an increased aortic diameter (aneurysm) and extensive aortic coverage with multiple stent grafts [16]. In 2 patients, persisting type II endoleak from the LSA was successfully treated by endovascular coil embolization on postoperative day (POD) #66 and #88 via percutaneous brachial artery access; however, 1 patient suffered a stroke. Therefore, our current management strategy of patients with persistent endoleaks consists of early treatment of type I and III endoleaks and a more conservative 'wait and watch' strategy for detection of potential aneurysm progression in patients with type II endoleaks [16, 20].

Secondary to endoleaks, stent graft infections and AOF/ABF (3.5%; $N = 13$ out of 371) were found to develop early during follow-up. Endovascular stent graft infection is reported to occur with an incidence rate of 0.05–4% with medical treatment alone resulting in a mortality rate of 100%. In our own experience [21], the treatment strategy for infected stent grafts with or without fistula formation was surgical and comprised aggressive debridement of the infected tissues and stent graft extirpation. Thoracic

endovascular aortic repair was not considered as a bridge to surgery in these high-risk patients so as not to delay curative treatment. Similar to our own observations, Cernohorsky *et al.* [22] reported a short interval (within 3 months) between TEVAR and clinical signs of stent graft infection, thereby emphasizing the important role of prophylactic antibiotics during and after the intervention. The use of rifampicin-soaked Dacron prostheses or autologous grafts (cryopreserved) remains another treatment strategy for stent graft infection with virulent organisms or frank purulence [23]. Extra-anatomical bypass may also be considered as an alternative surgical solution in patients with severe mediastinal infection.

The third most frequent indication for a secondary procedure was malperfusion syndrome. In particular, intentional LSA coverage was found to cause relevant malperfusion of the upper left limb or steal syndrome of the left vertebral artery in 6 patients. Endovascular LSA coverage has been shown to cause relevant subclavian steal syndrome, with stroke also being infrequently reported [24]. Therefore, previous subclavian transposition or carotid-to-subclavian bypass should be considered if intentional LSA coverage by elective TEVAR is planned. In 3 other patients, end-organ malperfusion was successfully overcome by stenting of the respective aortic branch.

Paraplegia remains of concern in the treatment of after TEVAR complications and was observed in 5.4% (3 out of 56 patients) of the study group (open surgery 4.0% versus reintervention 6.4%; $P = 0.68$). In one patient after open surgery, early paraplegia occurred on POD#1 after extended thoraco-abdominal repair, due to type II endoleak-associated aneurysm progression with complete visceral debranching. The operation was performed under mild hypothermia at 32°C with left heart bypass, CSF drainage and near-infrared spectroscopy to monitor the paraspinous collateral network to detect related spinal cord ischaemia [25]. All of the segmental aortic arteries were sacrificed intraoperatively. However, the patient suffered from severe haemorrhage postoperatively and required massive transfusion. Improvement of neurological symptoms was achieved by medical therapy with dexamethasone, reduction of CSF pressure and an increase in mean arterial pressure, but permanent motor deficits of the lower extremities remained.

In the other two cases, immediate paraplegia occurred after re-TEVAR and thoraco-abdominal segmental artery coil embolization (type II endoleak). The first patient underwent primary TEVAR due to acute TBAD complicated by abdominal malperfusion. Perioperative CSF drainage was utilized; however, the patient experienced immediate paraplegia after extended stent grafting of the thoraco-abdominal aorta. The second patient had undergone primary TEVAR for chronic TBAD-associated large aortic aneurysm. After TEVAR, a type II endoleak persisted for more than 3 months, originating from thoracic and lumbar aortic segmental arteries. The patient underwent complex coil embolization with closure of the proximal entry tear as well as the thoracic and lumbar segmental arteries. Shortly after the procedure, the patient developed the first signs of paraplegia. Despite the frequent use of CSF drainage and maintenance of supranormal mean arterial pressures, improvement of neurological symptoms was incomplete.

Other post-procedural complications were observed in both groups and included sepsis (16 vs 3.2%; $P = 0.09$), renal insufficiency (16 vs 3.2%; $P = 0.09$), malperfusion (4.0 vs 3.2%; $P = 0.82$) and reoperation as a tertiary procedure (8.0 vs 6.4%; $P = 0.87$). Tertiary procedures were required in only 4 (7.1%) out of the 56 patients; however, the rate for more than one additional operation/intervention may be as high as 42% [24]. Despite being relevant, the incidence of these complications did not significantly differ between patients treated either surgically or reinterventionally. However, respiratory insufficiency (12 vs 0%; $P = 0.04$) only occurred after conventional surgical repair, and therefore was found to be significantly different between treatment groups. The 3 patients who developed respiratory insufficiency were operated on via a left-sided thoracotomy for AOF ($n = 2$) and large descending aortic aneurysm ($n = 1$), which is *per se* associated with significant pain and may have a negative impact on postoperative pulmonary function. However, since TEVAR was not feasible—due to stent graft infection ($N = 2$) and lack of an adequate landing zone ($N = 1$)—no alternative treatment strategy to open surgery existed in these 3 cases.

The results that were observed in this study show that secondary procedures may be successfully performed with an acceptable outcome. Except for respiratory failure, no statistically differences were found regarding mortality and morbidity postoperatively as well as during early and mid-term follow-up. However, after TEVAR complications may occur with varying degrees of severity, thereby demanding early diagnosis and individual planning by an interdisciplinary team to treat each complication, for example stent graft infections and aortic fistulae, accordingly.

Limitations

The limitations of this study are inherent to the single-centre experience, the heterogeneity of the treated aortic pathologies and the retrospective nature of the analysis. In many cases, the respective endovascular reintervention strategy depended on the individual experience of the endovascular surgeon/interventionalist on call and our knowledge of published case reports. Currently, no treatment algorithm or standardized protocol for secondary procedures with regard to after TEVAR complications is defined, necessitating an interdisciplinary treatment strategy on an individual basis.

CONCLUSIONS

Complications after primary TEVAR seem to occur cumulatively during follow-up and often require secondary procedures for definite treatment. During early and mid-term follow-up, the predominant complications after TEVAR comprised endoleaks (Type Ia), malperfusion syndrome, stent graft infections, fistula formation and expanding aneurysm. Despite the high-risk nature of complications, individually planned secondary open surgical and interventional procedures may be successfully performed with an acceptable outcome. Owing to an increased incidence of early complications after TEVAR, close surveillance during follow-up is strongly recommended.

Conflict of interest: none declared.

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APPENDIX. CONFERENCE DISCUSSION

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Dr S. Folkmann *(Vienna, Austria):* This manuscript reports on a secondary intervention rate after TEVAR. Within 10 years, a cohort of 370 patients with all aortic pathologies were retrospectively recruited. 56 patients underwent secondary intervention, nearly half another endovascular treatment, and 44% had an open surgical repair.

So that leads me to my first question: How did you treat a type I endoleak? How did you make the decision?

And the second question would be, in your manuscript you mentioned that while the TEVAR procedure was done, the CSF drainage was used, I would like to know which patients this was done in and if it was performed at the primary or secondary intervention.

Dr M. Nozdrzykowski *(Leipzig, Germany):* Regarding the first question, to the best of our knowledge there is currently not any experience or any consensus on how one should treat a type I endoleak. In our cohort, we have about 40% of patients with type I endoleak, and it was the most common indication for secondary interventions, especially type Ia endoleak which was the indication for secondary intervention in approximately 27% of patients. Our current strategy in case of a type Ia endoleak is: if the proximal landing zone is 20 mm or more, and if we can place a new stent in the zone of 3 or 4, according to Ishimaru classifications, we use as a first choice approach for a second TEVAR procedure. In contrast, in cases of steep aortic arch angulation and if the proximal landing zone is shorter than expected, or if the aortic lesion is near or involving the aortic arch, we used as primary therapy open secondary intervention, I mean open surgical repair. Moreover, in young patients we use more frequently open surgical repair, because of unclear durability of the stent grafts.

Relating to your second question, we didn't commonly use cerebrospinal fluid drainage (CSF) in our patients. The use of CSF drainage was dependent on, whether it was the primary, or the secondary intervention. In the primary intervention we used CSF drainage only in patients who had previously thoracoabdominal aortic repair, because in these cases, the paraplegia rate is higher. Also in cases of a second TEVAR, we use CSF drainage, if the extended thoracic or thoracoabdominal aortic stent-graft placement was performed, for example, in cases of a type Ib endoleak or endoleak type III, most frequently in patients with DeBakey type III aneurysms.

To summarize, we used CSF drainage in elective cases and in approximately 40% of patients undergoing TEVAR a second time.

6.7 Surgical management of delayed retrograde type A aortic dissection following complete supra-aortic de-branching and stent-grafting of the transverse arch

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ORIGINAL ARTICLE

Surgical management of delayed retrograde type A aortic dissection following complete supra-aortic de-branching and stent-grafting of the transverse arch[†]

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Abstract

OBJECTIVES: Hybrid endovascular procedures are rapidly evolving and have recently been adopted for high-risk patients deemed unsuitable for conventional aortic arch surgery. We describe here our initial experience with this technique, including the management of 2 patients who developed a retrograde type A aortic dissection post-de-branching.

METHODS: Between May 2010 and October 2012, 109 patients underwent conventional aortic arch repair at our institution. A further 9 high-risk patients with complex aortic arch pathology (median logistic EuroSCORE: 26, range: 11–41) were deemed unsuitable for conventional total aortic arch replacement and therefore underwent hybrid aortic arch repair. Complete supra-aortic de-branching, followed by endovascular stent-grafting (TEVAR) of the transverse arch and descending aorta, was performed in these high-risk patients.

RESULTS: In-hospital mortality was zero and no patient developed paraplegia/paraparesis due to spinal cord ischaemia. However, 2 patients (22%) developed retrograde type A aortic dissection on Days 10 and 12 post-TEVAR. Both patients had a dilated ascending aorta and received a stent graft containing bare metal springs at the proximal end. Emergency ascending aortic replacement was performed during moderate-to-mild hypothermia (28–34°C) and bilateral antegrade cerebral perfusion *via* cannulation of the de-branching prosthesis. A Hemashield prosthetic graft was anastomosed to the proximal stent graft in an elephant trunk technique. Both patients suffered from minor non-debilitating stroke, with 1 being discharged home and 1 transferred to a neurological rehabilitation centre 2 and 3 weeks after reoperation, respectively.

CONCLUSIONS: Retrograde type A aortic dissection after hybrid endovascular treatment of the aortic arch represents a new—most likely under-reported—pathology that may be successfully treated with open surgical repair. The use of stent grafts with protruding proximal bare springs and the implementation of oversizing and post-deployment ballooning should be avoided in patients undergoing hybrid arch procedures, particularly if the ascending aorta is dilated.

