New techniques and principles in acute aortic pathologies requiring emergency surgical interventions

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PhD Thesis

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List of publications related to subject of thesis

I. **Göbölös L,** Philipp A, Foltan M, Wiebe K*: Surgical management for Stanford type A aortic dissection: direct cannulation of real lumen at the level of the Botallo's ligament by Seldinger technique.* Interact Cardiovasc Thorac Surg. 2008;7(6):1107-1109.

II. **Göbölös L,** Foltan M, Ugocsai M, Thrum A, Philipp A, Livesey SA, Tsang GM, Ohri SK. *Recent advances in the management of Acute Aortic Syndrome. In: Nazari S (editor): Front lines of Thoracic Surgery.* Milano: 2012; ISBN 978-953-307-915-918.

III. **Göbölös L,** Miskolczi Sz, Pousios D, Tsang GM, Livesey SA, Barlow CW, Kaarne M, Shambrook J, Lipnevicius A, Ohri SK. *Management options for aorto- oesophageal fistula: case histories and review of the literature.* Perfusion. 2013;28(4):286-290.

IV. **Göbölös L,** Philipp A, Ugocsai P, Foltan M, Thrum A, Miskolczi Sz, Pousios D, Khawaja S, Budra M, Ohri SK. *Reliability of different body temperature measurement sites during aortic surgery.* Perfusion. 2014;29(1):75-81.

V. **Göbölös L,** Ugocsai P, Foltan M, Philipp A, Thrum A, Miskolczi Sz, Malvindi PG, di Gregorio V, Pousios D, Navaratnarajah M, Ohri SK. *Central cannulation by Seldinger technique: A reliable method in Type A aortic dissection repairs.* Med Sci Monit. 2014;20:2386-2393.

VI. **Göbölös L,** Tsang GM, Curzen N, Calver AJ, Ohri SK. *Transapical perfusion for peri-arrest salvage during transcutaneous aortic valve implantation.* Perfusion. 2015;30(8):650-652.

VII. Miskolczi S, Sheppard MN, Bogáts G, **Göbölös L.** *Double-locus lymphoplasmacytic aortitis.* Asian Cardiovasc Thorac Ann. 2018;26(3):231-233.

VIII. Malvindi PG, Votano D, Ashoub A, Modi A, Miskolczi Sz, Velissaris Th, Barlow CW, Ohri SK, Tsang GM, Livesey SA, **Göbölös L.** *Age-related presentation of acute type A aortic dissection.* Asian Cardiovasc Thorac Ann. 2018;26(9):659-666.

IX. **Göbölös L,** Bajwa G, Ramahi J, Bergonzi PC, Bhatnagar G. *An aortic "supravalvular shelf" is not always innocuous.* NEMJ. 2020;2(1):3-5. ISSN: 0250-6882.

X. **Göbölös L,** Bonatti J, Bogáts G. *A comprehensive guide to new directions in thoracic aortic surgery. In: Horizons in World Cardiovascular Research.* Nova Science Publishers Inc., Hauppauge, NY: 2020; ISBN 978-1-53617-615-5. (In Press)

List of presentations related to subject of thesis

I. **Göbölös L**, Hejjel L, Philipp A, Foltan M, Imre J, Zelenka M, Birnbaum DE, Wiebe K: *Surgical management for Stanford type A aortic dissection: direct cannulation of the real lumen at the level of Botallo`s ligament by Seldinger technique.* 13th Annual Meeting of the Hungarian Society of Cardiac Surgery (2006)

II. **Göbölös L**, Philipp A, Thrum A, Foltan M, Lindenmayer-G. R, Wiebe K: *Antegrade selective carotid perfusion during surgical repair of the thoracic aorta.* Annual Meeting of the Hungarian Society of Cardiology (2008)

III. **Göbölös L,** Philipp A, Lindenmayer-G. R, Foltan M, Thrum A, Szabados S, Hejjel L, Lénárd L, Wiebe K: *Central cannulation by Seldinger technique: a reliable method in ascending aorta and aortic arch replacement.* 15th Annual Meeting of the Hungarian Society of Cardiac Surgery (2008)

IV. **Göbölös L**, Ugocsai P, Foltan M, Lindenmayer-G. R, Philipp A, Thrum A, Szabados S, Hejjel L, Lénárd L, Wiebe K: *Reliability of different body temperature measurement methods during aortic surgery.* 16th Annual Meeting of the Hungarian Society of Cardiac Surgery (2009)

V. **Göbölös L**, Miskolczi Sz, Pousios D, Tsang GM, Livesey SA, Kaarne M, Barlow CW, Shambrook J, Ohri SK: *Management options for aortooesophageal fistula.* Aortic Symposium of the AATS, New York (2012)

VI. **Invited lecture: Göbölös L,** Ugocsai P, Miskolczi Sz, Foltan M, Philipp A, Ther G, Ohri SK: *Management options for Acute Aortic Syndrome.* Yangtze River International Congress of Cardiology, Daping Hospital, Third Military Medical University, Chongqing, China (2013)

VII. **Invited presentation: Göbölös L**, Votano D, Ashoub A, Modi A, Miskolczi Sz, Malvindi PG. *Age-related presentation of acute type A aortic dissection.* 23rd Annual Meeting of the Hungarian Society of Cardiac Surgery (2016)

VIII. **Invited presentation: Göbölös L:** *Acute Aortic Syndrome - The Southampton Experience.* Emergency Medicine Forum, Debrecen, Hungary (2016)

IX. **Invited presentation: Göbölös L.** *Cornerstones in cardiosurgical stroke risk reduction: the CCAD opinion.* International Conference on Neurology and Cardiology, Dubai (2018)

Content

Glossary of terms and abbreviations

AAS	Acute Aortic Syndrome
ACP	Antegrade Cerebral Perfusion
AHA	American Heart Associantion
AOF	Aortooesophageal Fistula
AxS	Axillary/Subclavian Artery
BSA	Body Surface Area
CAD	Coronary Artery Disease
COPD	Chronic Obstructive Pulmonary Disease
CPB	Cardiopulmonary Bypass
CT	Computed Tomography
ECC	Extracorporeal Circulation
ECG	Electrocardiogram
FTAA	Familial Thoracic Aortic Aneurysms
GERAADA	German Registry for Acute Aortic Dissection Type A
HCA	Hypothermic Circulatory Arrest
ICU	Intensive Care Unit
IMH	Intramural Haematoma
IRAD	International Registry of Aortic Dissection
MMP	Matrix Metalloproteinase
MRI	Magnetic Resonance Imaging
NIRS	Near Infrared Spectroscopy
PAU	Penetrating Atherosclerotic Ulcer
SACP	Selective Antegrade Cerebral Perfusion
STJ	Sinotubular Junction
TAA	Thoracic Aortic Aneurysm
TAAD	Type A Aortic Dissection
TBAD	Type B Aortic Dissection
TEVAR	Transcatheter Endovascular Aortic Repair
TOE	Transoesophageal Echocardiogram
TTE	Transthoracic Echocardiogram
UACP	Unilateral Antegrade Cerebral Perfusion

Summary

Aortic surgery, especially for pathologies requiring urgent surgical intervention has undergone significant changes in the past twenty years, leading to major improvement in short- and long-term outcomes. This thesis aims to provide a comprehensive, up-to-date overview on clinical characteristics of acute aortic syndrome, with special emphasis on current operative treatment possibilities, including well-established and novel, innovative surgical approaches. Within this scheme, further specific goals are to analyse different cannulation and perfusion options, the role of core temperature management during hypothermic circulatory arrest and impact of age-related differences in surgical approach of AAS.

Ultrasound-guided direct cannulation on the concavity of aortic arch applying Seldinger technique is a reliable method in dissection repairs. Prompt antegrade perfusion provides not only cerebral, but also peripheral organ and tissue protection, which is an advantage in this high-risk group of patients. This alternative arterial inflow technique can be applied for prompt establishment of cardiopulmonary bypass in type A dissections or other aortic emergencies, especially during haemodynamic instability.

We have proven that tympanic temperature measurements correlate with arterial blood temperature monitoring during aortic surgery applying hypothermic circulatory arrest, therefore, should replace bladder and rectal measurements.

Early diagnosis and aggressive surgical approach without delay is a key factor in effective treatment for aortooesophageal fitulas. Endovascular treatment is essential to save the patient, but as a stand-alone procedure often ends-up with life threatening mid-term graft infection. Eliminating the source of bleeding as an emergency, resecting the oesophagus urgently to prevent sepsis and reconstructing the gastrointestinal continuity as an elective case after having the inflammatory processes settled seems to justify the sequence of endovascular aortic repair and subtotal oesophageal resection, followed by a gastro-oesophageal reconstruction, as an effective surgical approach.

More frequent proximal and distal progression of the dissection flap occurs in younger patients with acute type A aortic dissection. Older age is associated with a lower probability of an intimal tear at the level of sinus of Valsalva. These findings, associated with prognostic implications, account for the choice of more radical proximal procedures for repair of aortic dissection in younger patients.

Introduction

Aortic surgery, especially for pathologies requiring urgent surgical intervention has undergone significant changes in the past two decades leading to major improvement in short- and long-term outcomes. Better understanding of underlying diseases, improved guidelines and classifications have also contributed to more effective, prompt diagnosis and treatment of this high-risk segment of patient population. New imaging modalities, evolvement of perfusion methods, intra- and postoperative monitoring, improved intensive care are also of importance for achieving favourable outcomes. Nevertheless, continuous development of cardiac surgery itself is perhaps the most important component of this evolutionary process. As an example, the entry of catheter-based techniques including thoracic endovascular aortic repair and a combination of this method with conventional operative procedures resulted in novel devices, such as the "frozen elephant trunk", which led to reduced operative burden, lower mortality/morbidity and favourable long-term results.

The aim of this thesis is to provide a comprehensive, up-to-date overview on clinical characteristics of acute aortic syndrome, with special emphasis on current operative treatment possibilities, including well-established and novel, innovative surgical approaches. Within this scheme further specific goals were to analyze different cannulation and perfusion options, the role of core temperature management during hypothermic circulatory arrest and impact of age-related differences in surgical approach of AAS.

Acute aortic syndrome

AAS became a widely accepted term in the last decade, first mentioned by *Vilacosta et al* (1). By definition, AAS is an acute pathophysiological process involving the tunica media of the aortic wall, which results in rupture or any further life-threatening complications, and consists of aortic dissection, intramural haematoma and penetrating atherosclerotic ulcer. The incidence of AAS is approximately 30 patients/million/year; of which 80% is TAAD, 15% IMH, 5% PAU. 65.3% of patients suffering from AAS are men, mean age cumulates at 63 years (2). Peak frequency of AAS occurs between 8:00 am and 9:00 am, with increased likelihood during winter period (3). This severe disease leads to 20% prehospital mortality, 30% perioperative death and 20% loss within the following 10 years (4).

Acute aortic dissection

First historic record of the disease was registered by *Galenus* in 2nd century AC, the initial scientific description given by *Nicholls* in 1760 at autopsy of King George II. The definition of "aneurysma dissecans" originates from *Laënnec* (1819).

Classification

Classifications of thoracic aortic dissections aim to aid more accurate radiological diagnosis and also provide guidance on surgical versus medical management of patients. DeBakey divides dissections into 3 groups based on location of the entry and extension of aortic lesion:

- *Type I - Entry on the ascending aorta, with concomitant involvement of aortic arch, and descending aorta (60%)*
- *Type II - Confined to ascending aorta (10-15%)*
- *Type III - Confined to descending aorta (25-30%) (5).*

More convenient is the Stanford classification for everyday patient management based on involvement of the ascending aorta (6):

- Type A (TAAD) - involves the ascending aorta (featuring DeBakey types I and II)
- Type B (TBAD) - does not involve the ascendens (equivalent to DeBakey type III)

Usually, type A dissections require surgery, while type B dissections might be managed medically under most conditions.

Diagnostic modalities in AAS

Definitive diagnosis of thoracic aortic disease or one of its anatomic variants requires dedicated aortic imaging. Selection of the most appropriate imaging study may depend on patient related factors (i.e. haemodynamic status, kidney function, contrast allergy, etc.) and/or institutional capabilities (i.e. availability of imaging modalities, imaging specialist expertise, etc.) (7). Chest X-ray may reveal mediastinal widening or haemothorax, but does not provide exclusive diagnosis. ECG could show ischaemic signs, if the coronary ostia are involved in the pathological process, albeit not specific for TAAD. TTE might demonstrate a dissection flap in the ascending aorta and reveal acute aortic valve regurgitation. TOE could further investigate larger segments of the aorta; for initial preoperative assessment is not the

first choice as time consuming and not as sensitive as CT, but provides good real-time imaging intraoperatively. MRI scan represents the backbone of long-term postoperative follow-up as imposes no radiological burden on patients, but in the acute phase is not ideal as requires significantly more time at a critically ill patient than CT and not available in most of moderate size district general hospitals. These diagnostic modalities are analysed in Tables 1. and 2. (8).

	Transthoracic echocardiography	Transoesophageal echocardiography	Computed tomography	Magnetic resonance imaging
Availability	+++	++	+++	+
Portability	+++	+++	+-	-
Investigation tolerance	+++	+	++	+
Real-time follow-up	++	+++	-	-
Imaging speed	+++	++	+++	+

Table 1. Diagnostic features of imaging modalities in AAS

	Transthoracic echocardiography	Transoesophageal echocardiography	Computed tomography	Magnetic resonance imaging
Aortic dissection	+	++	+++	+++
Intramural haematoma	+-	++	+++	+++
Penetrating ulcer	-	+	+++	+++
Dissection entry	+	+++	++	+++
Periaortic haematoma	+-	+	+++	+++
Pericardial effusion	+++	+++	++	++
Aortic regurgitation	+++	+++	-	+++

Table 2. Efficacy of different imaging modalities in AAS

Initial management of AAS

Initial management of thoracic aortic dissections should be targeted to decrease aortic wall stress by controlling heart rate and blood pressure. In absence of contraindications, intravenous β-blockade (e.g. labetalol) should be administered and titrated to a target heart rate of 60/min or less. Beta-blockers should be administered cautiously in the setting of acute aortic regurgitation as they can block the compensatory tachycardia. In patients with clear

contraindications to β-blockade, non-dihydropyridine calcium channel–blocking agents (e.g. diltiazem, verapamil) should be utilized as an alternative for rate control. If systolic blood pressure remains ≥120 mmHg after adequate heart rate control has been obtained, then angiotensin-converting enzyme inhibitors and/or other vasodilators should be administered intravenously to further reduce blood pressure that maintains adequate end-organ perfusion. Sufficient pain control is usually achievable with the aid of morphine analogues (7).

Surgical considerations for AAS

In case of thoracic aortic dissection urgent surgical consultation should be undertaken regardless of the anatomic location (ascending versus descending) as soon as the diagnosis is established or highly suspected. TAAD should be urgently evaluated for emergent surgical repair due to the high risk of associated life-threatening complications, i.e. rupture. The mortality of TAAD is >40% in the first week (2). TBAD should be managed rather medically (10% mortality) unless life-threatening complications develop (i.e. malperfusion syndrome, progression of dissection, enlarging aneurysm, inability to control blood pressure or symptoms, progressive left haemothorax). Surgical approach of TBAD carries a risk of life approximately 30% (7) (2). In patients with TAAD, all aneurysmal aorta and proximal extent of the dissection should be resected. A partially dissected aortic root may be repaired with aortic valve resuspension. Extensive dissection of the aortic root should be treated with aortic root replacement with a composite graft or with a valve sparing root replacement. If a DeBakey Type II dissection is present, the entire dissected aorta should be replaced (7). Furthermore, the "frozen elephant trunk" technique could be considered in younger patients to avoid secondary operations (9). For TBAD, if surgical intervention is required, TEVAR would be the first treatment of choice as providing similar anatomical results as conventional surgery, but at a lower perioperative risk rate (2).

Intramural hematoma

IMH results from a haemorrhage into the aortic wall (tunica media) originating from the vasa vasorum without an intimal tear. Typical in elderly, mainly hypertensive patients, albeit can result sometimes from blunt chest trauma. IMH weakens the aortic wall and can penetrate to the outer aortic surface leading to rupture or propagate to the intimal surface creating an entry and progressing to a dissection. Therapeutic approach of IMH is similar to aortic dissection in the corresponding segment of the great vessel (7). Cases with TAAD analogue localisation

without progression and periaortic bleeding can be operated at a low risk. Elderly patients with significant comorbidities can be managed medically, but require intensive monitorisation for 2 weeks and repeat imaging to exclude IMH progression. Only a few limited papers examined this patient segment; Kaji *et al* observed complete haematoma involution in 40%, and in this group, there was no mortality in a period of 4 years (10). Evangelista-Masip found 34% spontaneous regression of IMH, 36% progression to dissection (12% to acute aortic dissection, 24% to localised dissection), 30% late aneurysm formation. It was also described that rupture or dissection is very rare <60 mm^2 extension of IMH (8).

Penetrating atherosclerotic ulcer

PAU is typical in elderly male patients with a history of hypertension (92%), smoking (77%), CAD (46%) and also associated with COPD (24-68%). PAU accounts for 5% of all AAS. In half of the cases there are concurrent aortic aneurysms, mainly abdominal (11). Patients usually present with symptoms of AAS, but sometimes PAU is asymptomatic and emerges as an incidental finding.

The term of PAU describes an ulcerating atherosclerotic lesion that penetrates the aortic intima and progresses into the media. In the early stages the lesion just ulcerates the intima and often asymptomatic. With further progression it may ulcerate the media and result in a medial hematoma of variable size (12).

PAU can resolve completely or stay stable, although can also lead to aortic dissection, saccular aortic saccular aneurysms or even spontaneous aortic rupture. There is a higher predilection to involve the mid to distal thoracic aorta (13).

Aortooesophageal fistula

Aortooesophageal fistula is a rare cause of gastrointestinal bleeding, albeit is a highly lethal condition, even when promptly diagnosed and treated. The exsanguination is imminent in most of the cases, many patients do not have the chance to reach a sufficient therapeutic facility as the aorta has a direct communication with the inner body surface. Main causes of AOF are lesions of the oesophageal wall resulting from a thoracic aortic aneurysm (in up to 54% of cases), ingestion of foreign bodies (in up to 19% of cases), trauma (usually iatrogenic), carcinoma, or seldom aortitis tuberculotica (14). Conservative treatment of AOF results in a high in-hospital mortality rate, and conventional surgical procedure has also a reported in-hospital mortality rate of nearly 40% (15). Transcatheter endovascular aortic repair as a stand-alone procedure has recently gained recognition as a possible technique for the emergent treatment of AOF, despite a considerable risk of infection (16), in contrast to the conventional solution of open thoracic surgery with higher mortality and morbidity. However, relatively little is known about long-term results of TEVAR for AOF due to its rarity and the lack of large clinical experience.

Perfusion options in aortic emergencies

TAAD, with or without involvement of the aortic arch, is a clinical emergency that requires immediate surgical intervention. Mortality rates of these operations have dramatically improved as the result of recent advances in preoperative preparation, intraoperative techniques, and postoperative care. Nevertheless, operations for aortic emergencies are still associated with a relatively high rate of mortality and postoperative morbidity compared to routine heart surgery, especially when the presentation is complicated by haemodynamic instability.

Establishing perfusion might be challenging as we aim to access the targeted diseased organ, the aorta. Classical femoral approach results in higher incidence of malperfusion, neurological complications and mortality (17). Cardiopulmonary bypass via axillary/subclavian artery has become popular as an alternative perfusion site in recent years predominantly for acute aortic dissections and patients with severe aortic atherosclerosis (18) (19) (20). AxS inflow may not be suitable for rapid establishment of antegrade perfusion in cases with hemodynamic instability, since the preparation is more time consuming. Obese patients might also represent a technical challenge; on the other side of the spectrum, in patients with small body surface

area, limitation of pump flow due to a narrow axillary artery could be a concern. In numerous studies failure rate and requirement for an alternative cannulation site of AxS measures 4.2% - 11%; albeit this is the most widely applied arterial access (21) (22) (23).

Anatomical variations, such as lusorian artery might also jeopardize the safe applicability of AxS and also unilateral antegrade cerebral perfusion. Furthermore, cannulation for extensive aortic lesion can be challenging either through AxS or lower limb arteries, if these vessels are involved in the pathological process (24). Therefore, other alternative approaches, especially central cannulations should be kept in evidence. In the light of the problems associated with peripheral cannulation techniques, we started to apply an innovative ultrasound-guided entry method on the usually uninvolved aortic wall segment on the concavity of aortic arch via Seldinger technique. As a further alternative or a bail-out for other unsuccessful arterial cannulation attempts, transapical approach of the heart-ascending aortic complex is also a feasible (25) (26).

Intraoperative body temperature monitoring

Accurate monitoring of core temperature during aortic surgery, especially with application of deep hypothermic circulatory arrest is an important component of routine perioperative care. Preservation of neurological function is one of the main goals in such patients. Increasing the tolerance of brain to ischaemia by application of systemic hypothermia allows for a safe period of circulatory arrest and has remained the mainstay of neuroprotection since decades (27) (28). The safety of this procedure relies on adequate systemic cooling under strict control. If this control is incomplete or fails, neurological injury may occur during HCA. Whereas hypothermia is neuroprotective, even mild hyperthermia is hazardous during cerebral ischaemia since it accelerates neuronal death (29). This results from oxygen free radical production (30), destabilization of cytoskeleton (31), intracellular acidosis (32) and increased blood-brain barrier permeability (33). Thus, to estimate actual brain temperature, different sites are used for perioperative temperature assessment, for example; urinary bladder, oesophagus, rectum and tympanic membrane. Body temperatures measured on these alternative sites may, however, substantially deviate from the actual cerebral temperature. Adequate neuroprotection requires meticulous temperature management to avoid too low or high temperatures leading to overcooling or overheating the patient due to inappropriate "slow responding" temperature monitoring.

Although application of hypothermia has been an important contribution to patient management as a neuroprotective method from the dawn of cardiac surgery (34), proper body temperature management relies on the accurate measurement of temperature, to enable adequate monitoring of changes during CPB and HCA. Oxygen consumption drops with lower body temperature, so that ischaemic tolerance is increased by cooling. Cerebral oxygen requirement decreases to approximately one-fifth of normothermic needs at 20°C (35) allowing a safe period of 45-50 minutes for HCA (Figure 1) (36). In addition, hypothermia may contribute to neuroprotection by a variety of complex mechanisms including decreased vascular permeability, reduced ion influx and decreased excitatory transmitter release (37). Albeit hypothermia is neuroprotective, it leads to platelet dysfunction, coagulation cascade blockade, vasoconstriction resulting in localized areas of hypoperfusion. During the rewarming phase of CPB, conventional temperature monitoring sites may not reflect true brain temperature so that cerebral hyperthermia may not be detected, if conventional temperature monitoring underestimates brain temperature or there is a delay with arterial heat exchange (38).
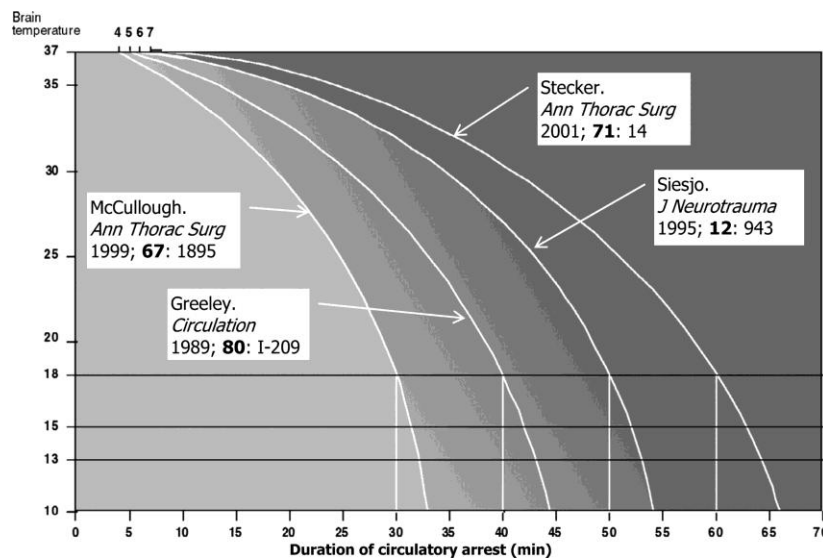
Figure 1. Relation of brain temperature and safe duration of HCA in the literature (36)

Cerebral oximetry

Classical complex aortic surgery, especially in combination with HCA represented high patient risk with significant postoperative morbidity - commonly associated with stroke - and mortality. One milestone in reduction of hazard in complex aortic procedures is tissue oximetry performed on the forehead, constantly monitoring brain tissue saturation on bases of

near infrared spectroscopy. Near infrared spectroscopy was initially published nearly four decades ago, utilizing the Lambert-Beer law as a measurement principle, where transmittance of material sample is related to its optical depth and to its absorbance. The radiation is emitted by a photodiode or laser undergoes reflection, absorption and deflection in the brain tissue, mainly on haemoglobin enabling concentration assessment of the substance. Standard wavelength of light applied in NIRS system measures 730-910 nm. The measurement is undertaken on mixed blood, although not able to differentiate between the arterial and venous phase, as pulsoximetry can. As 70% of absorption is resulting from venous blood, 25% from arterial phase, 5 % from the capillary bed; NIRS dominantly detects increased local O2 extraction, when the cerebral saturation value drops (39).The sensor measures oxygenation of the anterior and medial cerebral artery territories. As there is some individual variability in oxygenation parameters, the baseline value has to be established right before starting the surgical procedure, then intraoperative values can be interpreted in reference to the baseline (Figure 2). Intraoperative drop of 20% in comparison to baseline or saturations below 50% are strongly associated with postoperative stroke, cognitive dysfunction or coma. NIRS is a valuable tool in prevention of severe postoperative neurological dysfunction in aortic surgery (40).
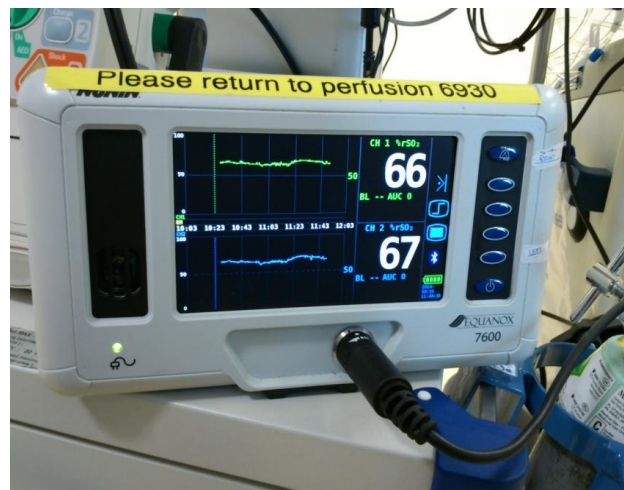

Figure 2. NIRS demonstrates a well conducted perfusion management in HCA

Cerebral blood supply challenges in major aortic surgery

In aortic emergencies patients have a good chance to end up in haemodynamical instability, therefore; well planned perfusion strategies are required to obtain optimal outcome. As we are working on a diseased aorta, this aim in not always easy to be achieved. To avoid malperfusion and protect organs, especially the cerebrum, prompt perfusion of the true lumen without any bias is mandatory. The classical femoral perfusion does not entirely fulfil all these requirements, alternative approaches were developed in the last two decades. As visible in the paragraph on HCA, safe duration of circulatory arrest measures 45-50 minutes at 20°C, which time span would not entirely satisfy requirements for some complex arch reconstruction. To avoid further neurological damage, cerebral perfusion has been implied in several institutions. Cerebral perfusion can be performed in an antegrade fashion either directly on both carotid arteries or non-selectively, through a branch of the aortic tree, i.e. AxS. Retrograde cerebral perfusion is usually performed through the superior vena cava, rarely via right internal jugular vein. Following initial enthusiasm, mid- and long-term results of loan retrograde cerebral perfusion were rather modest in comparison to the antegrade. Japan Cardiovascular Surgery Database Organization concluded from an analysis of 16,218 that although antegrade and retrograde cerebral perfusion demonstrate comparable clinical outcomes regarding mortality and stroke rates, but retrograde perfusion results in higher incidence of prolonged intensive care unit stay. Antegrade cerebral perfusion might be preferred as brain protection method for complex aortic arch procedures (41).