Keywords: Retrograde type A aortic dissection • Proximal landing zone • Ascending aorta • Hybrid aortic repair • TEVAR • Supra-aortic de-branching/re-routing • Aortic arch

INTRODUCTION

Conventional open 'two-stage' surgery for extensive thoracic aortic pathologies—including the aortic arch and the descending aorta—remains challenging, with an associated morbidity and mortality in the range of 13–36% [1–4]. Hybrid endovascular procedures are evolving and have recently been adopted for high-risk patients deemed to be unsuitable for conventional aortic arch surgery. Such procedures have been used to treat a wide range of aortic disease involving the transverse aortic arch and the descending thoracic aorta.

New less-invasive surgical strategies—involving off-pump partial or complete surgical re-routing of the supra-aortic branches followed by thoracic endovascular aortic repair (TEVAR)—have recently been introduced into clinical practice to treat aortic arch pathologies in high-risk patients with promising early results [5–7]. The main concept of 'supra-aortic de-branching' is the creation of a proximal landing zone (Zones 0, 1, 2) to allow for safe second-stage endovascular stent graft deployment to completely exclude transverse and distal arch pathologies, e.g. aneurysms, penetrating ulcers and dissections [8]. Although TEVAR has been developed as

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a less-invasive approach for the treatment of aortic pathologies, it is also associated with a dangerous and formerly unknown complication: retrograde type A aortic dissection (rAAD) [5, 9].

The risk of rAAD during and after hybrid de-branching procedures in the management of aortic arch pathologies remains unknown. However, the occurrence of rAAD during TEVAR seems to be multifactorial rather than directly related to intraoperative manipulation alone, particularly in the course of delayed rAAD [5].

We describe here our early experience with aortic de-branching procedures, with a particular focus on the diagnosis and management of patients who developed postoperative rAAD.

PATIENTS AND METHODS

Between May 2010 and October 2012, 109 patients underwent conventional aortic arch surgery at our institution. A further 9 high-risk patients with pathology of the aortic arch and descending aorta were deemed unsuitable for conventional surgery due to significant comorbidities (median logistic EuroSCORE: 26, range: 11–41), and were therefore admitted for hybrid endovascular aortic repair. Preoperative patient demographics and comorbidities are shown in Table 1.

Indications for hybrid treatment comprised extensive atherosclerotic arch aneurysm ($n = 7$) and arch aneurysm due to an aberrant subclavian artery ($n = 2$). Preoperative multislice computed tomography (CT), with subsequent 3D reconstruction of the entire aorta, was performed in order to identify an adequate proximal landing zone (Ishimaru classification) for endovascular stent-grafting and to exclude any major occlusive vessel disease of the supra-aortic and thoracoabdominal aortic branches [8]. To allow for complete stent-grafting of the transverse arch, a proximal landing zone of at least 2.0 cm in the distal ascending aorta (Zone 0) was chosen in all patients. Preoperative coronary angiography and echocardiography were performed in all patients.

Six operations were performed in a hybrid operation theatre equipped with an angiographic C-arm system allowing for concomitant TEVAR, while the other 3 patients underwent a staged procedure. The de-branching procedures were performed without cardiopulmonary bypass (CPB) in 6 patients, and with CPB in 1 patient who had a patent LIMA-LAD bypass graft post-CABG. Concomitant off-pump coronary artery bypass grafting (OPCAB) was performed in 2 patients. Later in the series, 2 patients with a dilated ascending aorta (diameter >40 mm) underwent supracoronary ascending aortic replacement followed by supra-aortic de-branching using a four-branched prosthetic graft (Lupiae graft, Vascutek Terumo, Scotland, UK). The ascending aorta was replaced in these patients during CPB in order to achieve an adequate proximal landing zone and to avoid the risk of rAAD.

Endovascular stent-grafting of the distal ascending aorta, transverse arch and proximal descending aorta was successfully performed retrogradely *via* the femoral artery under fluoroscopy followed by completion angiography in all cases. The TEVAR procedure was performed during the same operation as the de-branching procedure in 6 patients, and as a second-stage completion repair 5–8 days later in 3 patients. A postoperative routine follow-up CT scan was performed 1 week post-TEVAR in all patients.

Table 1: Patient demographics and preoperative comorbidities

Age ± SD, range	76.4 ± 4.8 (67–82) years
Male, *n* (%)	9 (100)
Hypertension, *n* (%)	9 (100)
Obesity, *n* (%)	2 (22)
Hyperlipidaemia, *n* (%)	6 (67)
Coronary artery disease, *n* (%)	4 (44)
Previous myocardial infarction, *n* (%)	1 (11)
Chronic obstructive pulmonary disease, *n* (%)	2 (22)
Diabetes mellitus, *n* (%)	4 (44)
Chronic renal failure, *n* (%)	1 (11)
Chronic pancreatitis, *n* (%)	1 (11)
Liver cirrhosis, *n* (%)	1 (11)
Previous cardiac operation, *n* (%)	2 (22)
Previous major surgery (non-cardiac), *n* (%)	6 (67)

RESULTS

Open supra-aortic de-branching, with ($n = 3$) or without ($n = 6$) the use of CPB was successfully performed in all patients. Concomitant OPCAB surgery was performed in 2 patients. No patient required intraoperative conversion to conventional open repair with deep hypothermic circulatory arrest.

Retrograde stent graft deployment *via* the femoral artery was successful in all 9 patients. Stent graft quantity depended on the individual extend of aortic pathology to allow for complete exclusion: 6 patients received three stent grafts (Valiant®, Medtronic Vascular, Santa Rosa, CA, USA)—covering the transverse arch and descending aorta up to the celiac trunk—and 2 were treated with one stent graft (Valiant®, Medtronic Vascular, Santa Rosa, CA, USA). Only 1 patient underwent TEVAR with two Zenith® (Cook, Inc., Bloomington, IN, USA) stent grafts.

Intraprocedural balloon dilatation of the aortic stent grafts was necessary in 4 cases and depended on individual aortic arch pathology and the occurrence of endoleaks immediately after stent graft deployment. No endoleaks were detected during the following clinical course.

Morbidity and mortality after hybrid arch repair

The median intensive care unit (ICU) stay and hospital stay were 11.3 ± 8.5 days (range 2–29 days) and 19.5 ± 12.1 days (range 7–42 days), respectively. In-hospital mortality was zero.

Perioperative stroke and transient postoperative delirium occurred in 2 and 3 patients, respectively. No postoperative transient or permanent spinal cord ischaemia (i.e. paraplegia/paraparesis) occurred, even in patients with coverage of the entire descending aorta to the celiac axis.

Five patients developed respiratory insufficiency postoperatively, and 3—one with chronic obstructive pulmonary disease—required percutaneous tracheostomy in order to be weaned from the ventilator. One patient with chronic renal insufficiency required temporary dialysis during the early postoperative course. Reoperation was required in 3 patients because of postoperative bleeding, acute innominate artery bypass occlusion and sternum instability in 1 patient each.

Two patients developed retrograde type A dissection post-TEVAR and are described in more detail below.

Case 1

At the beginning of the series, an 80-year old male patient presented with progressive back pain due to a large aneurysm of the distal aortic arch and descending aorta (max. diameter 60 mm) post-type B aortic dissection. The patient also suffered from several comorbidities including dyspnea at rest, obesity, atrial fibrillation, arterial hypertension, symptomatic hyperthyroidism and acute gastroenteritis. With regard to the medical history and the actual condition, this patient was deemed frail and high risk for open surgery.

He underwent off-pump supra-aortic de-branching and TEVAR of the entire descending aorta using three stent grafts. TEVAR coverage extended distally to the celiac axis, with good perfusion of the celiac trunk on completion angiography.

The procedure was successful and the patient recovered uneventfully. On the 10th postoperative day, however, he developed chest pain and acute cardiac tamponade requiring cardiopulmonary resuscitation. Emergency chest CT showed acute rAAD in close proximity to the proximal end of the stent graft and the anastomosed 'de-branching' graft (Fig. 1A and B). Replacement of the supracoronary ascending aorta was performed as an open emergency operation. Bilateral antegrade selective cerebral perfusion (800 ml/min) was performed *via* cannulation of the de-branching graft, during moderate hypothermia (28°C) and distal circulatory arrest. Intraoperatively, a dissection entry due to bare spring perforation of the enlarged ascending aorta (diameter 42 mm) was confirmed.

A Hemashield graft (32 mm) was anastomosed to the proximal end of the stent graft in an elephant trunk technique achieving good hemostasis (Fig. 1C and D). The right coronary sinus was dissected but the aortic valve was still competent. In view of the patient's age and comorbidities, the decision was made to glue together the layers of the right coronary sinus with fibrin glue, and the proximal anastomosis was completed thereafter. After finishing the proximal anastomosis, the de-branching graft was anastomosed end-to-side to the new ascending aortic graft. Circulatory arrest time was 35 min, aortic cross-clamp time was 82 min and CPB time was 158 min.

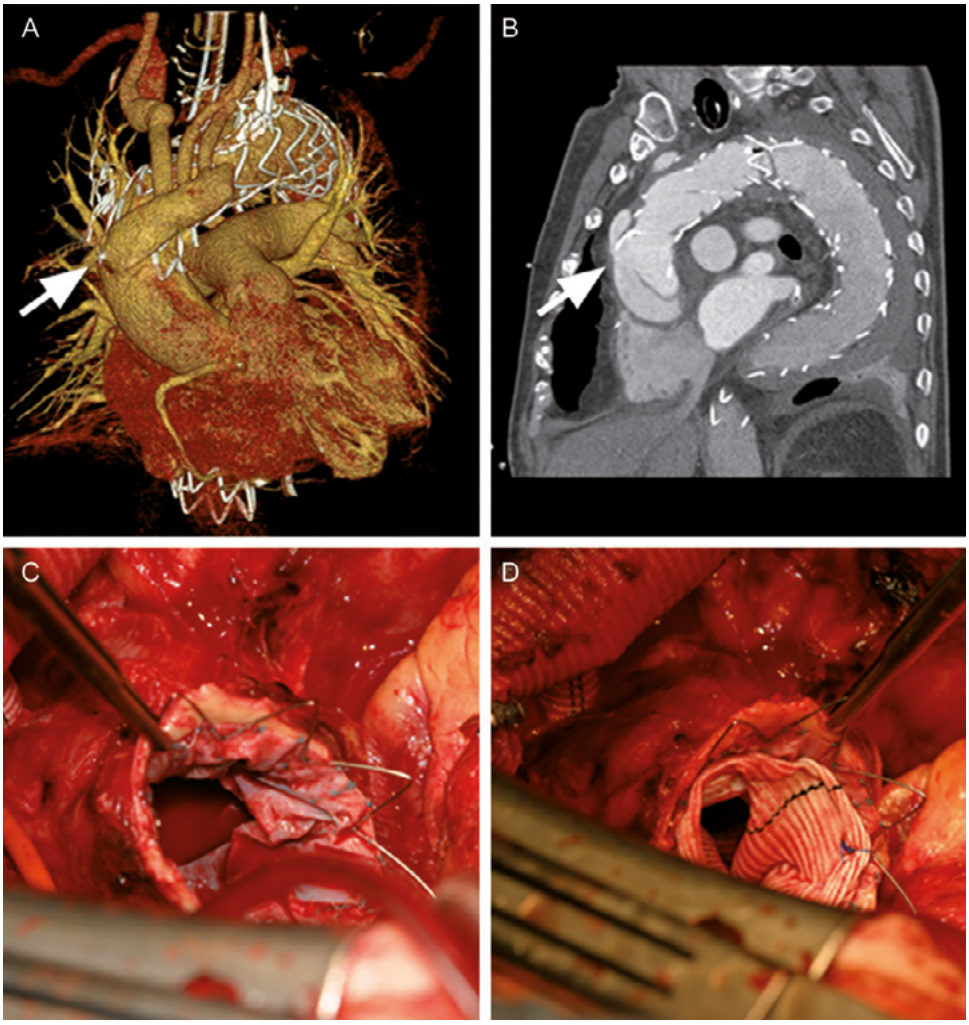

Figure 1: CT 3D reconstruction of the thoracic aorta after supra-aortic de-branching and thoracic endovascular stent graft repair showing retrograde aortic type A dissection (rAAD) due to proximal bare spring perforation (**A** and **B**). Intraoperative view of the proximal portion of the deployed stent graft after resection of the ascending aorta (**C**). An 'elephant trunk procedure' was performed by suturing a Hemashield graft to the proximal end of the stent graft (**D**); the bare springs can be cut off before or after completion of this anastomosis.

A postoperative cranial CT scan showed multiple infarction syndrome. Two weeks after reoperation for rAAD, the patient was responsive and able to weakly move all extremities, and was discharged to a neurological rehabilitation clinic.

Case 2

The second patient (age 67) had been admitted for an aberrant right subclavian artery aneurysm with involvement of the distal aortic arch, as well as significant left main coronary artery disease. The diameter of his native ascending aorta was 36 mm and therefore he was thought to be at low risk for rAAD. The medical history included arterial hypertension, diabetes mellitus, smoking (>40 pack years) and previous visceral surgery. The patient was deemed to be high risk for conventional open surgery because of the challenging location of his aortic aneurysm at the origin of the aberrant right subclavian artery (i.e. Kommerell's diverticulum).

The patient underwent supra-aortic de-branching and concomitant off-pump OPCAB surgery. TEVAR of the transverse arch, using one stent graft (Valiant®), was performed as a second-stage repair 1 week later. The postoperative course was uneventful; however, routine predischarge surveillance CT revealed an rAAD involving the non-coronary sinus and proximal ascending aorta, without signs of acute cardiac tamponade.

Urgent supracoronary ascending replacement with a 30-mm Hemashield prosthesis was performed. The de-branching prosthesis was cannulated in order to perform bilateral antegrade selective cerebral perfusion during mild hypothermic (34°C) arrest. Additional distal perfusion (2.5 l/min) of the lower body was performed *via* a balloon occlusion catheter that was placed within the arch stent graft, in order to lower the risk of ischaemic damage to the spinal cord and visceral organs. The dissection entry was located in the proximal ascending aorta directly adjacent to the bare metal springs of the stent graft. During antegrade cerebral and lower body (distal) perfusion, the ascending aorta was resected and an 'elephant trunk procedure' with a 30-mm Hemashield prosthetic graft was performed as described above. The aortic valve was competent and therefore the dissected layers of the non-coronary sinus were re-approximated with fibrin glue. Circulatory arrest time was 25 min, aortic cross-clamp time was 43 min and CPB time was 85 min.

The patient was extubated on the second postoperative day, but required another reoperation for sternal instability 10 days later. In addition, a right posterolateral cerebral infarction (3.7 × 2.7 cm) was diagnosed *via* cranial CT scan after the patient had developed left arm weakness. No further neurological deficits occurred and the patient was discharged home 6 weeks after the initial de-branching operation.

DISCUSSION

rAAD has been recognized as an uncommon but frequently lethal aortic disease in the era of transcutaneous thoracic aortic intervention [5, 9]. Post-TEVAR rAAD was initially reported as single case reports following the treatment of acute type B aortic dissection [10, 11]. In 2009, a multicentre study of the European Registry on Endovascular Aortic Repair Complications reported on an incidence of rAAD post-TEVAR for either acute or chronic type B dissection of 1.33% (95% CI 0.75–2.40) [12]. Although rAAD post-TEVAR is uncommon, its associated mortality is higher than that observed in patients presenting with conventional type A aortic dissection, being 50% if rAAD is diagnosed in-hospital and 70% if diagnosed during the TEVAR procedure [12].

Today, hybrid endovascular procedures are increasingly used in high-risk patients deemed unsuitable for conventional aortic arch surgery [5–7]. Most recently, the incidence of early rAAD after partial (Zone 1 and 2) and complete (Zone 0) supra-aortic re-routing followed by TEVAR of the aortic arch was reported to be 1.9%, with a 30-day hospital mortality rate of 33% [9]. However, the incidence of rAAD after stent graft deployment in the ascending aorta (Zone 0) with complete arch coverage was even higher when compared with more distal endografting of the aortic arch (Zone 1 or 2): 6.9 vs 1.4% [9]. Czerny *et al.* reported an overall rAAD incidence of 8% in a multicentre study of 66 patients with total arch de-branching and TEVAR (Zone 0), with an early (<7 days postoperatively) and delayed (>7 days postoperatively) incidence of 3 and 5%, respectively [5]. At our institution, 2 (22%) of 9 patients who underwent hybrid arch repair developed delayed rAAD. Even though emergency surgery was successful with no in-hospital mortality, the high occurrence of rAAD and the accompanying stroke rate raises concerns about the safety of complete supra-aortic de-branching and TEVAR of the aortic arch.

Williams *et al.* reviewed their institutional database with regard to supra-aortic de-branching and TEVAR of the aortic arch (Zones 0–2) and identified only 6 (1.9%) of 309 patients who developed early rAAD [9]. Their patient analysis revealed an increased rAAD incidence in patients with an aortic diameter of more than >40 mm and after stent graft deployment in the native ascending aorta (Zone 0) of 4.8 and 6.9%, respectively. A combination of increased ascending aortic diameter (>40 mm), a proximal landing zone in the native aorta (Zone 0), and the existence of dissection pathology increased the incidence of rAAD up to 25% [9]. All of these potential risk factors applied to the first patient of our series who developed rAAD: ascending aortic diameter of 42 mm, proximal landing zone in the native ascending aorta (Zone 0) and pre-existing type B aortic dissection. In addition, it was noted at the time of reoperation that the entry site was directly adjacent to the proximal bare springs of the stent graft.

Other investigators have noted an association between proximal bare springs and the occurrence of rAAD [12, 13]. However, a definite causation has not yet been established. Czerny *et al.* identified several factors that may contribute to the development of rAAD after surgical de-branching and complete TEVAR of the arch: ascending aortic injury after partial clamping for the proximal anastomosis, compliance mismatch (rigidity of the stent graft vs highly compliant ascending aorta) and blood flow alterations after transposition [5]. Aortic injury due to partial clamping of the ascending aorta was unlikely to have been the cause of rAAD in our second patient, since he underwent a repeat CT scan between his de-branching and TEVAR procedures. This interval CT did not reveal any evidence of rAAD, which was first diagnosed after the TEVAR procedure. Intraoperative examination again revealed an entry site that occurred directly adjacent to the proximal bare metal springs that may have caused the initial aortic wall injury. Kpodonu *et al.* suggested that stent graft oversizing to >20% with regard to aortic diameter may also be a potential risk factor for rAAD [14]. Of note, 4 patients in our series (including both patients with rAAD) required balloon expansion after stent graft deployment in the transverse arch.

Another issue regarding rAAD after TEVAR is the resulting neurological outcome after the reoperation. Both patients had been treated successfully with supra-aortic de-branching and TEVAR without any neurological complication postoperatively. However, both required emergent ascending aortic replacement with bilateral SCP—and ultimately suffered from stroke after reoperation. Clearly, any aortic operation bears a potential risk for occurrence of the new neurological events. However, CPR was required preoperatively in the first case and may have predisposed the patient to significant cerebral ischaemia. Avoiding rAAD—and thereby an aortic reoperation—is of outmost importance in these high-risk patients to lower the incidence of neurological complications and postoperative mortality.

The results of our study and others suggest that not every 'high-risk' patient deemed unsuitable for conventional aortic arch repair is a good candidate for off-pump supra-aortic de-branching and TEVAR of the aortic arch. When considering hybrid or conventional surgery, it is important to always individually estimate the patient's history, actual clinical status and anatomical variations. During a period of 29 months, we only classified 9 of 118 patients (7.6%) requiring aortic arch surgery as acceptable candidates for supra-aortic de-branching and TEVAR. However, the fact that both patients with rAAD (22%; $n = 2$) were successfully treated by emergent open surgery may even indicate that conventional surgery could have been successfully performed in the first place despite these significant comorbidities.

It is important for every surgeon to distinguish whether a patient is dying from aortic pathology (i.e. dissection or aneurysm) or with aortic pathology. Mack most recently described a method of patient selection for transcutaneous aortic valve replacement with regard to frailty and reported the usefulness of the 'eyeball test', grip strength and the 5-min walk test in order to assess whether a patient is best suited for conventional surgery, interventional treatment or conservative therapy [15]. Currently, there is no general consensus among the aortic experts in classifying 'fitness for open surgery', TEVAR or hybrid procedures, and therefore patient estimation of being 'too high risk' for open arch surgery depends on the surgeon's individual experience only!

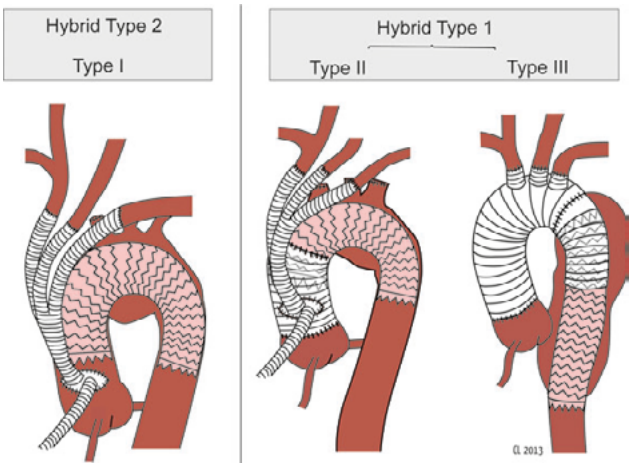

Figure 2: Suggested classification systems for hybrid aortic arch repair with regard to arch pathology by Koullias *et al.* [16] and Milewski *et al.* [7]. Supra-aortic de-branching followed by TEVAR of the arch; TEVAR procedure is primary (hybrid type 2/type I). Conventional hemiarch/arch replacement is performed; TEVAR procedure is secondary (hybrid type 1/type II and III).