Antergrade cerebral perfusion can be subdivided into selective antegrade cerebral perfusion providing direct bilateral brain supply and unilateral antegrade cerebral perfusion. At SACP both common carotid arteries are cannulated and direct perfusion is provided on the normal anatomical pathway at a total rate of 10 ml/kg/min constantly monitored by NIRS (Figure 3). To administer UACP, AxS represents the most convenient way, as the right axillary artery fills the right common carotid artery via innominate artery. Other alternative access for UACP is a direct cannulation of the internal carotid artery proposed by Urbanski *et al.* (42). Applying the standard technique, however, only the right hemisphere is continuously perfused, which can result in malperfusion of the contralateral hemisphere; as Merkkola *et al.* demonstrated, up to 17% of the patients have incomplete circle of Willis (43). Even with a complete circle of Willis, concern has been raised, if this type of perfusion alone can sufficiently supply the left hemisphere. Although UACP is simple, widely used method, but not the most physiological way of brain perfusion. A recent meta-analysis has concluded, albeit UACP and SACP did

not result in different mortality and neurologic morbidity rates, among prolonged HCA times UACP resulted in poorer outcomes with respect to SACP (44).
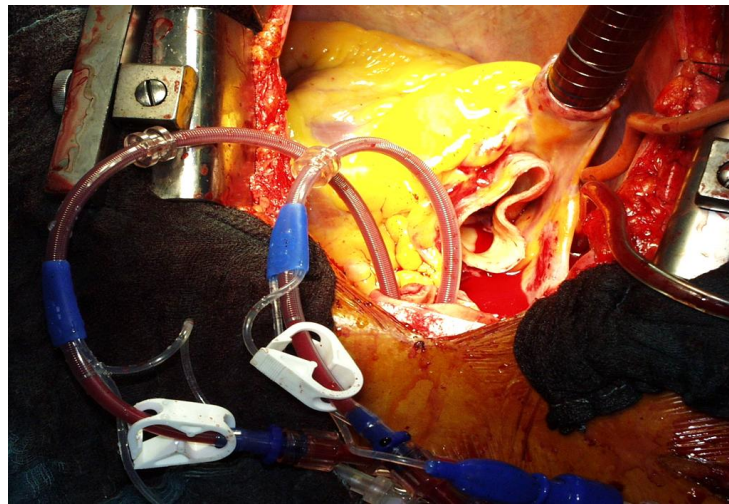

Figure 3. Selective antegrade carotid perfusion *in situ*

Surgical consideration in aortic emergencies

Conventional aortic surgery

Albeit aortic dissection, the most common aortic emergency is well known since centuries, Dubost utilized a homograft for abdominal aneurysm replacement in 1951 at first, and Gibbon created in 1953 the first relatively safe extarcorporeal system. In 1956 De Bakey replaced the ascending aorta, then the aortic arch (1967); one year later Bentall and De Bono implanted the first composite graft at an aortic root-ascending aorta replacement.

The most simple solution for surgical management of TAAD is an interposition graft replacement of the ascending aorta or also including in the replacement a large section of the lesser curvature of the arch; the so called "hemiarch" technique. In case of a simple ascending replacement no HCA is required, so long a "closed distal" anastomosis is with aortic cross clamp on performed. Current medical literature has the consensus, that in younger patients a "hemiarch technique" is desired, but in septua- and octogenarians, especially with significant comorbidities onboard, a "closed distal" technique is acceptable. Furthermore, this latter technique puts less operative burden on elderly; therefore, better recovery and survival can be achieved with a limited surgical procedure (45) (46). Surgical reconstruction of aortic root involvement has developed step-by-step from a simple valve resuspension, then valve

replacement to a mechanical composite root replacement. Later on, biological "full root" (e.g. Medtronic Freestyle™) substitutes came on the market, followed by root remodelling technique by Yacoub (47) and root reconstruction by David (48). Recently De Paulis (49) has published haemodynamic advantages of a Valsalva graft, which allows a better anatomical replacement of the aortic root. Combination of this graft with a biological valve prosthesis as "custom made" biological root proposed by Urbanski, enables easy redo valve surgery in the future (50).

Elephant trunk technique

In case of aortic arch involvement, next surgical step was an interposition graft replacement with island transposition of supraaortic vessels in HCA. As in younger patients the descending aorta has to be replaced often as a second stage procedure, Borst (51) introduced the"elephant trunk technique" to facilitate the second stage operation's proximal anastomosis with a hovering distal end of arch graft situated in the proximal descending aorta, such as the trunk of an elephant (Figure 4).
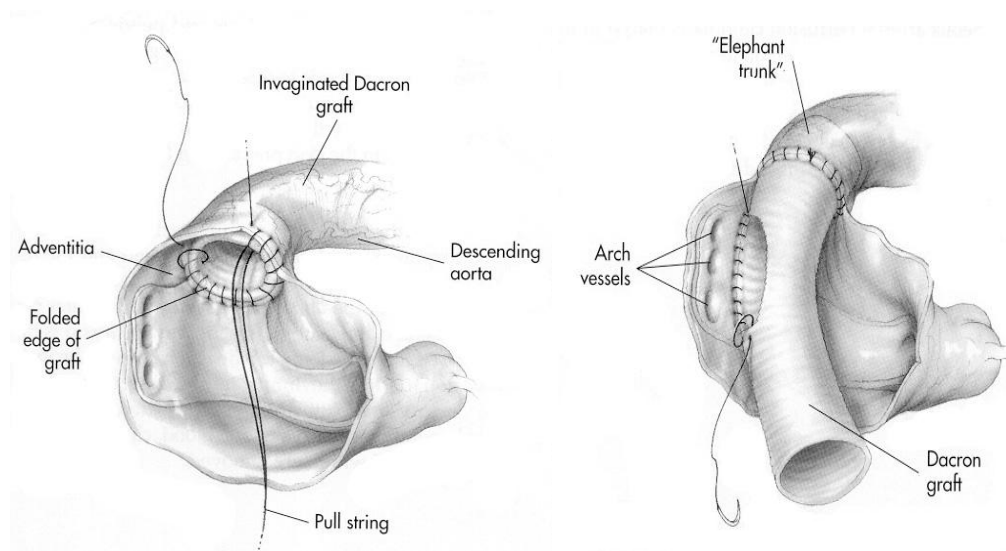

Figure 4. Elephant trunk technique by Hans Borst (52)

Transcatheter EndoVascular Aortic Repair

TEVAR has revolutionised noninvasive treatment of descending aortic aneursysms and TBADs. The initial idea came from Volodos, who developed Z-stents and fabric coated stents in 1980s (53). TEVAR grafts are intravascular expandable devices coated by fabric to

remodel the normal aortic lumen and to cover transvascular communication. In combination with debranching of the aortic arch, TEVAR can substitute even some complex arch operations. Requirements for sufficient stenting are a generous landing zone to well anchor the device, optimal radial pressure of stent frame to provide a good apposition of aortic wall with minimal trauma. Radial pressure is determined by stent frame geometry, length, spacing, wire material and correct oversizing. Following meticulous planning, TEVAR procedure is a relatively quick and low risk procedure in comparison to a surgical intervention in certain aortic pathologies (54).

Hybrid approach - 'Frozen elephant trunk' technique

Although "elephant trunk technique" has revolutionarized complex arch surgery with aim of facilitating a secondary descending aortic procedure, a significant proportion of patients was not suitable at all after 3-6 months following initial arch surgery to undergo a secondary procedure. Combination of the original "elephant trunk technique" with a TEVAR stent graft resulted in a hybrid device that allowed one stage completion of the previous double procedure. During HCA the aortic arch and some portion of proximal descending aorta is resected, then CT angiography guidance sized TEVAR portion of the Thoraflex Hybrid ™ (Vascutek Ltd, Inchinnan, Glasgow, UK) graft is inserted and expanded (Figure 5) distally. The device cuff is sutured to seal the descending aorta, after this the aortic arch plexus is anastomosed step-by-step to all supraaortic vessels, and at last the ascending anastomosis is completed. This unique device reduces operative burden in fragile patients (55).

Figure 5. Thoraflex Hybrid ™ device in situ (Vascutek Ltd, Inchinnan, Glasgow, UK) - image is courtesy of Vascutek Ltd, UK (Mr T. Pacuka)

Postoperative care following aortic emergencies

Intensive care therapy

Constant improvement in anaesthetic and intensive care therapy has significantly reduced postoperative mortality and morbidity following major aortic surgery in the last two decades. These advances enabled us to extend the operative indications for elderly patients with multiple co-morbidities, and improvement in surgical techniques have also contributed to reduction of previous patient selection limitations. Certain evolvement in respiratory therapy has reduced the incidence of lung related severe postoperative complications; continuous- and bilevel positive airway pressure (CPAP, BIPAP) have facilitated recruitment of the atelectatic lung fields following HCA and longer ECC times. Even tracheostomy has a smaller impact on recovery with availability of Seldinger type mini-tracheostomy. Kidney failure and major electrolyte/fluid imbalance is more effectively managed via continuous veno-venous filtration, and long-term dialysis also offers a better quality of life, then before. Improved understanding of the coagulation system led to development of prothrombin complex concentrate, recombinant fibrin, recombinant factor VIIa and several different surgical sealants as well, thus reducing intra- and postoperative blood loss. All the above factors have led to significant shortening of operative times and frequency of rethoracotomies, the major contributors in postoperative morbidity and mortality. German Registry for Acute Aortic Dissection Type A (GERAADA) has concluded after analysis of 1558 patients, that emergency aortic procedures for septuagenarians can be performed with acceptable mortality. Octogenarians showed up significantly higher 30-day mortality, although this was also lower, then the mortality without any surgical intervention (56).

Outpatient follow-up

As AAS mainly develops on a background of preexisting aortic aneurysms, this fact mandates regular follow-up in aortic patients to facilitate an elective intervention, if required. These elective procedures carry less risks, as the patient can be thoroughly prepared utilizing ideal imaging modalities, and pre-existing medical condition can be timely optimized for a major surgery. Regular postoperative outpatient follow-ups are essential in provision of excellent long-term outcomes by the opportunity of early endo-leak detection, monitoring aortopathy progression, managing hypertension, etc. The usual AAS population is relatively young, average age of affected individuals measures about sixty years, regular follow-ups

additionally contribute to restoration of health in this still relatively active age group. Patients with AAS possess a less favorable long-term outcome with a past medical history of previous cardiac surgery or generalized atherosclerosis (57). Blood pressure control is essential for these patients, aiming to maintain a pressure no more than 130/80 mmHg (58). If there is a well-known hereditary burden present, the patient´s complete family should be offered the opportunity to be genetically tested and counselled.

Some recent publications have highlighted the role of angiotensin II in progression of aortic aneurysms, although the relative contribution of its type 1 (AT1) and type 2 (AT2) receptors remain unknown. Habashi *et al.* demonstrated, that loss of AT2 expression accelerates aberrant growth and rupture of aorta in a mouse model of Marfan`s syndrome. Losartan, a selective AT1 blocker reduces aneurysm progression in mice; a full protection requires intact AT2 signaling. The angiotensin-converting enzyme inhibitor enalapril, which limits signaling through both receptors, is less effective. Both drugs attenuate transforming growth factor-ß (TGF ß) signaling in the aorta, but losartan uniquely inhibits TGF ß-mediated activation of extracellular signal-regulated kinase, by allowing continued signaling through AT2, which demonstrates a protective nature of AT2 signaling and a possible choice of therapy in aortic aneurysms (59). International multicentric studies are currently evaluating possible pharmacological prevention and postoperative medical supportive therapy options in Marfan´s syndrome provided by AT1 blockers, especially losartan in a combination with a ß-blocker, such as nebivolol. The key molecule in aortic aneurysms, TGF ß, normally attached to extracellular matrix, is free and activated. Under experimental circumstances, TGF ß blockade prevents aortic wall damage and dilation. AT1 blockers exert an anti-TGF ß effect; trials are now ongoing for evaluating the above effect of losartan compared with atenolol or nebivolol. The third generation ß-blocker nebivolol retains a ß-adrenergic blocker effect on heart rate, and further exerts an anti-stiffness effect, that is typically increased in aortic aneurysms (60). After thorough evaluation of ongoing human studies we are going to gain more insight into optimal pharmacological support of AAS and aortic aneurysms, which completes the therapeutic circle of this severe disease group.

Aims

Based on this background, we designed four clinical studies (Study I – IV) in the last decade aiming to improve diagnostics and treatment of aortic emergencies. The final goal of these protocols was to improve safety of this major surgical procedure.

The aim of Study I. was to develop a reliable central cannulation method in type A aortic dissection repairs. In Study II., the reliability of different body temperature measurement sites was investigated during aortic surgery; in Study III., management options for aortooesophageal fistulas; while in Study IV., age-related considerations of acute type A aortic dissection were analyzed.

Study I - Central cannulation by Seldinger technique in type A aortic dissection repairs

Background

Extensive aortic disease, such as giant aneurysms combined with atherosclerosis or dissections that involve the ascending aorta, can complicate the choice of cannulation site for cardiopulmonary bypass. Ideal perfusion during ascending aorta/arch surgery should allow easy implementation of antegrade cerebral perfusion while avoiding atheroembolization or false lumen perfusion in dissections. Alternative cannulation sites such as AxS or innominate artery have been recently preferred to femoral artery to improve postoperative outcomes in patients undergoing surgery of the thoracic aorta. Prompt establishment of antegrade perfusion may lead to favourable outcomes in type A dissections, especially in case of hemodynamic instability. We started to employ direct cannulation of the true lumen targeting the concavity of aortic arch by Seldinger technique in aortic dissections, later this method was applied in ascending/arch aneurysm resections too. We have evaluated the efficacy of this access technique as an alternative arterial inflow pathway in aortic surgery.

Patients and methods

Within a period of 2.5 years, 24 consecutive patients (mean age: 59±14 years, CI: 53.0 - 64.8; 17 men and 7 women) underwent procedures of the thoracic aorta. In all patients a standard operative technique for acute aortic dissection was applied and the only difference in surgical strategy was the choice of arterial cannulation site. Direct cannulation by Seldinger technique was utilized in 14 cases (58%), subclavian access in 6 patients (25%), and femoral entry on 4 occasions (17%). Further preoperative data is provided in Table 3.

Characteristics	Direct	Subclavian	Femoral
N^o of patients	14	6	4
Male	8	6	3
Female	6	0	1
Age (years (median))	65±10 (66)	51±17 (49) [N.S. p=0.11]	51±13 (46) [N.S. p=0.13]
Hypertension	13	5	3
Preoperative ventilated	4	4	3
Preoperative renal insufficiency	2	2	0

Table 3. Demographic and preoperative data. Statistical analyses are provided as comparisons to the group with direct cannulation

The preoperative diagnosis was established on basis of emergency computed tomography with additional intraoperative transoesophageal echocardiography support in all patients. Aortography or coronary angiography was not performed for preoperative evaluation. The standard operative technique for aortic dissection repair at our institution has been graft replacement of the ascending aorta and proximal aortic arch ("hemiarch technique"). Inspection of the supraaortic vessels was always carried out to decide whether to perform a concomitant island transposition depending on the supraaortic status. The patient was placed in standard supine position. The arms were horizontal beside the body as for a usual cardiac procedure. Monitoring of arterial pressure was performed by placing three lines routinely in both radials and the right femoral artery. The ascending aorta and aortic arch were exposed through a median sternotomy, then the concavity of aortic arch at level of Botallo`s ligament (ligamentum arteriosum) was cannulated applying a minimal invasive technique with dilation steps, as described by Seldinger (Fem-Flex Femoral Arterial Cannula®, 24 Fr TFA 02425H Edwards Lifesciences LLC, Irvine, USA; Joline Special Dilatatorset®, Hechingen, Germany) (Fig. 6). No purse-string sutures are required in this area; the arterial line is fixed with a stitch to the cranial sternotomy skin incision corner to avoid accidental dislocation. Correct position of the guide wire and cannula in the aorta during the cannulation procedure was routinely confirmed by TOE, or epiaortic ultrasound in a rare case of technical difficulty with echocardiography. The same type of cannula was inserted in both peripheral access sites. CPB was instituted between the arterial cannulation site and right atrium. The patient was cooled to a tympanic temperature of 19-20°C (Mon-a-therm® Thermistor YSI 400 Series tympanic temperature probe, Mallinckrodt Inc, St Louis, USA), rectal (Thermocouple probe, Mallinckrodt Medical, USA) and bladder (Curity®, Degania, Israel) temperatures were also followed-up simultaneously throughout the procedures as well. After cross-clamping an ascending aortic incision was performed, antegrade crystalloid cardioplegic solution (2000 ml Custodiol® HTK-Solution by Brettschneider, Dr. F. Köhler Chemie, Hähnlein, Germany) was administered proportionally through both coronary orifices. During HCA, selective antegrade cerebral perfusion was applied via both carotid arteries (DLP Retrograde Coronary Sinus Perfusion Cannula with manual Inflating Cuff®, Medtronic Inc, Minneapolis, USA) at a flow rate adapted to maintain a constant cerebral O_2 saturation on each side, providing a perfusion pressure of 35-40 mmHg. Cerebral monitoring was performed with NIRS (INVOS® cerebral oxymeter, Somanetics Inc, Troy, USA), brain tissue oxygen saturation measured 60-70% continuously during perfusion, which corresponded to the induction values.
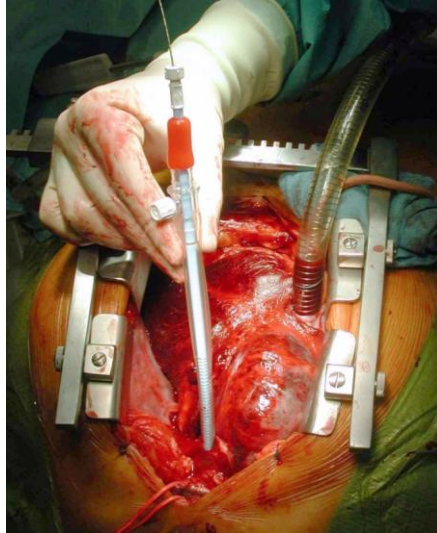
Figure 6. Direct aortic cannulation via Seldinger technique

Reconstruction of the aorta was undertaken with a woven Dacron side-branched vascular prosthesis (Hemashield Platinum Woven Double Velour Vascular Graft®, Boston Scientific Inc, Wayne, USA) including the island type reinsertion of all supraaortic vessels, if applicable. The false lumen was eradicated with 45% bovine serum albumin-10% glutaraldehyde glue (BioGlue®, CryoLife International Inc, Kennesaw, USA); aortic valve commissures were re-fixed applying the resuspension suture technique. The valve was replaced, if appeared diseased. Composite valve graft replacement was performed in patients with Marfan's syndrome, or if intraoperatively severe local involvement of the aortic wall could be observed. The decision, whether to implant a composite graft did not depend on a maximal diameter of the aortic root but was based on presence of Marfan's syndrome or severity of wall destruction. Systemic reperfusion with concomitant rewarming was started through the graft side-branch. Summary of performed surgical procedures is presented in Table 4.

Surgical procedure	Direct	Subclavian	Femoral
Ascending aorta + hemiarch	13	6	4
Ascending aorta + total arch	1	*	*
° David reconstruction	1	*	*
° Yacoub reconstruction	2	1	1
° Bentall procedure	3	1	*
° Coronary bypass grafting		1	*

° marks an additional procedure of aortic graft implantation

Table 4. Surgical procedures

Statistical analysis was undertaken using SPSS v15.0 software (IBM Corporation, Armonk, New York, USA). For statistical comparison of the groups Mann-Whitney's U test and Chi-square test were applied. Although the number of cases in two groups; femoral cannulation and subclavian approach was relatively low (4 and 6 cases, respectively), we considered a p-value <0.05 to be significant to enhance the statistical power of comparisons. Where appropriate, confidence interval (CI) was calculated with a confidence level of 95%. Data are presented as mean values ± SD and, where applicable, corresponding CI are shown in parentheses.

Results

There were no intraoperative deaths; cumulative 30-day mortality rate measured 25% (6) for the entire patient population; 3 of 14 (21%) in the direct group, 2 of 6 (33%) subclavian, 1 of 4 (25%) femoral cannulated patients (p=0.24 and p=0.46, respectively), all due to multiorgan failure. Direct aortic cannulation was safely performed in all cases; there was no need to switch to an alternative cannulation site. The adventitia of the dissected aorta was firm enough to support a cannula being inserted with Seldinger technique utilizing staged dilatators, and there was no case of complicated local massive haemorrhage on the cannulation site. No malperfusion or apparent thromboembolism due to cannulation procedure was observed. Malperfusion would have been anticipated, if a cerebral saturation difference of 10% occurred compared to preoperative values, and/or a pressure difference between the peripheral arteries greater than 20 mmHg found. Permanent neurological deficits were not present, in one patient transient changes occurred (4%) in the direct group. Since the Seldinger technique was easier and quicker to apply, than the peripheral approaches (Table 5) and showed certain advantages in the preliminary results, we have permanently changed our cannulation method to direct aortic entry in all patients. Transoesophageal echo guidance along with colour Doppler imaging was helpful for following-up the aortic cannulation procedure; the imaging provided additional real-time information about true lumen antegrade perfusion.

Mean extracorporeal perfusion duration measured 183±63 minutes (156.4 - 209.6), mean time demand to reach circulatory arrest was 28±14 minutes (23.1 - 34.9) in the entire cohort, with no significant differences between the groups (Table 5). Initial SACP flow was comparable in all three groups, however, we observed a significant difference in SACP flow requirements to maintain the initial cerebral saturation at constant blood pressure by the end of cerebral perfusion period between direct cannulation group (right: 196±37 ml/min [177.3 - 227.4]; left:

227±68 ml/min [184.8 - 247.2]), and both femoral (right: 350±54 ml/min [264.1 – 435.9] [p=0.006]; left: 275±64 ml/min [173.2 – 376.8] [p=0.24]) and subclavian access groups (right: 282±56 ml/min [223.2 – 340.8] [p=0.02]; left: 283±49 ml/min [231.6 - 334.4] [p=0.05]), in favour of direct cannulation. Further intraoperative data were evaluated to identify reliability and benefits of direct cannulation method and are presented in Table 5.

Time requirement to reach circulatory arrest was the shortest in the direct access group with a mean value of 27±11 (20.6 - 33-3) minutes; at femoral cannulation it measured 43±22 (28.0 – 78.0) minutes (p=0.058); at subclavian entry 32±8 (23.6 – 40.4) minutes (p=0.34), respectively.

Intraoperative data	Direct	Subclavian	Femoral
	Mean ± SD (Median)		
Time to HCA (min)	27±11 (26)	32±8 (31)	43±22 (48)
CPB time (min)	181±77 (149)	188±32 (193)	180±52 (200)
HCA time (min)	51±20 (52)	51±22 (50)	53±31 (48)
SACP time (min)	39±18 (39)	36±24 (25)	41±29 (31)
SACP flow right start (ml/min)	201±41 (200)	218±52 (200)	258±59 (250)
SACP flow right end (ml/min)	196±37 (185)	282±56 (300)	350±54 (330)
SACP flow left start (ml/min)	216±54 (205)	243±99 (275)	240±37 (240)
SACP flow left end (ml/min)	227±68 (220)	283±49 (300)	275±64 (275)
Tympanic temperature minimum	20.8±0.9 (20.8)	19.5±1.0 (19.7)	20.8±0.3 (20.9)
Rectal temperature minimum	26.9±3.3 (27.3)	26.8±4.3 (27.6)	26.0±2.3 (26.0)
Urinary bladder temperature minimum	26.0±4.8 (25.6)	24.8±3.4 (24.8)	23.8±2.3 (23.7)

HCA: Hypothermic circulatory arrest, CBP: Cardiopulmonary bypass

SACP: Selective antegrade cerebral perfusion

Table 5. Intraoperative data. Statistical analyses are given as comparisons to the group with direct cannulation.

Direct arch cannulation resulted in the best renal function on the first postoperative day with a creatinine level of mean 140±48 mmol/L (112.3 - 167.7); femoral entry showed 179±79 mmol/L (53.4 – 304.6; p=0.08); at subclavian access we found 199±69 mmol/L (89.3 – 308.7;

p=0.25). Although a clear tendency between creatinine levels in direct cannulation group and the other two approaches can be observed in favour of the direct cannulation technique, these differences did not reach the level of significance due to a relatively low number of patients in the subclavian and femoral access groups. Figure 7 demonstrates plasma creatinine levels during the first 72 postoperative hours. 2 of direct and 2 of subclavian cannulated patients were excluded from the statistical analysis due to preoperative renal impairment. Similar characteristics could be observed in lactic acid levels, as a marker of perioperative global ischemia on intensive care unit following up our patients; results are depicted in Figure 8. Four of direct, one of femoral and two of subclavian artery perfused patients were not considered for statistical analysis with an initial lactic acid level over 2 mmol/l.

Lenght of intensive care unit stay over 5 days could be observed at 5 of 14 (36%) patients in the direct group, 4 of 6 (66%; p=0.21) in subclavian, 2 of 4 (50%; p=0.51) at femoral cannulated patients.