Koullias and Wheatly suggested a new hybrid classification system for high-risk patients with regard to anatomy to allow for better decision making when deciding to replace the transverse arch surgically or to exclude the underlying aortic pathology by TEVAR: hybrid type 1 vs hybrid type 2 [16] (Fig. 2). With regard to their classification, the frozen elephant trunk technique could be used in patients requiring a hybrid type 1 repair, while off-pump supra-aortic de-branching with TEVAR of the arch would be indicated in a hybrid type 2 [16]. The Philadelphia group published another classification system (Type I–III) to address the varying pathologies of the transverse arch [7] (Fig. 2). They suggested the use of supra-aortic de-branching and TEVAR of the transverse arch in the 'classic' saccular aneurysm (Type I), while Type II and III have no suitable proximal landing zone (and distal landing zone in Type III) and therefore require reconstruction of Zone 0 by ascending aortic replacement [7]. In Type II or III, TEVAR may be performed antegradely during the same session (Type II, IIIa) or retrogradely *via* the femoral artery as a second-stage repair (Type IIIb).

Perioperative diagnostics and imaging are of outmost importance to diagnose post-TEVAR rAAD. Intraoperative transoesophageal echocardiogram (TEE) allows for the detection of acute rAAD during TEVAR, and therefore should be applied in every case [9]. A high degree of clinical suspicion should be used in the postoperative period, particularly if sudden hypotension occurs. At our institution, postoperative routine chest CT scan is performed 1 week post-TEVAR in order to exclude any procedure-related complications (e.g. subacute rAAD, endoleaks etc.), and to verify the therapeutic success (e.g. aneurysm exclusion).

Although our incidence of rAAD is worrisomely high in this small patient cohort, it is possible that the true incidence of post-TEVAR rAAD is under-reported in the current literature. We strongly believe that routine predischarge CT scan examination should be performed in all patients treated by TEVAR regardless of symptoms or clinical suspection.

As a result of our high incidence of rAAD after hybrid aortic de-branching and stent-grafting in patients (with extensive aortic pathologies involving the arch and the descending aorta), we now electively perform ascending aortic replacement with a four-branched prefabricated graft in all patients with ascending aortic ectasia (aortic diameter >4.0 cm) or aneurysm (hybrid type 2/Type II and III as described above), in order to achieve an extended proximal landing zone (3–4 cm in length) and to avoid the potential risk of rAAD. Moreover, we also avoid the use of conventional endovascular stent graft prostheses with protruding, rigid proximal bare springs during all hybrid de-branching procedures, particularly in patients with a dilated ascending aorta or distorted vascular anatomy. Finally, we are very selective when identifying patients for hybrid therapy, with conventional aortic arch surgery being our procedure of choice in the vast majority of patients.

CONCLUSION

rAAD represents a new and possibly under-reported complication after hybrid endovascular treatment of the aortic arch. The use of stent grafts with protruding proximal bare stents and the implementation of oversizing and post-deployment ballooning should be avoided in this high-risk cohort, particularly if the ascending aorta is dilated. An expert consensus should attempt to more accurately identify high-risk patients unsuitable for

conventional surgery who will benefit most from hybrid arch procedures.

Conflict of interest: none declared.

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6.8 Emergency open surgery for aorto-oesophageal and aorto-bronchial fistulae after thoracic endovascular aortic repair: a single-centre experience

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ORIGINAL ARTICLE

Emergency open surgery for aorto-oesophageal and aorto-bronchial fistulae after thoracic endovascular aortic repair: a single-centre experience†

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Abstract

OBJECTIVES: Severe complications after thoracic endovascular aortic repair (TEVAR), such as secondary aorto-oesophageal (AOF) or aorto-bronchial fistulae (ABF), are most likely under-reported; however, once detected, emergent surgery becomes necessary.

METHODS: Between June 2002 and September 2013, 10 (2.6%) of 374 patients (8 males; mean age 68 years, range: 49–77) were admitted with AOF ($n = 8$) or ABF ($n = 2$) post-TEVAR during follow-up (mean 12.9 months, range 0.2–48.1). The respective Ishimaru landing zones were 0 ($n = 1$), 2 ($n = 3$), 3 ($n = 4$) and 4 ($n = 2$). Median interval between TEVAR and AOF/ABF formation was 18.1 months (range 0.1–65.1). Symptoms on admission included haematemesis ($n = 4$), haemoptysis ($n = 2$), melena ($n = 1$), elevated C-reactive protein ($n = 10$), new-onset fever ($n = 3$), positive blood cultures ($n = 8$), dysphagia ($n = 1$), chest pain ($n = 4$), previous syncope ($n = 1$) and vertigo ($n = 1$). In 6 patients with AOF, stent graft removal required ascending aortic ($n = 1$), aortic arch ($n = 1$), left hemiarch ($n = 2$) and descending aortic ($n = 6$) replacement with concomitant oesophagectomy ($n = 4$) and cervical oesophagostomy ($n = 1$) or oesophageal repair ($n = 2$); another patient with AOF underwent oesophagectomy and cervical oesophagostomy via posterolateral thoracotomy without stent graft removal as a first-stage operation. One patient with ABF was treated by stent graft removal, aortic arch and descending aortic replacement in combination with bronchial repair. Two patients were deemed inoperable and treated conservatively.

RESULTS: All patients survived the operation. Reoperation due to postoperative mediastinitis, haemorrhage, pericardial tamponade and wound infection was required in 4 (50%, 95% confidence interval [CI] [22, 78]) patients. In-hospital mortality was 25% ($n = 2$; 95% CI [7, 59]) due to mediastinitis with resulting multiorgan failure ($n = 1$) and aortic rupture with haemorrhagic shock ($n = 1$). One patient died due to unknown cause on postoperative day 158. No neurological complications occurred postoperatively. Postoperative complications comprised acute renal failure with temporary dependence on haemodialysis ($n = 2$) and respiratory insufficiency ($n = 4$) requiring percutaneous tracheostomy ($n = 2$). Both patients treated conservatively died after 4 and 81 days due to pulmonary haemorrhage and fulminant mediastinitis, respectively.

CONCLUSIONS: AOF and ABF represent uncommon but fatal complications—if treated conservatively—after TEVAR that may occur during short- and mid-term follow-up. Surgery for AOF/ABF requires early diagnosis and should be performed promptly and in a radical fashion to totally excise all infected tissues in these high-risk patients.

Keywords: Aorto-oesophageal fistula • Aorto-bronchial fistula • Thoracic endovascular aortic repair • Stent graft infection • Aortic erosion • Postinterventional complication

INTRODUCTION

Thoracic endovascular aortic repair (TEVAR) has been clinically introduced in the mid-90s and is now increasingly advocated by many surgeons and interventionalists as the method of choice to treat thoracic aortic disease [1]. However, despite a reported low early postoperative mortality, stent grafts—if compared with open aortic surgery—may result in a higher incidence of long-term complications [2], potentially causing severe collateral damage to adjacent mediastinal structures [3], while associated with an equally increased risk of postoperative paraplegia [4].

Secondary aorto-oesophageal (AOF) and aorto-bronchial (ABF) fistulae have been known to be uncommon but fatal complications after open thoracic and thoracoabdominal aortic surgery [5].

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More recently, the incidence of AOF and ABF post-TEVAR has been described to be 1.5–1.9% [5–7]. However, the incidence of secondary AOF and ABF is most likely under-reported due to patients that are lost during follow-up and might even increase in the future, since TEVAR is nowadays not exclusively used in aortic emergencies or elderly high-risk patients [2, 3].

Since secondary AOF and ABF are uncommon and optimal treatment remains controversial, the purpose of this study was to report on the incidence, clinical presentation and outcomes after radical surgery in this high-risk cohort of post-TEVAR patients.

PATIENTS AND METHODS

A total of 374 patients underwent TEVAR at our institution between June 2002 and September 2013. We retrospectively identified 10 patients who were admitted either due to AOF ($n = 8$) or due to ABF ($n = 2$). The mean patient age was 67.6 ± 8.1 years (range 49–77) and 8 (80%, 95% confidence interval (CI) [49, 94]) were males. Follow-up post-TEVAR was 100% complete (mean 12.9 months; range 0.2–48.1). The patients' demographics and comorbidities are given in Table 1.

Endovascular procedures

The indications for TEVAR in the 10 patients were descending aortic aneurysm ($n = 5$), chronic ($n = 2$) or acute ($n = 1$) type B aortic dissection (TBAD), penetrating atherosclerotic ulcer (PAU; $n = 1$) and aberrant right subclavian artery aneurysm with aortic arch involvement ($n = 1$). Three different endovascular stent graft systems were used: Valiant (Medtronic Vascular, Santa Rosa, CA, USA) in 7 patients, Excluder (TAG; W.L. Gore and Associates, Inc., Flagstaff, AZ, USA) in 2 patients and Talent (Medtronic Vascular) in 1 patient. Retrograde stent graft deployment via the femoral artery ($n = 10$) was performed in the ascending aorta after complete supra-aortic debranching ($n = 1$), the aortic arch ($n = 3$) and the descending aorta ($n = 6$); the respective Ishimaru landing zones were 0 ($n = 1$), 2 ($n = 3$), 3 ($n = 4$) and 4 ($n = 2$). The single patient with stent graft deployment in landing zone 0 had received supra-aortic debranching prior to TEVAR. In 3 patients with an Ishimaru landing zone 2, intentional left subclavian artery (LSA) overstenting was performed; 1 of the 3 patients initially received left common carotid to LSA bypass before TEVAR. Another patient was initially treated with 1 stent graft for successful exclusion of a large descending aortic aneurysm but he required stent graft extension 5 years later due to aneurysmal progression of the distal landing zone. No endoleaks were noted during post-procedural angiography; post-deployment ballooning with stent graft oversizing of > 20%, 10–19% and 0–9% was performed in 5, 2 and 3 patients, respectively.

Table 1: Preoperative comorbidities and intraoperative data

Characteristics	Number of patients (% [95% CI])
Overall	10
Age (years, mean ± SD)	67.6 ± 8.1
Gender (male)	9 (90 [60, 99.5])
Hypertension	9 (90 [60, 99.5])
Coronary artery disease	4 (40 [17, 69])
Cardiomyopathy (EF < 30%)	2 (20 [6, 51])
Chronic obstructive pulmonary disease (COPD)	3 (30 [11, 60])
Previous pneumonia	4 (40 [17, 69])
Renal insufficiency	3 (30 [11, 60])
Diabetes mellitus	6 (60 [31, 83])
Obesity	4 (40 [17, 69])
Hyperlipidaemia	3 (30 [11, 60])
Peripheral vascular disease	3 (30 [11, 60])
Previous cardiac surgery	2 (20 [6, 51])
Previous cerebral infarction	1 (10 [0.5, 40])
Intraoperative data; patients ($n = 8$)	
CPB time, mean ± SD (range)	175 ± 77.7 min (117–220)
Femoral artery cannulation, *n* (% [95% CI])	7 (88 [53, 99.4])
Axillary artery cannulation, *n* (% [95% CI])	2 (25 [7, 59])
SCP, *n* (% [95% CI])	3 (38 [14, 69])
Distal aortic perfusion, *n* (% [95% CI])	6 (75 [31, 83])
Overall HCA temperature, mean (range)	26.1°C (21–32)
Deep-to-moderate HCA, mean (range)	22.2°C (21–24)
Mild HCA, mean (range)	31.3°C (30–32)
HCA time, mean ± SD (range)	13.5 ± 6.3 min (3–22)

CPB: cardiopulmonary bypass; SCP: selective cerebral perfusion; HCA: hypothermic circulatory arrest; CI: confidence interval.