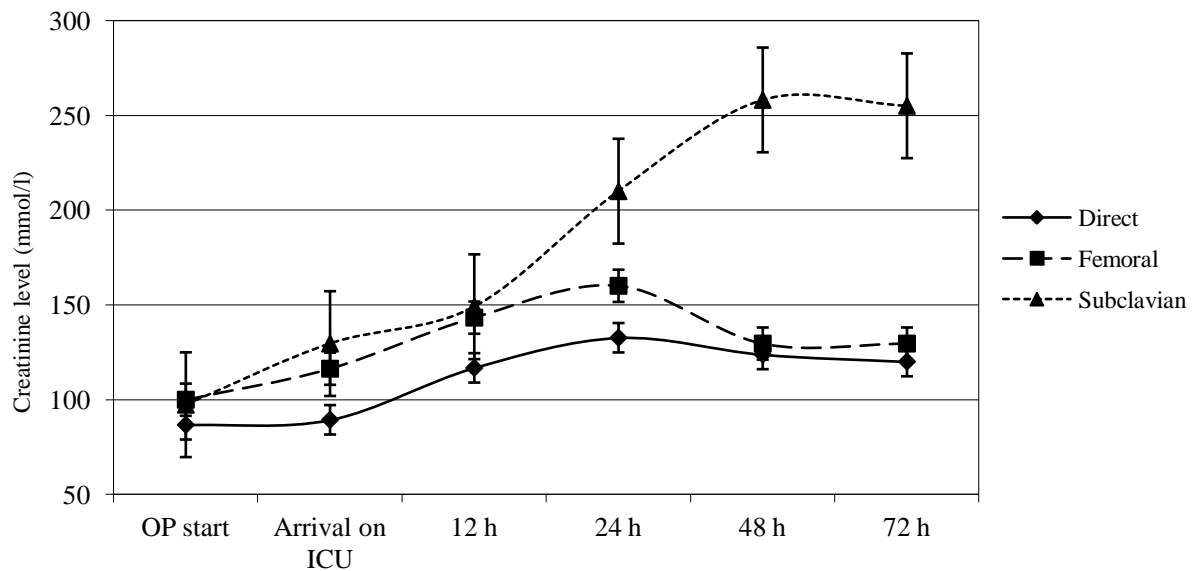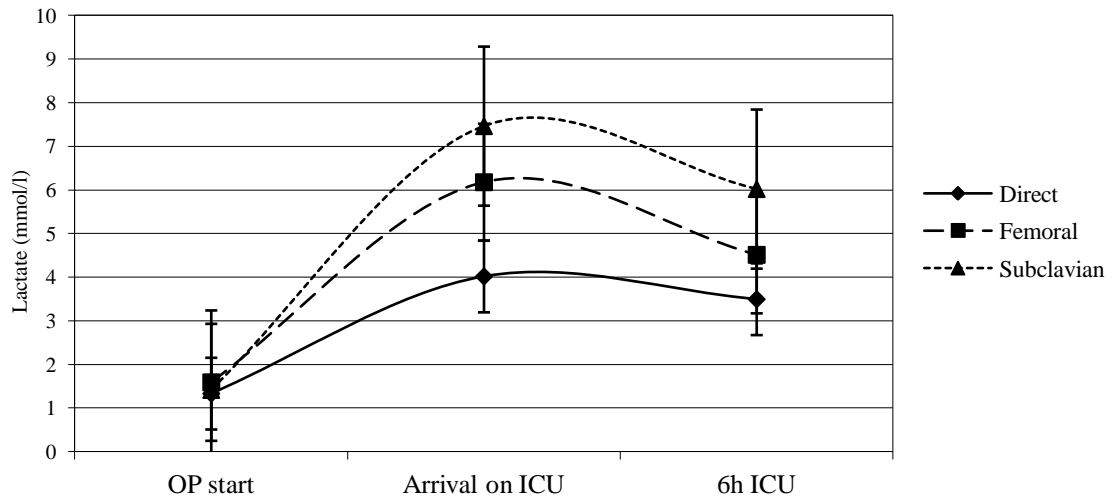Figure 7. Changes in creatinine levels at different cannulation methods

Figure 8. Lactate screen of the three perfusion groups

Conclusion

Arterial access for establishing CPB, especially in patients requiring repair of acute type A aortic dissection, is a controversial subject in the current literature (61). Minimal invasive central cannulation by Seldinger on the concavity of aortic arch is technically feasible and safe. It may avoid cerebral embolization and organ malperfusion; therefore, may reduce the rate of neurological and malperfusion complications. This alternative arterial inflow technique can be applied for prompt establishment of CPB in type A dissections, especially during hemodynamic instability.

Study II - Body temperature measurement sites in aortic surgery

Background

We performed a retrospective, comparative analysis of different, but widely used temperature measurement sites during surgical repair of thoracic aorta in HCA to determine reliability of methods for intraoperative core temperature monitoring. Preservation of neurological function is one of the main goals in such patients. Safety of this type of procedure relies on adequate systemic cooling under strict control. If this control is incomplete or fails neurological injury may occur during HCA.

Patients and methods

22 patients (mean age: 63±12 years, 12 men and 10 women) underwent operations on the thoracic aorta. In all patients a standard operative technique for acute aortic dissection or aneurysm resection was used at our institution. CBP was established via arterial cannulation performed on the concavity of aortic arch applying the Seldinger technique, and during HCA selective bilateral antegrade carotid perfusion was used. Indications for surgery included: acute type A dissection (n=14, 64%), degenerative aneurysm (n=6, 27%), aortic infiltration of thymic carcinoma (n=1, 4.5%) and intraaortic stent refixation (n=1, 4.5%). Fifteen patients (68%) underwent emergency operations. Preoperative patient characteristics are provided in Table 6.

Diagnosis was confirmed by contrast-enhanced computed tomography and intraoperative TOE in all patients. Aortography or coronary angiography was not performed in emergency cases.

Characteristics	
N^o of patients	22
Male	12
Female	10
Mean age in years±standard deviation	63±12
Emergency operations	15
Indications	
Type A dissection	14
Degenerative aneurysm	6
Aortic infiltration of thymic carcinoma	1
Intra-aortic stent refixation	1
Hypertension	16
Preoperative ventilation	4
Preoperative renal insufficiency	3

Table 6. Preoperative patient characteristics

The standard institutional operative technique for aortic dissection or aortic aneurysm at our institution was applied, as described in Study I; exactly same intra- and perioperative management and decision making algorythm was undertaken in all patients. Summary of performed surgical procedures is presented in Table 7.

Surgical procedure	n
Ascending aorta + hemiarch	20
Ascending aorta + total arch	2
° David reconstruction	3
° Yacoub reconstruction	4
° Bentall procedure	4
° Coronary bypass grafting	4

° *marks an additional procedure of aortic graft implantation*

Table 7. Surgical procedures performed

Statistical analysis for body temperature measurement sites was undertaken by univariate analyses (Pearson's correlation and Student's t-test) with SPSS v17.0 (SPSS Inc. Chicago, Illinois, USA) to identify the best reference point for arterial blood temperature assessment during HCA and SACP. A p value <0.05 was considered as significant.

Results

Perioperative data

There were no operative deaths; cumulative 30-day mortality rated 13% (n=3). The cause of death was multiorgan failure in all 3. Eight patients (36%) stayed in the intensive care unit >5 days. Direct aortic cannulation was safely performed in all cases; there was no need to switch to an alternative cannulation site, and there was no case of complicated local massive haemorrhage on the cannulation site. TOE guidance was useful for aortic cannulation along with colour Doppler imaging, which provided information about the true lumen antegrade perfusion. No malperfusion or apparent thrombo-embolism due to cannulation was observed. Malperfusion was defined by a cerebral saturation difference of 10% compared to pre-operative values and/or pressure difference between the peripheral arteries >20 mmHg. There were no permanent neurological deficits, but two patients (9%) suffered from transient neurological dysfunction. Mean CPB time measured 176±63 minutes (median: 158), mean duration to reach HCA was 25±12 minutes (median: 21), mean HCA time was 46±21 minutes (median: 45) and mean selective antegrade carotid perfusion time was 36±18 minutes (median: 34). Intraoperative patient data is shown in Table 8.

Intraoperative data	Mean ± SD (Median)
Time to HCA (min)	25±12 (21)
CPB time (min)	176±63 (158)
HCA time (min)	46±21 (45)
SACP time (min)	36±18 (34)
SACP flow right start (ml/min)	216±55 (200)
SACP flow right end (ml/min)	199±40 (190)
SACP flow left start (ml/min)	224±55 (210)
SACP flow left end (ml/min)	230±61 (220)

Table 8. Intraoperative data

Core temperature evaluation

Statistical analysis revealed strong association between tympanic temperature and arterial blood temperature during HCA, while rectal and bladder values did not represent the core temperature adequately. The difference between rectal and arterial blood temperatures was significantly greater than the difference between tympanic and arterial blood temperatures [average temperature difference (rectal minus arterial): 7.9 (pre HCA), 8.3 (pre SACP), 5.6°C (end SACP); average temperature difference (tympanic minus arterial): 1.9, 1.7, 0.3°C, respectively; (p<0.001)]. There was a similar relationship between the bladder and tympanic temperatures (average temperature difference (bladder minus arterial): 7.3, 6.7, 4.8°C, respectively; average temperature difference (tympanic minus arterial): 1.9, 1.7, 0.3°C, respectively; (p<0.001)]. Figure 9 shows the temperature detected at different sites during the course of the operation.
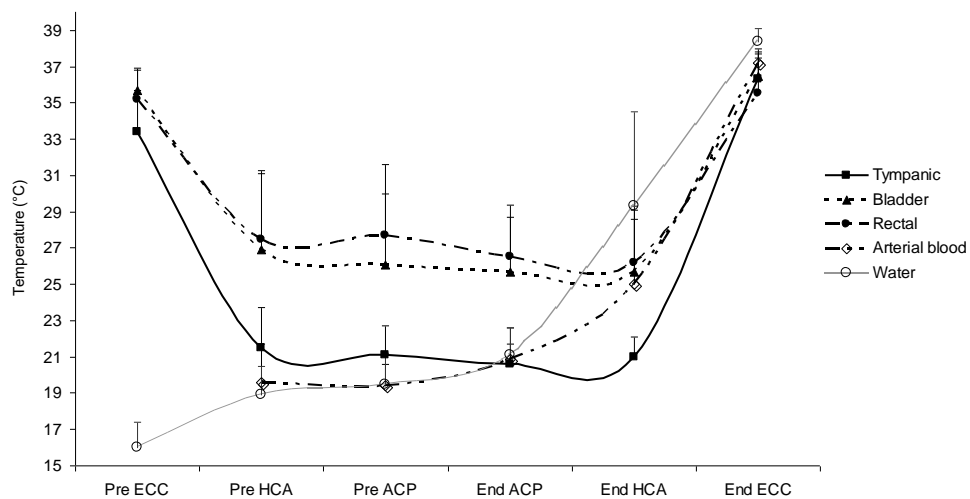

Figure 9. Temperature changes at different measurement sites during ECC, HCA and SACP

Analysis of rewarming phase revealed strong correlation between tympanic and arterial blood temperature (r= 0.9541; p<0.001) as well as between the arterial blood and heat exchanger water temperature (r=0.9879; p<0.001). Urinary bladder and rectal values showed less correlation with the arterial blood (r=0.7939, p= n.s.; r=0.7654, p= n.s., respectively). Figure 10 shows core temperature detected at different sites during the rewarming phase.

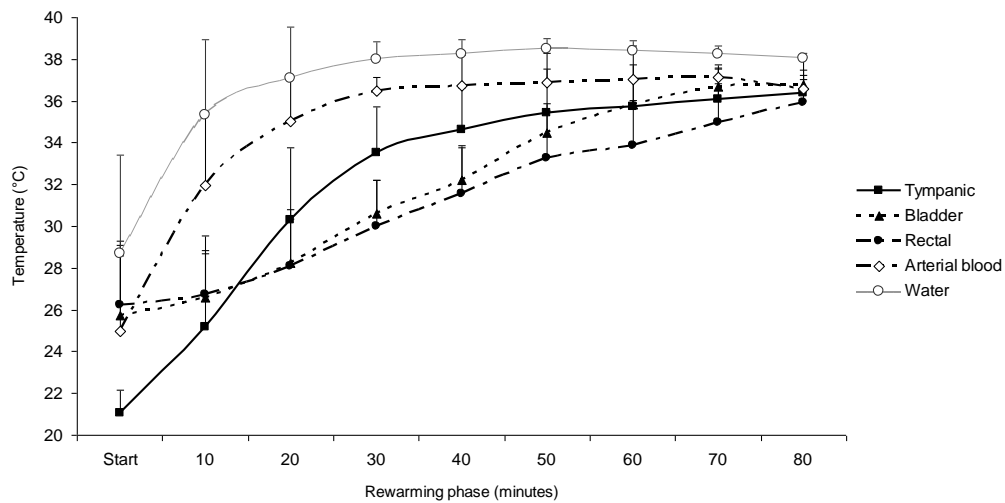Figure 10. Core temperature at various intervals during rewarming from HCA

Conclusion

We recommend multiple temperature measurement sites during aortic surgery applying HCA and SACP to be able to assess homogenous cooling and rewarming of the patient. To achieve good postoperative neurological outcome, we believe that tympanic values are highly reliable as a guide to temperature changes of the brain during HCA and rewarming.

Study III - Management options for aortooesophageal fistula

Background

Aortooesophageal fistula is a very rare clinical entity often leading to a life-threatening gastrointestinal bleeding. Thoracic aortic aneurysms are the most common cause of aortooesophageal fistula, further causes involve foreign body ingestion, trauma, which is in most of the cases iatrogenic, carcinoma, or very rarely aortitis tuberculotica. Conservative treatment of AOF results in a high in-hospital mortality rate, and conventional surgical procedure has a reported in-hospital mortality rate of nearly 40% (62). TEVAR as a stand-alone procedure has recently gained recognition as a possible technique for emergent treatment of AOF, despite a considerable risk of infection (16); in contrast to conventional solution of open thoracic surgery with higher mortality and morbidity. However, relatively little is known about long-term results of TEVAR for AOF due to its rarity and lack of large clinical experience.

Patients and methods

We retrospectively analysed all our patients with AOF in a period of two consecutive years undergoing different management approaches by separate surgeons. There were all together 5 patients treated by TEVAR and oesophagectomy, due to the low number and also lack of homogenous matching size control group, no statistical analysis could have been performed. We have demonstrated pros and cons of different therapeutic strategies, since each of them represent a possible management pathway in this group of patients with different advantages and disadvantages through one characteristic case each. The current literature has been also reviewed for treatment options, low number of isolated case reports are present, even much limited number of larger scale single centre analyses show up usually less than ten patients.

Management by EVAR and subtotal oesophageal resection followed by gastrooesophageal reconstruction

Our most challenging, but educational TEVAR case, a 69-year-old man presented with 3 days of central chest pain, coughing and haematemesis. Past medical history included hypertension, hyperlipidemia and gastrooesophageal reflux disease. Laboratory findings showed increased inflammatory markers. Computed tomography revealed a saccular mycotic aneurysm of the

mid-descending thoracic aorta in a close relation to the thickened wall oesophagus anteriorly. Air inclusions were visible within the aneurysm thrombus. No pathological lymph nodes were present. A communication between the descending aorta and oesophagus was demonstrated on computed tomography (Figure 11). The patient underwent massive blood- and blood product transfusions to maintain haemodynamic stability. Urgent TEVAR was performed as a life saving procedure, which successfully isolated the aneurysm (Figure 12).
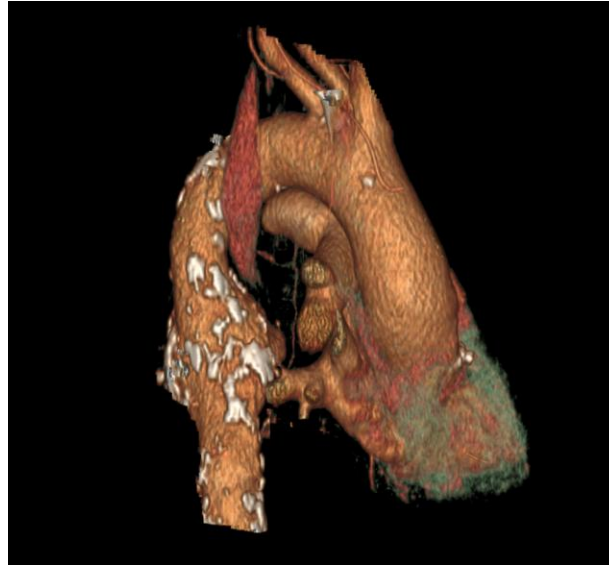
Figure 11. 3D reconstruction of the aortooesophageal relation at AOF, contrast enhancement outlines the oesophageal silhouette

Total oesophageal resection, evacuation of infected thrombus and a tunnelled feeding jejunostomy was undertaken thereafter to prevent sepsis on the next day. Surprisingly, histology of the resected specimen showed a clearly defined fistula tract on basis of a moderately differentiated squamous cell carcinoma colonised by E. coli, suggesting that this rather than pressure was the aetiology of the AOF.

Figure 12. Pre- and postoperative diagnostic images of TEVAR treatment in AOF

Panel A – Arrow marks the level of AOF, note the contrast enhancement inside the oesophagus

Panel B – Saccular aneurysm of the mid-descending thoracic aorta on fluoroscopic image

Panel C – Arrow shows TEVAR in position, note the absence of oesophagus
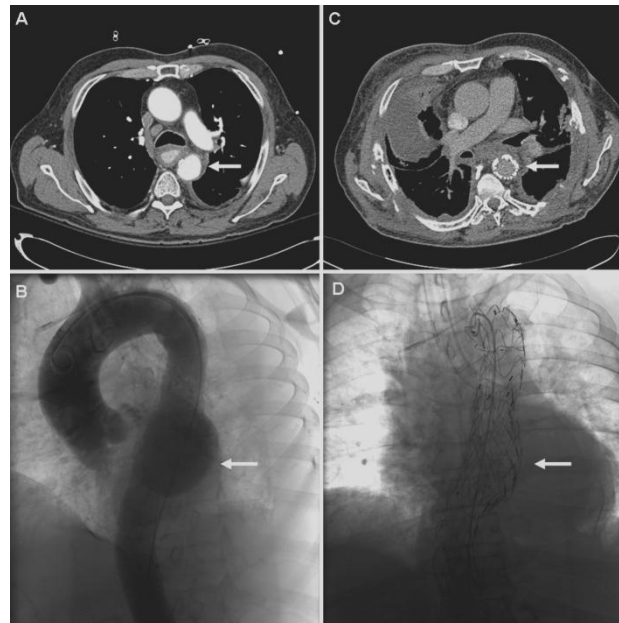
Panel D – Fluoroscopic image of endovascular stent graft in situ

Patient's prolonged postoperative course was complicated by respiratory distress syndrome and acute renal failure, which were both successfully managed. The patient was discharged well recovered after 71 days postoperatively with normal inflammatory markers. Outpatient rehabilitation was undertaken prior to gastrooesophageal reconstruction which was scheduled six months following TEVAR.

Management by open thoracic surgery

A 30-year-old patient was admitted as emergency after having an electromechanical dissociation arrest during oesophago-gastroscopy for gastrointestinal bleeding. OGD showed an oesophageal ulcer. Computed tomography demonstrated a communication with the descending aorta, where an aneurysm was situated.

An aortic repair was performed with a 30-mm-diameter gelatin-coated woven polyester interposition tube graft (Gelwave; Vascutek, Inchinnan, UK) followed by a McKeown

oesophagectomy and a gastrooesophageal reconstruction with orthotopic gastric interposition at the same operation. For this approach the surgical decision was based on the patient's young age, good general condition and a limited oesophageal laesion. Postoperatively he became septic with Pseudomonas in the blood cultures and developed a left upper lobe lung infarct. A redo thoracotomy was undertaken, the necrotic left upper lobe was removed followed by a pleurectomy.

During the patient`s regular outpatient follow-up repeat CT scan after six months showed a fluid collection around the graft anastomosis with some inflammatory signs. The graft was replaced by a homograft as an urgent procedure. After this surgical intervention the patient was discharged after 15 days in a good general condition.

Conservative management of postoperative graft infection

A 62-year-old male patient presented with back pain and severe shortness of breath. He had no significant past medical history. A computed tomography angiogram showed a Crawford type I descending aortic aneurysm extending from the left subclavian artery and ending at the renal arteries. Diameter of descending aorta was 6-7 cm at the beginning, the maximum diameter reached 10 cm at the level of tracheal bifurcation with an obvious rupture and a large haematoma compressing both trachea and oesophagus; there was an oesophageal communication also demonstrated. The aneurysm was replaced by an interpositional Dacron tube graft, the oesophageal rupture orifice was closed with a bovine pericardial patch so that Dacron graft could have been separated from trachea and oesophagus.

After a couple of days, a recurrent oesophageal leakage was demonstrated on per oral feeding. The patient refused a radical oesophageal surgery, so he was further treated conservatively with the aid of antibiotics. In the following weeks his general condition was stabilized and he was discharged on a six months course of antibiotics. The patient was reluctant to carry on with the prescribed treatment after one month; later on he was readmitted with recurrent graft infection. This time he also refused further surgical intervention, under a long-term (one year) antibiotic therapy he could be discharged following a prolonged inpatient care. Once more he had a relapse as not taking the prescribed medication meticulously, refused again invasive therapy, therefore, after longish recovery his was discharged on life-long antibiotic coverage.

Results

No statistical outcome could have been achieved from this limited number of treatments, which still represents a higher range of single centre AOF experience in the current medical literature.

Conclusion

Our empirical conclusion is, that early diagnosis and aggressive surgical approach without delay is the key for effective treatment for AOF. TEVAR treatment is essential to save the patient, but as the process is usually situated in an infected environment due to communication with the inner body surface; TEVAR as a stand-alone procedure would often end-up with life threatening mid-term graft infection. Therefore, following short-term vital stabilization, the oesophagus should be removed and the infected posterior mediastinal area cleared. After sufficient recovery, a second stage interval gastrooesophageal reconstruction may lead to the most optimal long-term results.

Study IV - Age-related considerations in acute type A aortic dissection

Background

Our aim was to investigate on clinical and anatomic presentation of TAAD according to patients' age. Only a limited number of reports in literature are focused on preoperative features and their correlation with age of patients presenting with TAAD. On this basis, we have studied clinical and anatomic presentation of TAAD, characterized their relationship with patients' age and evaluated possible implications in terms of pathologic background and surgical management.

Patients and Methods

Population

Internal database of Wessex Cardiothoracic Centre at University Hospital of Southampton, United Kingdom was interrogated and 235 patients were identified, who had undergone repair of spontaneous TAAD between January 2000 and December 2014.

Study design

Retrospective cohort study. We investigated on clinical presentation, anatomic features of TAAD and operative techniques for aortic repair. Distribution of intimal tear was coded according to involvement of the aortic root, isolated to ascending aorta or affecting the aortic arch. Extension of dissection was reported based on presence of a dissecting flap in the aortic root, aortic arch, descending thoracic aorta and the abdominal aorta.

Statistical analysis

Continuous data are presented as mean±SD, categorical variables are represented as counts and percentages. Student t-test was utilized to compare age between groups defined by clinical presentation, anatomical presentation and surgical procedures. Influence of age on probability of anatomical presentation was assessed with logistic regression.

Statistical analyses were performed with Stat-View Statistical Software Package 5.0 (SAS Institute, Inc. Cary, NC) and NCSS 2001 (Number Chruncher Statistical System, Kaysville, Utah).

Results

Demographic and preoperative clinical presentation

Figure 13 provides details on age distribution in our population; patients younger than 40 years represent 6% of total number of patients, who underwent surgical repair of TAAD, 18% were younger than 50 years and 32% older than 70 years. Male patients experienced acute dissection earlier in their life. Age of patients with a known connective tissue disorder or bicuspid aortic valve was significantly lower than those without any syndromic features and presenting with a tricuspid aortic valve. No significant differences in preoperative clinical presentation were found, but predominant signs of myocardial ischaemia, which were more common in younger patients ($\leq$ 50 years). Table 9 provides further details on preoperative clinical characteristics.
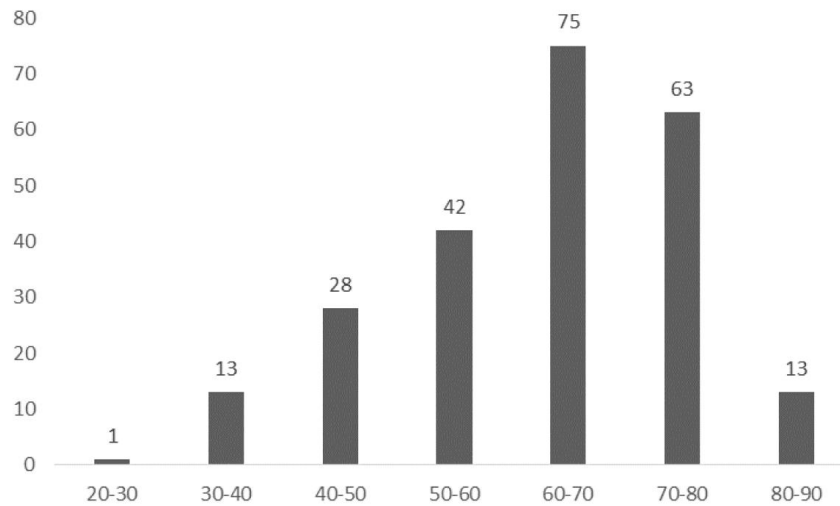
Figure 13. Age distribution of patients who underwent TAAD repair

Variables	No (%)	Age (mean±SD) years		p value
		Variable YES	Variable NO	
Gender (male)	154 (66%)	61.4±12.6	68.0±12.1	<0.0001
Presentation				
Myocardial ischaemia	36 (15%)	60.0±14.8	64.9±13.5	0.04
Tamponade	39 (17%)	66.2±18.3	63.6±13.5	0.24
New onset of cerebral stroke	18 (8%)	65.6±22.9	63.9±13.4	0.59
Mechanical ventilation	16 (7%)	61.6±22.1	64.2±13.4	0.41
Acute Renal Failure	12 (5%)	64.9±25.2	64.1±13.4	0.82
Limb ischaemia	12 (5%)	62.7±25.2	64.0±14.0	0.72
Abdominal ischaemia	2 (1%)			
Cardiopulmonary resuscitation	10 (4%)	67.3±27.5	63.9±13.4	0.41
Connective tissue disorders/BAV	22 (9%)	50.1±17.2	64.5±12.6	0.004
Marfan syndrome	6 (3%)	45.5±22.4	64.3±13.3	<0.0001
Previous cardiac surgery	14 (6%)	62.6±25.4	64.2±13.1	0.65

Table 9. Preoperative clinical characteristics

Extension of dissection flap and sites of intimal tear

The more extensive dissecting process is associated with more frequent involvement of the coronary sinus(es), additional descending thoracic and abdominal aorta progression. The above features characterize the anatomic presentation in younger patients. Investigations of distribution of primary tear sites showed that significantly lower age was associated with presence of intimal tear at level of the aortic root. We found similar results regarding proximal aorta involvement, even when analysed the population excluding patients with syndromic disorders and bicuspid aortic valve. Table 10 summarizes all these findings. Probability of aortic dissection extension into the coronary sinus(es), descending thoracic aorta and abdominal aorta involvement decreases with patients' age; OR 0.96, 95% CI: 0.933-0.980; OR 0.97, 95% CI: 0.95-0.99; OR 0.97, 95% CI: 0.95-0.99, respectively. A higher age was associated with lower probability of intimal tear in the aortic root, OR 0.95, 95% CI: 0.93-0.98 (Figure 14).
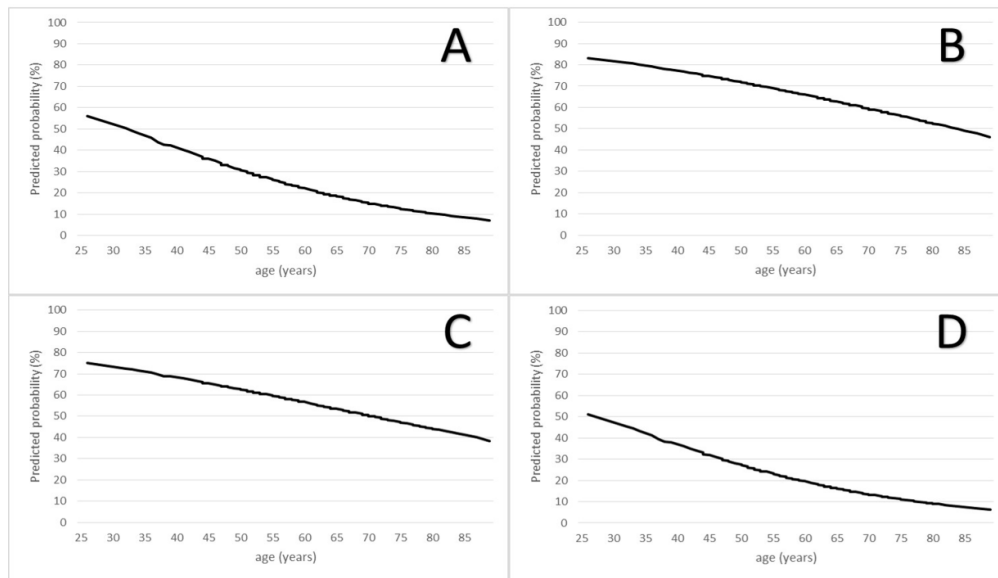