Surgical procedures

All patients diagnosed with AOF or ABF were generally classified as surgical emergencies. The optimal treatment strategy was discussed on an individual basis by an interdisciplinary team including a cardiovascular surgeon, a general/visceral surgeon, a vascular interventionalist and a radiologist. However, re-TEVAR was not considered as a potential treatment option in these patients due to the underlying infectious process of the mediastinum with involvement of the previously implanted endovascular prostheses. Two patients were deemed inoperable and treated conservatively.

The details of our institutional surgical technique to address secondary surgical procedures after TEVAR have been described elsewhere [8, 9]. In brief, surgical access was achieved via a left-sited posterolateral thoracotomy ($n = 6$) or in combination with a full sternotomy ($n = 2$). Arterial cannulation for cardiopulmonary bypass (CPB; $n = 7$) was performed via the femoral ($n = 5$), the axillary artery ($n = 1$) or both ($n = 1$). The right axillary artery was cannulated to allow selective cerebral perfusion (SCP) along with direct cannulation of the right atrium for venous drainage ($n = 2$). Median CPB time was 17 5 ± 77.7 min (range 117–220).

Hypothermic circulatory arrest (HCA) was induced at deep-to-moderate hypothermia of 21–24°C ($n = 4$) by cross-clamping the lower descending aortic segment. However, intraoperative body core temperatures for hypothermic circulatory arrest (HCA) have been gradually increased to mild hypothermic conditions (30–33°C; $n = 3$) in the past few years. HCA without SCP was utilized in 5 patients (mean HCA duration 13.5 min; range 3–22). The head was packed externally in ice during HCA.

In all patients with aortic replacement—except 1 patient who was operated on at deep-to-moderate HCA of 22°C in combination with SCP—moderate distal aortic perfusion (25–32°C; 3 l/min) was performed retrogradely via the femoral artery ($n = 6$) for adequate visceral and spinal cord protection during the entire procedure. Perioperative cerebrospinal fluid (CSF) drainage as an additional measure to minimize the risk of paraplegia was used up to 72 h postoperatively. Intraoperative perfusion data are summarized in Table 1.

In 6 patients with AOF, stent graft removal required ascending aortic ($n = 1$), aortic arch ($n = 1$), left hemiarch ($n = 2$) and descending aortic ($n = 6$) replacement with concomitant oesophagectomy ($n = 4$) and cervical oesophagostomy ($n = 1$) or oesophageal repair by suture ($n = 2$) (Fig. 1); 2 of the 6 patients underwent a staged procedure: primary oesophagoectomy with cervical oesophagostomy via a left-sited posterolateral thoracotomy followed by aortic replacement in a second procedure ($n = 1$) and vice versa ($n = 1$). One patient with AOF—initially treated by supra-aortic debranching prior to TEVAR—who had been diagnosed with severe mediastinitis and several oesophageal abscesses underwent oesophagectomy and cervical oesophagostomy via a left-sited posterolateral thoracotomy without stent graft removal as a first-stage operation. Four AOF patients also received a percutaneous endoscopic gastrostomy tube to allow enteral nutrition postoperatively. The single patient with ABF underwent aortic arch and descending aortic replacement due to extensive aneurysm progression with bronchial repair. Table 2 gives an overview of the performed operative procedures.

Smear tests of the mediastinum and the infected prostheses were performed in all cases. All patients were treated either with broad-spectrum antibiotics (institutional protocol) or calculated antibiotic therapy with regard to previously isolated bacteria from the individual patient's blood cultures.

Study variables and definitions

The operative reports and clinical charts of all patients were retrospectively reviewed. The local ethics committee did not require additional patient consent.

Definite diagnosis of AOF or ABF fistula was defined as documented imaging results by endoscopy, CT, oesophagography or bronchioscopy.

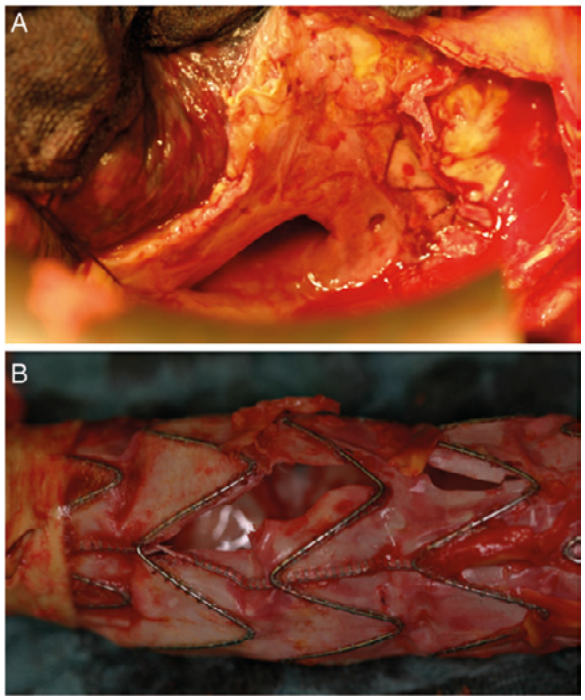

Figure 1: Intraoperative exposure of an aorto-oesophageal fistula after stent graft removal (**A**). Explanted endovascular stent graft; the prosthetic material has been dissolved by the infectious process (**B**).

HCA was defined as time of complete circulatory arrest (without SCP or distal aortic perfusion).

Renal failure was defined as an increase in serum creatinine of >1.5 mg/dl and temporary (resolved by the time of discharge) or permanent need for haemodialysis. Respiratory insufficiency was defined as weaning failure from mechanical ventilation by means of prolonged ventilation (>7 days) or requirement of reintubation or tracheostomy. Hospital mortality was defined according to current guidelines as death in hospital prior to discharge or within 30 days of surgery (regardless of location).

Follow-up was 100% complete with a mean follow-up time of 12.9 months (range 0.2–48.1). Follow-up was ascertained by a mailed paper questionnaire or a phone call to the patient or family members, or by contact with the family physician. It was performed by study personnel and consisted of information on patient vital status, symptomatology, and reoperations or hospitalisations. Supplemental information on CT or endoscopy findings was obtained when possible.

Statistical methods

Categorical data are reported as frequencies (percentages) and continuous variables as mean (range). 95% CIs were calculated following the method of Wilson by means of the R package binom.

RESULTS

Incidence and clinical presentation

Among the 374 patients treated by TEVAR between January 2002 and February 2013, the overall incidence of either AOF or ABF was 2.6% ($n = 10$); the respective incidence of AOF and ABF were 2.1%, 95% CI [1.1, 4.2]% ($n = 8$) and 0.5%, 95% CI [0.15, 1.9]% ($n = 2$).

Mean interval between TEVAR and development of AOF/ABF was 18.1 ± 24.8 months (range 0.1–65.1). Clinical symptoms on admission included haematemesis ($n = 4$), melena ($n = 1$) or haemoptysis ($n = 2$) with haemorrhagic shock ($n = 4$), new-onset fever ($n = 3$), elevated inflammatory laboratory parameters ($n = 10$), dysphagia ($n = 1$), dyspnea ($n = 1$), chest pain ($n = 4$), vertigo ($n = 1$) and previous syncope ($n = 1$).

At the time of admission, 8 (80%) patients were found to have positive blood cultures with bacteria. Mediastinal smear tests were positive in 6 cases. Antibiotics were continued for at least 3 months postoperatively. Table 3 gives an overview of the obtained microbiological data.

The initial diagnosis of AOF/ABF was performed via endoscopy ($n = 7$), CT ($n = 4$), bronchoscopy ($n = 1$) or oesophagography ($n = 1$) (Fig. 2). However, all patients received a CT of the thoracic and thoracoabdominal aorta (aortic protocol) prior to surgery; 1 patient had developed a type I endoleak and 4 patients were diagnosed with an endoleak type II fed by the LSA ($n = 3$) or a thoracic aortic segmental artery ($n = 1$) prior to open surgery.

Clinical symptoms of all patients at the time of admission for AOF/ABF are summarized in Table 4.

Hospital mortality and longevity

The respective in-hospital, 6-month mortality and 1-year mortality rates were 25% ($n = 2$), 37.5% ($n = 3$) and 37.5% ($n = 3$) for operated and 50% ($n = 1$), 100% ($n = 2$), 100% ($n = 2$) for conservatively

Table 2: Aetiologies, procedures and complications

Patient, age (yrs)	Aetiology	Previous TEVAR stent graft (*n*), length (mm)	Prox. LZ/ oversizing (%)	Type of fistula (length)/ Incidence of Endoleak	Operation aortic replacement; AOF or ABF repair	Postoperative complications	Hospital mortality
#1, 61	Acute TBAD	Valiant (1), 28 × 157	Z3/21	AOF (5 cm)/yes	DA replacement; oesophagectomy	–/–	No
#2, 71	DAA	Talent (1), 42 × 114	Z2/0	AOF (1.5 × 1.5 cm)/yes	Asc Ao, AA, DA replacement; oesophageal repair/staged cervical oesophagostomy	Rethoracotomy: mediastinitis, PE; Pneumonia, temp. dialysis, multi-organ failure	Yes
#3, 75	DAA	Valiant (1), 32–36 × 150	Z4/11	AOF (3 × 4 cm)/ no	DA replacement; oesophagectomy	Tracheostomy	No
#4, 49	PAU	Gore TAG (1), 31 × 100	Z2/26	AOF (5 × 2 cm)/ no	Left hemiarch, DA replacement; oesophagectomy/staged cervical oesophagostomy	Rethoracotomy: haemorrhage, PE, mediastinitis; Resp. insufficiency, wound infection	No
#5, 70	DAA	Gore TAG (1), 34 × 200; Talent (1) 34 × 114	Z4/21	AOF (0.5 cm)/no	DA, upper TAA replacement; oesophageal repair	Rethoracotomy: wound infection; Temp. dialysis	No
#6, 73	Aberrant RSAA	Valiant (1), 38 × 200	Z0/21	AOF (2 cm)/yes	-/Oesophagectomy and cervical oesophagostomy	Rethoracotomy: haemorrhage (x2)	Yes
#7, 66	Chronic TBAD	Valiant (1), 46 × 150	Z2/9	ABF (N.A.)/no	AA, DA replacement/bronchial repair	Splenectomy	No
#8, 74	DAA	Valiant (1), 34 × 160	Z3/18	AOF (6 cm)/yes	Oesophagectomy and cervical oesophagostomy/staged left hemiarch, DA replacement	Tracheostomy, pneumonia	No
#9, 77	DAA	Valiant (1), 44 × 200	Z3/21	AOF (5 cm)/no	–/–	–/–	–/–
#10, 59	Chronic TBAD	Valiant (1), 32 × 32 × 150	Z3/9	ABF (N.A.)/yes	–/–	–/–	–/–

TEVAR: throacic endovascular arotic repair; LZ: landing zone; AOF: aorto-oesophageal fistula; ABF: aorto-bronchial fistula; TBAD: type B aortic dissection; DAA: desecening aortic aneurysm; RSAA: right subclavian artery aneurysm; AscAo: ascending aorta; AA: aortic arch; DA: descending aorta; TAA: thoracoabdominal aorta; PE: pericardial effusion; N.A.: not available.

Table 3: Laboratory and microbiological data

Patient	C-reactive protein (CRP) mg/l	Leucocytes per microliter	New-onset fever	Blood cultures	Mediastinal smear test
#1	102	10200	Yes	Staphylococcus aureus	Staphylococcus aureus
#2	231	22200	Yes	No growth	No growth
#3	65	7080	No	Citrobacter freundii (ESBL)	Staphylococcus epidermidis, Proteus mirabilis, Citrobacter freundii, Steptococcus mitis, Prevotella oralis
#4	232	14400	Yes	Staphylococcus aureus	Staphylococcus aureus, Streptococcus mitis/oralis, Prevotella oralis (Bacteroides oralis), Candida albicans
#5	291	15100	No	No growth	Candida glabrata (Torulopsis glabrata), Propionibacterium acnes
#6	198	6160	No	Streptococcus anginosus	Streptococcus anginosus
#7	40	9660	No	Staphylococcus epidermidis	No growth
#8	29	8550	No	Staphylococcus anginosus, Escherichia coli (ESBL)	Streptococcus anginosus, Escherichia coli (ESBL) extended spectrum ß-lactamase
#9	404	9800	No	Lactobacillus species	–
#10	70	9660	No	Salmonella enteritis, Staphylococcus epidermidis	–

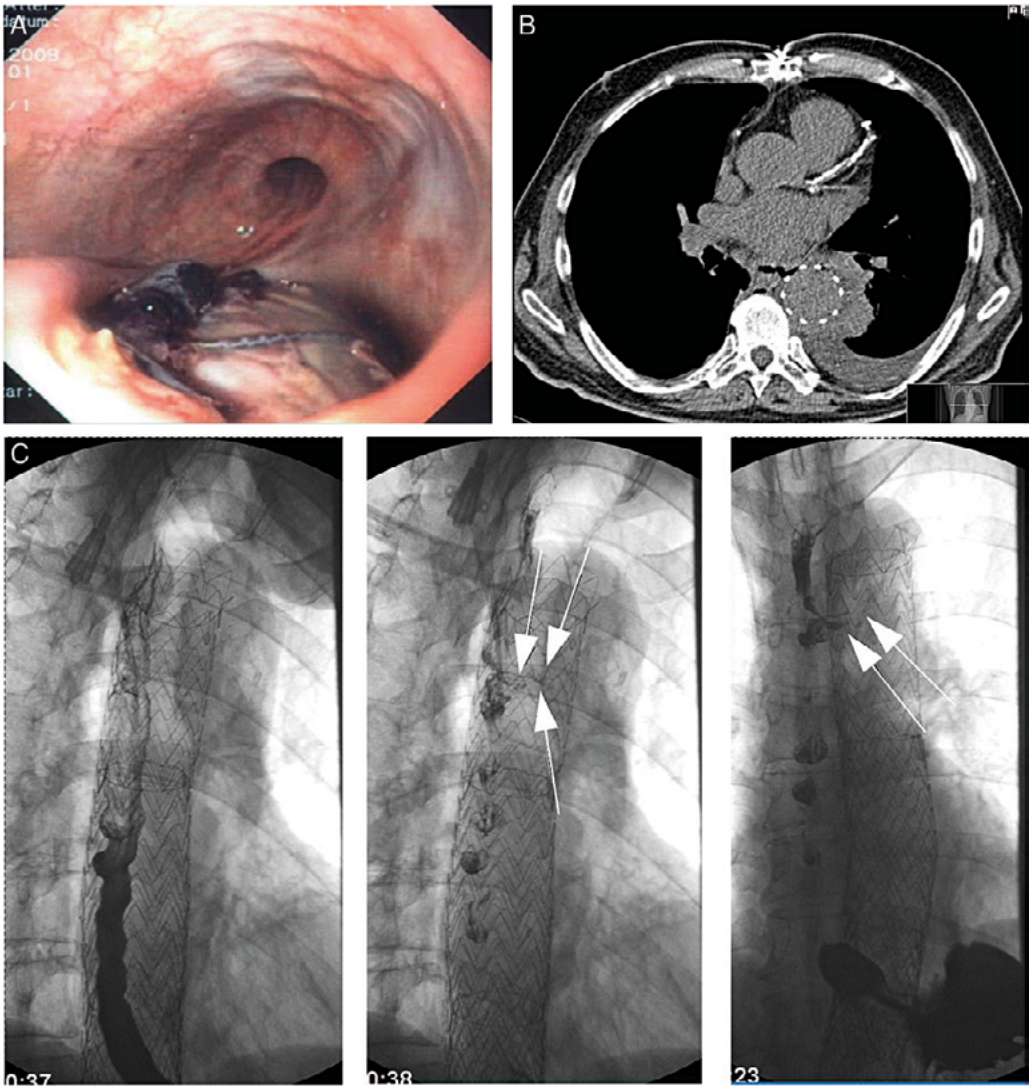

Figure 2: Diagnosis of aorto-oesophageal fistulae by endoscopy (**A**), computed tomography (**B**) or oesophagography (white arrows) (**C**).

treated patients. Postoperative follow-up was available for all patients and 100% complete. After a mean period of 12.9 months, 5 (62.5%) patients were still alive.

All initial open surgical procedures for stent graft removal and/or oesophageal resection were technically successful. However, 2 patients died within 40 days, resulting in an in-hospital mortality of 25%.

The first patient had been admitted in septic shock due to fulminant mediastinitis caused by AOF 4 months post-TEVAR (Fig. 3). He underwent oesophagectomy and cervical oesophagostomy via left posterolateral thoracotomy and secondary aortic surgery was planned after clinical stabilization. Six days later, he developed right-sited haemothorax with acute rupture of the ascending aorta and died as a result of hypovolemic shock in the operating theatre.

The second patient had been admitted due to AOF and was treated by aortic replacement with oesophageal repair and subsequent coverage by a pericardial patch. Postoperatively, the patient required prolonged mechanical ventilation. On postoperative day (POD) 14 the patient became septic and haemodynamically instable. Chest CT revealed a pneumomediastinum and reoccurrence of the AOF and pericardial effusion. After pericardial drainage, the patient successfully underwent oesophagoectomy with cervical oesophagostomy. However, the patient ultimately developed multiorgan failure during the following clinical course and died on POD 40.

Postoperative complications

Complications leading to rethoracotomy occurred in 4 (50%) patients and were in detail: mediastinitis ($n = 2$), postoperative haemorrhage ($n = 2$), pericardial tamponade ($n = 2$) and wound infection ($n = 2$). Another patient with chronic TBAD required splenectomy via a left-sited laparotomy due to preoperative infarction of the spleen.

Four patients—including 2 individuals with chronic obstructive pulmonary disease—developed respiratory insufficiency. Percutaneous tracheostomy was required in 1 patient with COPD and 1 patient due to postoperative pneumonia in order to be weaned from the ventilator. Temporary dialysis due to acute renal failure occurred in 2 (25%) patients—with 1 of them developing

Table 4: Patient presentation and diagnostics

Incidence of AOF/ABF; patients (n = 10)	
Overall, n (% [95% CI])	10 (2.7 [1.5, 4.9])
AOF, n (% [95% CI])	8 (2.1 [1.1, 4.2])
ABF, n (% [95% CI])	2 (0.5 [0.15, 1.9])
Timing	
Months since TEVAR, mean ± SD (range)	18.1 ± 24.8 (0.1–65.1)
Clinical symptoms	
Elevated C-reactive protein, mg/ l ± SD (range)	166.2 ± 118.3 (29–404)
New-onset fever, n (% [95% CI])	3 (30 [11, 60])
Positive blood cultures, n (% [95% CI])	8 (80 [49, 94])
Haematemesis, n (% [95% CI])	4 (40 [17, 69])
Haemoptysis, n (% [95% CI])	2 (20 [6, 51])
Melena, n (% [95% CI])	1 (10 [0.5, 40])
Haemorrhagic shock, n (% [95% CI])	4 (40 [17, 69])
Chest pain, n (% [95% CI])	4 (40 [17, 69])
Dysphagia, n (% [95% CI])	1 (10 [0.5, 40])
Dyspnoea, n (% [95% CI])	1 (10 [0.5, 40])
Vertigo, n (% [95% CI])	1 (10 [0.5, 40])
Syncope, n (% [95% CI])	1 (10 [0.5, 40])
Exhaustion, n (% [95% CI])	1 (10 [0.5, 40])
Evidentiary preoperative diagnostics	
Computed tomography, n (% [95% CI])	4 (40 [17, 69])
Endoscopy, n (% [95% CI])	7 (70 [40, 89])
Oesophagography, n (% [95% CI])	1 (10 [0.5, 40])
Bronchoscopy, n (% [95% CI])	1 (10 [0.5, 40])

TEVAR: thoracic endovascular aortic repair; AOF: aorto-oesophageal fistula; ABF: aorto-bronchial fistula; CI: confidence interval.

multiorgan failure during his clinical course. No new neurological complications occurred postoperatively.

Overall mean time to hospital discharge was 30 ± 21.4 days (range 3–68). Postoperative complications are listed in Table 2.

Non-surgical treatment

Two patients with AOF (n = 1) and ABF (n = 1) were deemed inoperable at the time of diagnosis, and therefore were treated conservatively.

The first patient had successfully undergone emergency TEVAR for chronic TBAD with covered aortic rupture. On POD 5 surveillance CT of the chest revealed an endoleak type I that was treated by intra-aortic angioplasty with ballooning at the proximal and distal end of the prosthesis on the same day; postinterventional angiography showed no persisting endoleak. However, on the next day, he developed haemoptysis and was transferred to the ICU due to haemodynamic instability. Chest CT revealed an ABF of the left main bronchus (Fig. 4). On POD 7, he acutely developed massive haemoptysis—including small parts of lung tissue—requiring reintubation with a double lumen endotracheal tube and cardiopulmonary resuscitation. However, the patient died shortly after successful CPR due to significant pulmonary bleeding and subsequent haemorrhagic shock.

The second patient had been initially treated endovascularly for acute rupture of her descending aortic aneurysm but returned 42 days post-TEVAR due to development of an AOF. Patient history revealed chest pain and haematemesis prior to syncope. On admission, the patient was already intubated and sedated. Endoscopy revealed a large AOF (length: 5 cm) located in the mid-oesophagus without an active bleeding source. Due to various other comorbidities, including ongoing left-sited pneumonia and urinary tract infection, the patient was treated medically and died after 81 days due to fulminant mediastinitis.