Figure 14. Relation of age and probability of dissection in different aortic regions

Panel A –Coronary sinus(es) dissection (p=0.0003)

Panel B – Descending thoracic aorta dissection (p=0.016)

Panel C – Abdominal aorta dissection (p=0.029)

Panel D – Intimal tear affecting the aortic root (p=0.0017)

Variables	No (%)	Age (mean±SD) years		p value
		Variable YES	Variable NO	
Overall population (n=235)				
Extension				
Coronary sinus(es)	50/235 (21%)	57.8±13.2	65.4±13.1	0.0002
Aortic Arch	205/235 (87%)	63.6±12.4	65.5±18.7	0.44
Descending thoracic Aorta	129/175 (74%)	62.0±12.9	66.6±14.8	0.014
Abdominal Aorta	109/171 (64%)	61.9±12.8	66.0±14.5	0.03
Intimal tear				
Tear identified	196/221 (89%)			
Tear root	36 (19%)	57.3±13.0	65.2±13.1	0.0007
Tear ascending aorta	103 (53%)	64.7±13.6	63.1±13.3	0.34
Tear arch	57 (28%)	66.1±11.0	63.1±14.0	0.13
Excluding connective tissue disorders and bicuspid aortic valve (n=213)				
Extension				
Coronary sinus(es)	45/213 (21%)	58.4±13.4	65.9±13.1	0.0004
Aortic Arch	184/213 (86%)	64.4±12.1	64.5±19.7	0.96
Descending thoracic Aorta	118/161 (73%)	62.8±13.5	66.3±16.8	0.13
Abdominal Aorta	100/155 (64%)	62.9±12.7	66.8±14.3	0.06
Intimal tear				
Tear identified	175/200 (88%)			
Tear root	32 (18%)	57.8±12.4	66.0±13.6	0.0009
Tear ascending aorta	91 (52%)	65.6±13.4	63.3±12.1	0.24
Tear arch	52 (30%)	66.6±10.7	63.5±13.6	0.14

Table 10. Anatomical findings

Surgical techniques

No difference in patients' age was found regarding distal repair strategy. A higher mean age characterized patients, who underwent associated isolated aortic valve replacement; in contrast to significantly younger age of patients, who had a full root replacement (Table 11).

Variables	No (%)	Age (mean±SD) years		p value
		Variable YES	Variable NO	
Aortic valve replacement	13 (6%)	71.1±10.7	63.7±13.3	0.04
Aortic root replacement	61 (26%)	57.2±12.1	66.5±12.9	<0.0001
Aortic valve sparing	2 (1%)			
Hemiarch replacement	65 (28%)	64.2±11.7	64.1±13.8	0.93
Total arch replacement	13 (6%)	58.4±12.0	64.4±13.3	0.09
30-day mortality	26 (11%)	67.0±11.2	63.7±12.7	0.19

Table 11. Operative procedures for dissection repair

Conclusion

Clinical presentation and occurrence of dissection related malperfusion syndrome were not associated - apart from presence of signs of myocardial ischaemia and syndromic connective disorders - with the age of patients presenting with TAAD. More extensive involvement of proximal and distal aorta characterized younger patients. Different pathologic background promoting onset of TAAD in young and elderly patients could explain this finding. Higher rate of connective tissue disorders and a wide prevalence of undiagnosed intrinsic underlying disease of proximal aortic wall may account for this peculiar presentation in the young. An intimal tear localization in the aortic root is more common at lower age of presentation. This finding associated with prognostic reasons supports the higher requirement for a full root replacement in younger patients.

Discussion

Study I

This study demonstrates that direct cannulation on concavity of the aortic arch instead of femoral or right subclavian artery may improve outcomes of ascending aorta and aortic arch replacement, especially in case of haemodynamic instability, although it is an observational study because the three groups are not balanced.

Albeit the idea of cannulating ascending aorta in type A aortic dissection was described decades ago (63), direct cannulation of ascending aorta has only been performed occasionally as an emergency technique to avoid retrograde malperfusion (64). Recently, successful attempts have been made to establish antegrade perfusion via ascending aorta primarily for type A dissections (65) (66) (67). Ascending aorta or arch cannulation may have the great advantage of technical simplicity, especially when there is haemodynamic instability or at dissected limb arteries (68) (69) (70) (71). According to these reports this technique can be performed safely under ultrasound-guidance. An access point at level of Botallo`s ligament utilizing the Seldinger technique could provide a useful alternative to establish rapid arterial entry. At this section of aorta the pulmonary bifurcation is firmly connected by a massive connective tissue, which usually prevents a complete dissection in this area. With the aid of this rapid and atraumatic cannulation method CPB can be established, thereby reducing likelihood of perioperative shock, which would lead to an increased mortality (72). Although time demand to reach circulatory arrest was remarkably lower applying the direct cannulation technique compared to the other two accession methods, level of significance was not reached because of a relatively low number of patients in the other two groups, and greater standard deviation values.

Rapid establishment of arterial access facilitates quicker initiation of antegrade systemic perfusion and core cooling, which also contributes to effective reduction of surgical procedural duration. This may result in lower morbidity through enhanced organ perfusion and reduction of coagulation disorder probability. Our method of aortic cannulation has additional advantages. One additional benefit of this type of arch cannulation is having the tip of the cannula located in the proximal descending aorta. Consequently, turbulence at the tip of cannula occurs in the proximal descending aorta, thereby reducing the risk of embolization of debris into the carotid arteries. Further advantage of proximal descending aortic perfusion is a

reduction of fluid jet stream – Coanda`s - effect that can be associated with relative carotid hypoperfusion in patients undergoing perfusion with a short cannula from the ascending aorta (73). Most patients suffering from TAAD undergo at least a "hemiarch replacement" in our practice, so the cannulations site is removed with the affected aortic wall segment and the repositioned cannula fits perfectly into the side-branched prosthesis.

In addition, transoesophageal or epiaortic ultrasonographic guidance may also be indispensable for reliable real lumen cannulation, which examinations are simple methods to obtain imaging information of ascending aorta and proximal arch. Although preoperative computed tomographic scan is mandatory to obtain correct operative planning, the ultrasonographic control provides real-time information on location of intimal tear, intimal flap, true and false lumen; as this intraluminal situation can change progressively following the tomographic scan. Moreover, the guide wire and correct position of the cannula can be checked continuously, so false lumen perfusion is surely avoided, which is not always the case at peripheral approaches. Simultaneous application of ultrasonographic control and cerebral monitoring by NIRS reduces the likelihood of malperfusion, thromboembolism and subsequent extension of false lumen. We have observed no local complications with Seldinger technique, but were always prepared to perform an apical cannulation described by Wada *et al* (25; 20) as a bail-out procedure.

The challenge of neurological injury resulting from embolic events and cerebral malperfusion in aortic dissections should be discussed with having a regard to that there are a number of different cannulation approaches. Femoral cannulation is well known associated with a higher risk of retrograde embolization and potential perfusion of false lumen via a distal re-entry point, although in our cohort there were no perfusion complications in this group. In this view, techniques providing antegrade flow may offer a better option, especially in patients with Stanford A dissections (74).

In our practice, Seldinger cannulation on concavity of aortic arch became the standard approach for arterial access in both elective and emergency cases as by the Hannover group (66) (75). This cannulation technique is fast and simple, which can be an important issue, especially in haemodynamically unstable patients. It avoids additional time-consuming incisions, thereby avoiding additional surgical trauma and possible local complications at peripheral cannulation sites. In combination with cold SACP and deep/moderate HCA, this technique allows adequate protection for the body and is not associated with higher risk of

cerebral microemboli (76) (77). Efficacy of SACP as an adjunctive to hypothermic arrest has been proven in numerous publications (78) (79).

As with other surgical approaches, there are some disadvantages, which need to be recognised. This includes cannulation of the false lumen with potential malperfusion or even complete rupture of the cannulated aorta. For those emergency situations, alternative strategies have to be available. In the above mentioned cases there are basically three major goals to be achieved; cerebral protection, myocardium conservation and finally a proper perfusion of the lower body. This stepwise approach necessitates an efficient cooperation of anaesthesiologist, perfusionist and surgeon to obtain optimal results.

Reece *et al* applied the Seldinger technique for cannulation in 24 patients, resulting in no misplacement (80). However, their study was not randomized, and various aortic pathologies were excluded, leading to a potential selection bias. Furthermore, the cannula is held in position manually during the cooling phase, not allowing further surgical activity during this period; the authors are not convinced that sutures in the dissected aorta remain stable. With our technique there is no need for sutures in the aorta; the cannula is fixed to the cranial skin incision corner by a suture and sits also deep enough in the proximal descending aorta not requiring any further support. Inoue et al report an experience in 32 cases, also using the Seldinger technique, controlled by epiaortic ultrasound. Prior to ascending aortic cannulation, they cannulated the femoral artery to be able to regulate the aortic pressure (70). Although no malperfusion occurred in their series, a double arterial approach is questionable in context of avoiding time-consuming preparations and potential retrograde embolism or further dissection (81).

Kitamura *et al* have presented recently the "Samurai cannulation" in AAS; 61 patients were cannulated within a period of six years, and have reported favourable postoperative stroke and in-hospital mortality rates in comparison to other cannulation methods of their patient population. Their central access is not novel, Kitamura applies a long-ago published bail-out method of Hannover group, where the patient is exsanguinated via venous drainage, the aorta is transsected, and the aortic cannula is placed into the exposed true lumen under direct visual control. Their potential hazard relies on normothermic circulatory arrest for minimum one minute leaving not much leverage to react on emerging complications, and air embolization is also more likely in case of an open aorta, where a short period of de-airing is available only under normothermic conditions (82).

Transapical cannulation is another elegant method for achieving reliable antegrade access, as described by Wada *et al* (25). In large cohort of 138 patients, the cannula was inserted through a 1 cm apical incision direct into the true lumen via the aortic valve under TOE guidance. The impact of causing an acute aortic insufficiency in this context is not discussed in detail. Both Wada's technique and Reece`s method have disadvantages of resulting in prolonged cardiopulmonary bypass times, since no additional procedures can be performed during cooling, such as inspection and preparation of the aortic root.

AxS is also an elegant, widely applied method for arterial access during aortic arch surgery (83). However, it is presumably more time consuming, and carries the possibility of failure rates up to 4.2%-11% (21). Nevertheless, it provides an opportunity of continuous unilateral cerebral blood flow without interruption (23). Applying the standard technique, however, only the right hemisphere is continuously perfused, which can result in malperfusion of contralateral hemisphere, as Merkkola *et al* demonstrated that up to 17% of patients have an incomplete circle of Willis (43). Even in presence of a complete circle of Willis, it is still an open question, if the exclusively right sided perfusion can sufficiently supply the left hemisphere. Our results with SACP demonstrate too, that the lowest perfusion volume is necessary to maintain a proper bilateral cerebral oxygenation in the direct cannulated group. Since the brachiocephalic trunk divides anatomically into two nearly equivalent branches, namely the right carotid and subclavian artery, the provided flow through the latter vessel on CPB can lead to a relative hyperperfusion of the right carotid parallel to a relative hypoperfusion of the aorta. This could explain our findings regarding SACP flow values and peripheral organic perfusion monitored by renal function and lactate level. The Seldinger technique delivers rapid arterial access, which results in a shorter ischemic period both cerebral and peripheral. AxS perfusion provides sufficient oxygenation for the right hemisphere but may not for the contralateral side, so the required initial right SACP flow is similar to the direct group, but the left shows such values as in the femoral group. Additionally, a constant relative hyperperfusion of right hemisphere most probably leads to an intracerebral oedema, which elevates SACP flow requirements to maintain a proper cerebral saturation at the end of HCA. Relative hypoperfusion of the body is characterized by diminished renal function at subclavian cannulation. It has to be considered as well, that at AxS approach usually smaller size cannulas can be applied due to the anatomical situation. Femoral access is more time consuming to be established resulting in relative cerebral hypoperfusion/longer ischemic period demonstrated by higher initial SACP flow requirements

in this group. Femoral perfusion, in case of no malperfusion, provides a proper renal blood supply, thus the renal function is better preserved than at subclavian access, but the initial hypoxia due to delayed establishment of perfusion is visible comparing the creatinine levels in this group to the direct cohort. Peripheral arterial access is not only challenging in dissected vessel, but also at high body mass index, or on the other side of the spectrum, in patients with a delicate stature, e.g. in East-Asia.

Cakir *et al* have demonstrated beneficial perfusion effects of a bidirectional novel innominate cannula in an experimental model, achieving higher perfusion readings than with AxS approach. This experimental model well supports our outcomes that perfusion in close vicinity of both carotid origins leads to most favourable cerebral supply in aortic surgery (84).

Moizumi *et al* could not use AxS access in 5.5% of their aortic dissection cohort, as pathological changes extended into the axillary artery (85). Our first experience with the Seldinger technique was also a patient having dissection in all limb arteries (69). Carotid artery cannulation, performed by Urbanski over 100 patients so far, including some with Stanford A dissections, seems to be another alternative method, but also carries a risk of brain malperfusion and later complications in the vessel (42). The experience with innominate artery cannulation by Di Eusanio *et al* includes 55 patients with only two in acute aortic dissections (86). In the past couple of years the latter two authors have shared their increasing number of patient experience regarding the own cannulation method, although the above techniques are still applied rather in elective aneurysm surgery, than in AAS.

The Kiel group has published Ramihi's 5-year experience regarding transatrial cannulation in TAAD, where 46 patients were cannulated through right upper pulmonary vein and the cannula tip was progressed into the left ventricle. They also report shorter procedural times, lower stroke and renal failure rate, and in-hospital morality. Despite the excellent outcomes strongly supporting our findings with direct aortic cannulation in AAS, some potential drawbacks have to be recognised regarding Ramihi's method; no manipulations are possible on the aorta until reaching HCA, mitral regurgitation may lead to pulmonary flooding endangering early postoperative ventilation. Another potential complication may emerge from the most common location of the aortic tear itself, as situated often on greater aortic curvature right above the STJ. Retraction for right upper pulmonary vein access may result in AAS progression, even in acute aortic rupture (87).