DISCUSSION

Described for the first time by Dubrueil in 1818 and Girardet in 1914, primary AOF and ABF have been known to be extremely rare but lethal clinical entities [10, 11]. Secondary AOF/ABF after open thoracic aortic surgery occur with an increased incidence in up to 1.7% of patients following open thoracic aortic surgery [5].

Although long-term outcomes (>10 years) after stent grafting of the thoracic aorta are still unknown, TEVAR is now being proclaimed by many interventionalists as the method of choice to address thoracic aortic pathologies [2]. With increased use of TEVAR, formerly unknown complications such as retrograde aortic dissection [12] and other uncommon severe complications have been described [4, 6]. In this context, the clinical incidence of secondary AOF and ABF post-TEVAR is currently reported to be 1.5–1.9% [5–7].

We report an overall incidence of AOF/ABF of 2.6% in a consecutive patient cohort of 374 patients over a period of more than 10 years as a single-centre experience—with a respective incidence of AOF and ABF of 2.1 and 0.5%.

The mean time interval between TEVAR and AOF/ABF development was 18 months, with 7 (70%) patients being readmitted within the first year after treatment (< 12 months). In 2009, Chiesa *et al*. reported a mean interval to AOF (68%), ABF (5%) or combined AOF/ABF (26%) after thoracic stent grafting of 11 months (10.9 ± 15.4 months). Most recently, data by the European Registry of Endovascular Aortic Repair Complications (EuREC) showed a median TEVAR-to-AOF time of ∼3 months (90 days) [6]. However, the underlying mechanisms of secondary AOF and ABF development post-TEVAR are still unknown.

Czerny *et al*. [6] hypothesized that AOF development may be associated with the need for an emergency procedure and the presence of mediastinal haematoma prior to TEVAR. Secondary oesophageal ischaemia may be the result of elevated pressures within the posterior mediastinum, ultimately leading to AOF formation. Similarly, ABF may occur if the bronchial artery is completely excluded during TEVAR, resulting in bronchopulmonary ischaemia [13]. Chronic inflammation—due to resorption of the haematoma or aortic compression and erosion by the implanted stent graft—is another theory of AOF/ABF development [5, 6].

Endoleaks after endovascular stent grafting during follow-up have also been reported to represent a potential cause of AOF/ABF development [7, 8]. In our series, 5 of 10 patients (50%) with AOF/ABF developed an endoleak (type I: n = 1, type II: n = 4), including 2 patients with intentional LSA coverage. Although intentional LSA coverage may be performed safely to achieve an adequate proximal landing zone, this strategy may increase the risk of a persisting endoleak type II and possible AOF/ABF formation. LSA transposition, ligation with left common carotid artery to LSA bypass or LSA embolization post-TEVAR could prevent potential type II endoleaks (risk for steal from the left vertebral artery) or neurological complications in cases with a proximal Ishimaru landing zone within the arch 0–2 [14]. Type II endoleak post-TEVAR also occurred in 1 patient due to back bleeding from a prominent thoracic aortic segmental artery; this represents

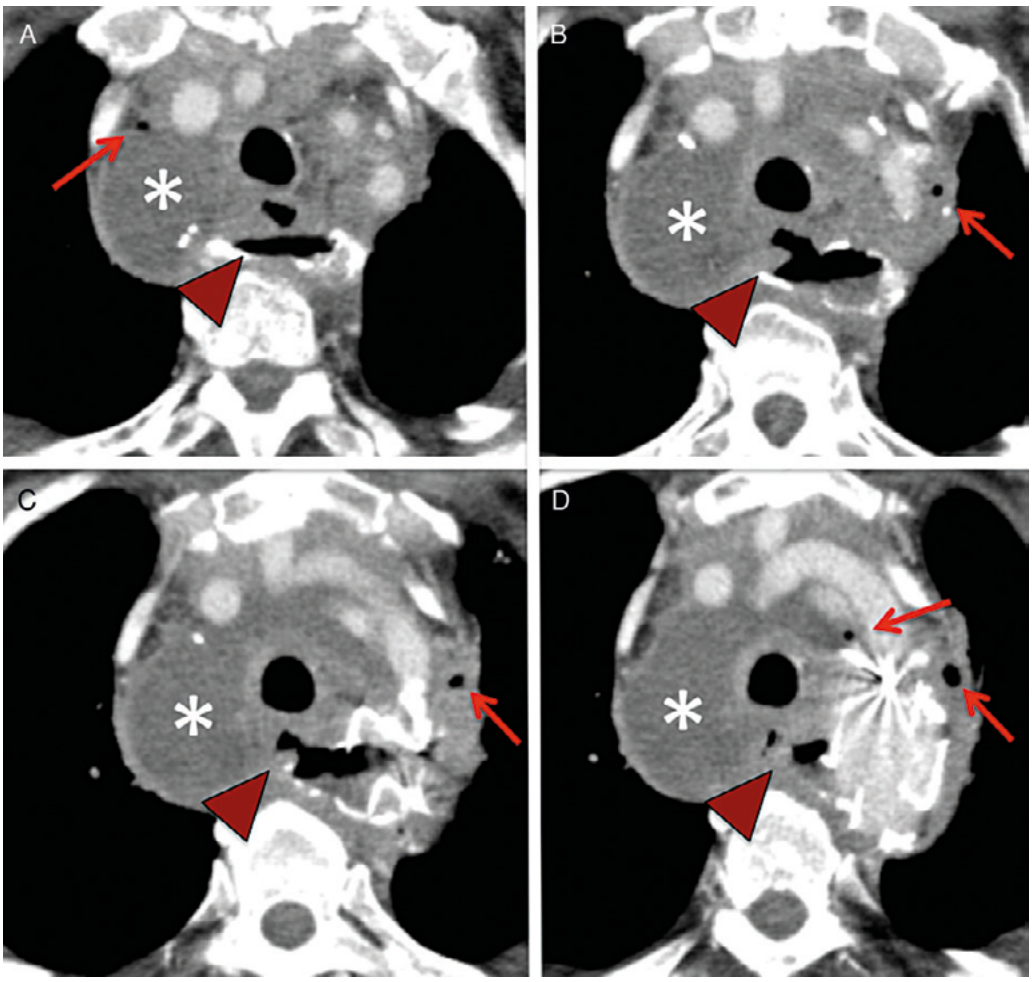

Figure 3: Computed tomography after readmission showing mediastinits (asterisk) and an aorto-oesophageal fistula (dark red arrow heads) after TEVAR at the level of the transverse arch (**A–D**). Ectopic gas can be found within the mediastinum (red arrows).

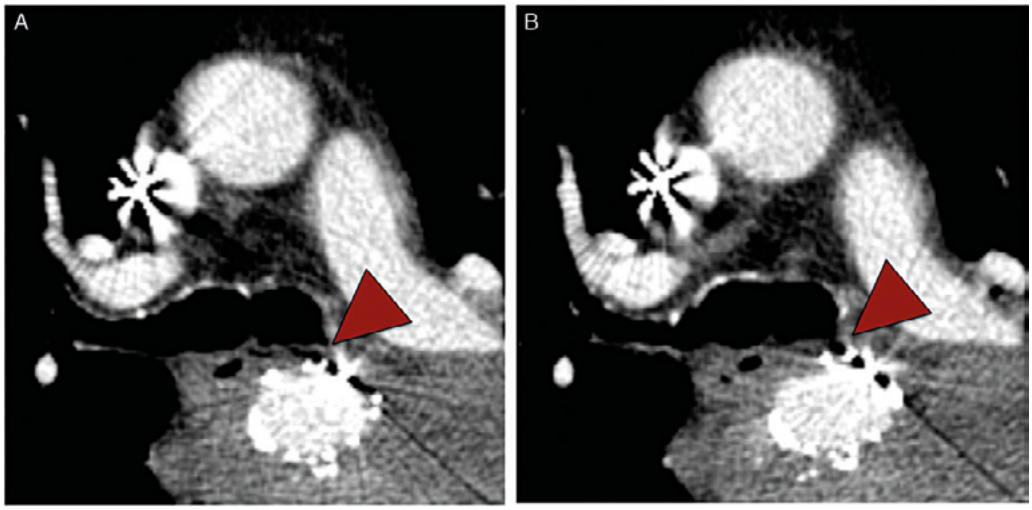

Figure 4: Computed tomography of the chest showing an aorto-bronchial fistula with a communication between the left main bronchus and the stent graft at the level of the descending aorta (dark red arrow heads; **A** and **B**).

another unsolved problem of TEVAR, especially after extensive endovascular thoracic and thoracoabdominal aortic coverage. New innovative strategies, such as segmental artery coil embolization prior to TEVAR, are currently under investigation to address this issue [15].

During stent graft deployment, oversizing may be necessary to achieve an optimal result on post-procedural angiography. However, oversizing may increase the risk of aortic wall deterioration and fistula formation [5, 12]. Stent graft oversizing was performed in almost all patients of our series ($n = 9$; Table 2), including 5 (50%) patients with an intra-procedural oversizing of >20%. We can conclude that oversizing of more than 20% should be avoided if possible during TEVAR [5].

Recently, the use of stent grafts with rigid, proximal bare springs has also been noted to bare a potential risk of aortic intimal erosion, retrograde aortic dissection, free rupture and/or aortic penetration with damage to adjacent mediastinal structures causing a state of chronic inflammation [3, 6, 12, 16]. We have previously demonstrated that proximal bare springs may increase the risk for aortic intimal damage—and potential AOF/ABF formation—in patients with an ectatic/dilated native thoracic aorta [12] (Fig. 3).

Patients with AOF/ABF present with a variety of clinical symptoms, which may lead to a significant delay in diagnosis and treatment. Patients frequently have a history of self-limited haematemesis or haemoptysis ('sentinel' or 'herald bleedings', Table 4) with no significant decrease in haemoglobin [5, 7, 17]. At the time of bleeding recurrence, patients often present with haemorrhagic shock requiring emergent surgical treatment [8]. Therefore, a history of bleeding (haematemesis, haempotysis, melena, etc.) should raise the suspicion of secondary fistula formation after TEVAR and further diagnostics such as CT, endoscopy and/or bronchioscopy should be performed promptly.

Of note, only 3 patients in this series presented with new-onset fever but all ($n = 10$; 100%) were found to have elevated inflammatory laboratory parameters and positive blood cultures with bacteria ($n = 8$; 80%) at the time of AOF/ABF diagnosis. Intraoperative mediastinal smear tests detected bacteria ($n = 6$; 75%) or fungi ($n = 2$; 25%) in 6 of 8 patients (see Table 3).

One of our patients presented with nonspecific symptoms (i.e. vertigo and chest pain) and the diagnosis of AOF was made only after CT imaging (Fig. 2). Other nonspecific symptoms—such as dyspnea, dysphagia, previous syncope, new onset fever or exhaustion—were always accompanied by more definite symptoms suggestive of AOF or ABF (i.e. haemoptysis or haematemesis). We therefore suggest to closely follow all patients post-TEVAR and to expect late complications after endovascular treatment even if patients present with uncommon or unspecific clinical symptoms.

The optimal treatment for secondary AOF/ABF has been discussed controversially in the literature. Medical treatment alone is known to be inadequate with a mortality rate of 100% [5–7, 18].

Re-TEVAR as a treatment option for AOF/ABF has been reported by some investigators [19, 20], but seems very questionable since the infected prosthesis remains in place and debridement of infected tissue cannot be performed [20, 21]. Moreover, life-long antibiotic therapy would be necessary in these high-risk patients. We believe that emergency TEVAR for AOF should only be used as a 'bridge-to-surgery' in haemodynamically unstable patients [9, 22].

It has been suggested that open surgery offers the best outcome in the treatment of primary and secondary AOF/ABF, but no consensus about the optimal surgical strategy exists [6, 18]. Mortality after open repair for AOF/ABF has been reported to be 64% [5] with a 1-year survival between 16 and 57% [5, 6].

Extra-anatomic aortic bypass has been initially reported by Yonago *et al.* [17] in 1969 and is still considered an alternative surgical strategy to manage a primary or secondary AOF/ABF. An omental flap has been reported for patients with aorto-enteric fistula [23]. Most recently, Okita *et al.* presented their results for open surgery of primary and secondary AOF (post-TEVAR patients: $n = 4$) at the 27th EACTS Annual Meeting in Vienna and reported a low hospital mortality rate of 26.7%. Their surgical strategy comprised simultaneous resection of the aorta and the oesophagus followed by *in situ* reconstruction of the descending aorta using a rifampicin-soaked Dacron graft with additional coverage of an omental (or intercostal muscle) flap [22].

Others investigators favour the use of cryopreserved aortic allografts (homografts) and have achieved similar results with an equally low mortality rate of 27% [24]. However, homografts may not always be available at a time and usually tend to be too short and of a small diameter to allow aortic replacement in AOF/ABF cases. A promising alternative could be the use of 2–3 self-made pericardial tubes, e.g. by wrapping around a conventional 15 × 10 cm pericardial patch to get a 3.5 cm tube.

Canaud *et al.* [25] most recently reported on their results after secondary open surgery in a heterogeneous post-TEVAR cohort of 14 of 236 patients and reported an extraordinary low hospital mortality of 14.3% with a 2-year survival rate of 87.7%. However, their surgical series of 14 patients included only 7 patients (50%) with AOF ($n = 1$) and ABF ($n = 6$).

We are convinced that prompt and radical surgical therapy represents the treatment of choice in patients with post-TEVAR complications [8, 9]. In AOF patients, we perform a staged surgical approach: oesophagectomy (with or without oesophagostomy) with radical excision of all infected tissue, stent graft removal and aortic replacement followed by second-stage oesophageal reconstruction, e.g. gastric pull-up operation. For patients with ABF, we perform a similar approach to the aorta/stent along with appropriate bronchial repair, e.g. flap coverage or lobectomy.

CONCLUSIONS

AOF and ABF represent uncommon but fatal complications after TEVAR that may occur during short- and mid-term follow-up. Surgery for AOF/ABF requires detailed planning and should be performed promptly and in a radical fashion to excise all infected tissues. However, more data is required on the surgical outcome of patients with fistula formation after TEVAR in order to determine the optimal surgical strategy of these challenging patients.

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APPENDIX. CONFERENCE DISCUSSION

Dr M. Schepens *(Brugge, Belgium)*: I just have a brief question. I didn't notice from your data that you use omentoplasty to treat this kind of severe problem. Do you think it has any place in the treatment?

Dr Etz: I personally think this is an option if the patient presents with severe mediastinitis. In this cohort there was only one patient in whom it was considered, but we would rather go for radical resection right now. Presently, data is scarce and we do not utilize omentoplasty much in Leipzig. In this cohort there was only one patient who had a pericardial patch but there was no one that received an omentoplasty. Nevertheless, I think it is a valid option.

Dr Schepens: What is your opinion about complete resection of the aneurysmal wall, since the previous speaker really said that it was important to remove the whole aneurysm?

Dr Etz: The way I was trained by Dr Griepp is to remove as much diseased aneurysmal tissue as possible, particularly when you are in doubt. If infection is excluded, I think it's okay to leave aneurysmal wall behind if you have a bleeding issue as a major problem, for instance.

Dr Y. Okita *(Kobe, Japan)*: I have two questions. This is a postop TEVAR experience.

Dr Etz: Right.

Dr Okita: In Leipzig, how many had a primary aorto-oesophageal fistula? If you know, please tell us.

Dr Etz: A primary aneurysm?

Dr Okita: An aorto-oesophageal fistula.

Dr Etz: So primary after TEVAR or primary -

Dr Okita: No, no, before.

Dr Etz: In Leipzig it is very rare that a patient comes with a primary untreated aneurysm that's eroding the oesophagus. The raw numbers do not tell us much about the incidence because we neither know the true denominator nor the number of patients that never reach the hospital because of an acute and fatal haemorrhage after rupture.

Dr Okita: This is rare, right?

Dr Etz: It is rare.

Dr Okita: And the second question. You are comparing the results of aorto-oesophageal and aortobronchial. Can you find any difference regarding the mortality between the two of them?

Dr Etz: With the small numbers we have, there is really no way to tell, particularly with only two patients presenting with an aortobronchial fistula. The way these patients present is often quite dramatic as we all know, sometimes with recurrent haematemesis or haemoptysis as direct heralds of imminent rupture. This is one of the reasons why it's probably an under-reported complication. These patients die a sudden death and you don't see them in the hospital.

Dr Okita: Did you do a lung resection as well?

Dr Etz: No, but if it's necessary, if the aneurysm is eroding the lung for instance, we would.

Dr C. Knosalla *(Berlin, Germany)*: I have three questions. First, I would like to know what your current strategy is when dealing with aorto-oesophageal fistula. In which cases do you try to repair the oesophagus? Or do you immediately resort to oesophagectomy to really eradicate it?

And my second question is, as I did my vascular training with Edouard Kieffer in Paris, where do you see the value of allografts in this indication?

And thirdly, you did these operations over quite a period of time and you said you have 100% follow-up in your hospital. So I would imagine that you can give us some more details about recurrence rates after one year.

Dr Etz: Let's start with the first question, what I think about oesophageal repair as opposed to a staged radical resection. In our experience, there was only one patient that had an oesophageal repair, and his survival was poor. First of all, it is always an individual decision, of course, and there is no large experience that we could base it on. But whenever you have a case that goes wrong and you are in doubt whether oesophageal repair is feasible, then it is probably better to perform radical resection, and since we had an experience with this one case we are hesitant with regard to repair. If it is a very small lesion (and possibly depending on who is on call), I would not categorically declare that it would never undergo repair, but we do not generally recommend it.

Regarding your second question, usually we have a number of proximal homografts available and only a few thoracic homografts. If there's availability and we think that the inflammation is a major problem and that there may be difficulties with the proximal anastomosis, for instance, then we would opt for a homograft, if available, yes. And the last question was, again?

Dr Knosalla: The recurrence rate after one year, because these cases really can have late reinfections, particularly if you use prosthetic grafts.

Dr Etz: I believe, and this is what I was taught by Dr Griepp, in reporting one-year mortality as a measure of operative success: this is the true number; reporting hospital mortality, 60-day, and whatever, is not. These are very extensive surgeries and one-year survival is the true number. So that's what we have been reporting; in our series it was 62.5%. I think this is probably the best you can get at this point with these desperate cases at one year.

And you're absolutely right, the study is over a long time period and some of the patients had been operated on before I joined the Leipzig team. Even so, I think our data are resilient, because we have a lot of research personnel thoroughly questioning not only the patients themselves, but also calling the GPs, and if there is any doubt, then the previous operating surgeon is contacted as well.

Dr A. Apaydin *(Izmir, Turkey)*: The homografts, they have a short-term risk of rupture; I think it's about 11%. So they are not very safe, you should keep it in mind.

Dr J. Bachet *(Paris, France)*: You said one thing that intrigues me. You say, 'of course homografts.' These patients are completely unexpected patients, and I suppose that you don't have homografts on the shelf like we have valves.

Dr Etz: Exactly. What I said is, of course, we consider their use.

Dr Bachet: Well, you can consider everything you like.

Dr Etz: If we have homografts available (and Leipzig is a large institution so we have a little more in stock probably than other institutions), yes, we would consider using them. But I totally share your concern.

Dr Bachet: But I suppose they are not very often available, as you said.

Dr Etz: That's right.

Dr Bachet: On the other hand, what do you think of what Thierry Carrel's group proposed, which is to use systemically preserved pericardium? They have published very good results.

Dr Etz: It is also used, yes, of course. It's a good option, I think.

Dr M. Borger *(Leipzig, Germany)*: Just a comment to Dr Bachet. We only have one descending thoracic aortic homograft at a time in our institution. The other more important problem is that they tend to have quite a small diameter and you can't match the size of the homograft to the size of the native aorta, which is usually dilated. Especially by the time you take out the stent, you are often left with this long segment of dilated aorta that needs to be replaced, which is difficult with a homograft.

Until now, we have performed repair of aorto-oesophageal fistula with a standard prosthetic graft. However, we've used bovine pericardium, as you are referring to, in patients with mycotic aneurysms where the area of involved aortic pathology tends to be much shorter. Since we have been very happy with pericardium for mycotic aneurysms, we will probably start using this technique for oesophageal fistulae. However, one would need to sew together three of these pericardial tubes, in order to achieve the correct length and diameter. That is, you take a 15×10 cm pericardial patch, wrap it around and sew the edges together in order to achieve a 3.5 cm diameter tube and then sew enough of these tubes together in order to replace the affected aorta.

Dr W. Harringer *(Braunschweig, Germany)*: This is an excellent technical explanation of how you do it, especially if you don't have homografts of the appropriate size available. I personally still prefer homografts. We also have some of them on the shelf. But this is clearly an individual situation. If you don't have them, then either (as Professor Okita's group) use soaked Dacron or use pericardium as an alternative to prosthetic material. It's not an invention by the Bern group because it has been done before by others, years before, because they didn't have alternatives. But it seems to be an excellent choice if you don't have other material available in these infective situations.

But let me ask you one more thing. The one-year survival rate came down, of course. How many of these patients died of infection or reinfection? What were the reasons for death, do you know that?

Dr Etz: Two patients that died had been deemed to be inoperable. One was already presenting with signs of infection, so in this case we know the cause. The other one died after fulminant haemorrhage. However, once they are home after surgery, the follow-up on the cause of death is very difficult.

Dr M. Picichè *(Rome, Italy)*: My question is about the interval between the beginning of massive haemoptysis and the operation, because, of course, this requires management. What do you do? Do you use a Carlens tube and occlude one side in order to avoid blood flooding into the other side of the bronchus, in case of aorto-oesophageal fistula?

Dr Etz: Fortunately, sentinel bleeding often occurs, which raises our suspicions. We are very alert in these acute emergencies but we have not routinely used a Sengstaken–Blakemore tube, although we used a bronchus blocker in one case – whatever you need to get the patient alive to the OR suite. There is no protocol as such.