Fusco *et al* presented their results in femoral artery cannulation (88), with a conversion rate of 2.5% to ascending aortic cannulation, they conclude that femoral cannulation is appropriate and yields excellent clinical results. They have, however, not considered the problem of retrograde embolism from the downstream aorta, probably since atherosclerosis is less common in dissection patients in their experience.

Recent meta-analyses have also revealed advantages of central cannulation methods in complex aortic aneurysms and AAS surgery; proximal arterial cannulation adds-on a useful armamentarium for management of complex aortic disease in various aortic pathologies (89) (90) (91). Both Ma *et al* (2018) and Shimura *et al* (2019) have emphasized safety and advantages of ultrasound guided central aortic cannulation in TAAD regarding 33 and 208 patients in their series, respectively (92) (93).

Seldinger technique delivers rapid arterial access, which results in shorter ischemic periods both cerebral and peripheral (94). Potential drawbacks of the technique are requirement for a smoothly operating team, which emphasises the importance of specialised aortic teams; technical ability to perform transapical cannulation as a bail-out; local dissection in cannulation area is extremely rare.

As eventual drawbacks do not impose significant challenges in moderate size cardiac centres and real-time ultrasonographic monitoring provides a safe procedure; the Seldinger cannulation on the lesser curvature is a good-to-know central arterial access in case of failing peripheral methods.

Study II

Our other study on intraoperative core temperature monitoring demonstrates that tympanic measurements provide reliable temperature estimation during aortic surgery performed under HCA. This may aid in improved postoperative outcomes due to a reduced cooling phase and adequate rewarming. Although application of hypothermia has been an important contribution to patient management as a neuroprotective method from the dawn of cardiac surgery (34) (95), proper body temperature management relies on accurate measurement of temperature, to enable adequate monitoring of changes during CPB and HCA. Oxygen consumption drops with lower body temperature so that ischaemic tolerance is increased by cooling. Cerebral oxygen requirement decreases to approximately one-fifth of normothermic needs at 20°C (35) allowing a safe period of 45-50 minutes for HCA. In addition, hypothermia may contribute to neuroprotection by a variety of complex mechanisms including decreased vascular permeability, reduced ion influx and decreased excitatory transmitter release (37). During the rewarming phase of CPB, conventional temperature monitoring sites may not reflect true brain temperature so that cerebral hyperthermia may not be detected, if conventional temperature monitoring underestimates brain temperature or there is a delay with arterial heat exchange (96) (38). Monitoring rectal or urinary bladder temperature to control intraoperative core temperature is standard in many institutions all over the world. Rewarming, which aims to normalise temperature after HCA, relies on measured data from the above sites. We have shown that temperature measurement at these sites could be misleading, possibly due to latency in the heat exchange process at these points. Clinicians are often concerned about risks of postoperative hypothermia, such as shivering leading to increased myocardial oxygen consumption, arrhythmias, coagulopathy, greater risk of wound infections and extended hospital stay (97) (98) (99) (100), but possible side effects of cerebral hyperthermia are rarely taken into account. Thus, the rewarming phase must be carefully monitored and managed to avoid cerebral hyperthermia, since it elevates the risk of post-ischaemic tissue injury (101) (102), and intraoperative hyperthermia is well known to be associated with post-operative neurological impairment (103) (104).

Arterial blood temperature is considered to be the most accurate indicator of cerebral temperature (105) (106). It is not surprising as this is the medium for heat exchange for the brain during HCA and SACP. According to our results, tympanic temperatures correlate well with arterial blood temperatures and hence with cerebral temperatures, not only during HCA but also during the rewarming phase of the surgical procedure. Urinary bladder and rectal

temperatures lag behind arterial blood temperatures, therefore, these measurement sites cannot be relied upon to provide accurate estimation of temperature change. This affects management of these patients at various phases of cooling and re-warming. The tympanic membrane is situated in the immediate vicinity of internal carotid artery and is supplied by its branches. Thus, the tympanic temperature is well-placed to closely represent cerebral thermal state. Although some authors consider tympanic temperature as a good standard for cerebral temperature monitoring reflecting the hypothalamic status [107] [108], others have suggested that tympanic temperature can be influenced by changes in ambient temperature [109] [110]. If prior to insertion of a tympanic probe, a debris-free status of the auditory channel is confirmed via otoscopic examination along with careful insulation by cotton swabs and the probe is securely fixed by tape and gauze bandage over the external ear, so the ambient temperature influence on tympanic measurement can be effectively diminished. Variations in urinary flow, which is a usual phenomenon during CPB and especially with HCA may affect the bladder temperature sensors [111]. On the other hand, rectal probes can become lodged in faecal matter, which insulates them from the surrounding tissues [112]. The above factors contribute to a weak correlation of these temperature measurements with those of arterial blood.

In our institute we do not use nasopharyngeal/oesophageal temperature monitoring in HCA as standard measurement site, as it has been shown in several studies to modestly, but significantly over- and underestimating brain temperatures during the cooling and rewarming phase, respectively [113] [114] [115]. Probably this is a result of the suboptimal heat exchange environment as these probes are situated in larger air containing cavities. Although oesophageal probes are placed relatively close to the descending aorta, the open chest or eventually applied topical cooling in the pericardium could also influence measurement accuracy. Akata *et al.* have furthermore demonstrated, that pulmonary artery temperatures closely reflect changes in brain temperatures, but nasopharyngeal/oesophageal measurements could not be considered as a reliable index of brain temperature at all during rapid induction of moderate/deep hypothermia [116].

We can conclude that tympanic temperature measurements correlate with arterial blood temperature monitoring during aortic surgery with HCA and SACP, and therefore should replace bladder and rectal measurements.

Study III

Aortooesophageal fistula is a rare cause of gastrointestinal bleeding, characterized by significant morbidity and mortality, even with early diagnosis and intervention. Several therapeutical management options have been reported in literature, although all rely on the same principle; urgent management of the aortic tear with immediate or delayed repair of the oesophageal lesion. There are many approaches to treat AOF, but the treatment has to be adapted to the patient's wishes in some cases. In our experience the most straight-forward therapeutic option is emergency TEVAR followed by an urgent subtotal oesophageal resection, the therapeutic circle is completed by a second stage gastrooesophageal reconstruction. Securing the bleeding source as emergency, removing the oesophagus urgently to prevent sepsis, and subsequent elective reconstruction of gastrointestinal continuity appears to be a justified surgical approach, as in the current available literature also states, although there are no large studies available. TEVAR is a new, lower risk emergency alternative, although stand-alone TEVAR leaves the oesophageal defect untreated, contributing to a higher risk of mediastinitis and increased mortality and morbidity (16). A similar conclusion resulted from the Regensburg experience; TEVAR is an effective emergency alternative to prevent early fatal exsanguinations, however, can rarely be utilized as a stand-alone procedure (117). A nationwide, multicentric Italian study provided information on 25 aortooesophageal and aortobronchial fistulas that were treated with TEVAR. The results demonstrated that patients, who underwent combined TEVAR and tracheobronchial/oesophageal intervention, had lower graft infection rates and better survival than patients receiving TEVAR treatment exclusively (118). Most probably, the long-term prognosis is affected by a concomitant mediastinal infection and graft contamination.

Surgical approach of the oesophageal lesion is controversial in the literature. Snyder *et al* reported a primary suture of the oesophageal defect with minimal mediastinal contamination, although it was associated with a higher risk of dehiscence and fistula recurrence, probably due to local ischaemia (119). Instant oesophago-gastric anastomosis after subtotal oesophagectomy may be another alternative (120), although associated with increased risk of perioperative death, but this risk could be reduced by omentopexy around the tube graft. Subtotal oesophageal resection followed by gastric or jejuneal interposition as a second stage surgical intervention could minimize the hazard of graft infection (121) (122). For feeding, transdiaphragmatic or transthoracic gastrostomy are reliable solutions that both avoid further opening of the abdomen for a separate gastrostomy or jejunostomy and minimizes damage to

the stomach, but maintains patency of the upper gastrointestinal tract. Another interesting complex solution to prevent late thoracic interposition graft infections has been described by Aleksic *et al* and Aizawa *et al* Although with different etiology, they both demonstrated reasonable long-term results after implantation of an extraanatomic ascending-descending aortic interposition tube graft bypass with stump closure of the affected descending aorta, with or without omentopexy around the descending stump (123) (124). Our personal experience with extraanatomical bypasses is limited to extensive chronic TBADs, in which cases the distal abdominal and lower limb perfusion was severely compromised. The operative solution of bilateral subclaviofemoral bypasses provided acceptable perfusion results, although the long-term patency was significantly influenced by the efficacy of anticoagulation. Müller *et al* have investigated 33 patients with anatomic and extraanatomic repair following mycotic aneurysms of the thoracic and abdominal aorta, their conclusion shows that in situ reconstructions did not carry a higher risk of morbidity and mortality than extraanatomic counterparts (125).

Similar conclusions to our therapeutic considerations were drawn by the so far largest multicentric database analysed by Japanese Association for Thoracic Surgery in 2014. 47 AOF cases were reported from whole Japan, their conclusion was that TEVAR alone for AOF management is associated with high mid-term mortality and does not improve mid-term outcome; therefore, not be considered as a definitive stand-alone therapeutic option. In addition, oesophageal reconstruction might be acceptable for single stage operations in patients in a stable condition, as no significant differences were observed between patients treated with oesophageal reconstruction at the same or a different occasion (126).

In conclusion, early diagnosis and aggressive surgical approach without delay is the only option for effective treatment for AOF. Second stage interval gastrooesophageal reconstruction may lead to most optimal long-term results as majority of patients are in a poor condition at the initial life-saving TEVAR and oesophagectomy. Imaging examination is essential in the primary diagnosis; computerized tomography is a safe, reliable, non-invasive method in early recognition of this highly lethal entity. We have to emphasise the importance of multidisciplinary character of the treatment involving radiologists, gastroenterologists, upper-gastrointestinal- and cardiothoracic surgeons to obtain the most favourable results in management of AOF.

Study IV

TAAD is more common from seventh decade of life, albeit it is an unexpected pathology in healthy subjects; it represents one of well recognized causes of sudden death in young people (127) (128). Our data entirely supports previous findings reporting that among patients undergoing TAAD repair 6% is younger than 40 years, and 20% is aged less than 50 years (129) (130). Several triggers including hypertension, smoking habit, cocaine abuse and amphetamine have been associated with occurrence of this catastrophic event in the young (131) (132), but the presence of underlying connective tissue disorder has been extensively recognized as a fundamental predisposing factor strongly bound to this population (130) (133). It is not surprising that patients with known connective tissue disorders came to our attention at a significantly lower age than those without any syndromic disease and presenting with a tricuspid aortic valve. An inherited pathology of the aortic wall leads to a faster development of aortic aneurysms and to a higher risk of aortic complications. This early pathologic evolution does not characterize only syndromic patients, who represent only a small subgroup in surgical series, and a minority among young patients. IRAD investigators reported that people under 40 years with positive family history showed a significantly increased size of aortic root and ascending aorta when compared with older patients (133). This finding was common both in Marfan and non-Marfan patients. Several non-syndromic genetic conditions can lead to early development of thoracic aortic aneurysms, which are further characterized by rapid dilation, and high risk of dissection. These non-syndromic Familial Thoracic Aortic Aneurysms are related to genetically heterogeneous disorders, and are estimated to represent 20% of cases in diagnosed thoracic aneurysms (134). Mutations in five genes (MYH11, TGFßR1, TGFßR2, MYLK, and ACTA2) have been identified so far with all autosomal dominant inheritance (135). From molecular point of view, consequences of genetic alterations translate into a degenerative remodelling of the aortic medial extracellular matrix resulting in progressive loss of elastic properties (136) (137). Clinical, anatomical, genetic and molecular evidences suggest that prevalence of inherited aortic wall disorders in young people presenting with aortic complications is probably higher than expected and diagnosed.

This pathologic background can have an important role in extension of dissection. In our series, a significantly lower mean age characterized the presentation with a more prominent involvement of the aortic root and distal aorta. Within the characteristics of our population, we have confirmed the findings coming from the experience of Nishida *et al* (138), describing a strategy for aortic root repair, and from the analysis of the large GERAADA database,

which reported that probability of TAAD extension into the supraaortic vessels and abdominal aorta decreases with patients' increasing age (130). Even after excluding patients from the analysis having syndromic disorders or bicuspid aortic valve, we found that more severe involvement of the aortic root and coronary sinus(es) were present in younger than in patients having a proximal flap of dissection involving just the ascending aorta and limited to the non-coronary sinus. Association of lower age and dissection of coronary sinus(es) may further account for the preoperative presenting sign of myocardial ischaemia. This event has been associated with aortic root complication after dissection repair and can be seen as a marker of severe proximal aortic tissue disruption (139).

Intimal tear at the level of the aortic root is a feature of the younger subgroup and this result was additionally confirmed via analysis following exclusion of patients with known connective tissue disorders or bicuspid aortic valve. In a different population, Ma *et al.* (140) described a similar distribution of intimal tear site and reported age and hypertension as risk factors for an arch entry tear. Alongside genetic and metabolic alterations, the aortic flow properties play a key role in progression of the wall disease (141) (142), and maybe an active variable in promoting the onset of dissection. Recent studies investigated on aortic flow patterns and wall stress with the aid computational fluid dynamics. Wall shear stress seems to have a significant impact in triggering and progression of medial degeneration, and represents a mechanical force able to separate aortic layers once imbalance between the tissue strength and flow-induced wall stress occurs (143) (144). Numata *et al* investigated on six different anatomical models of aortic disease. In all patients the oscillatory shear index (a parameter describing the deviation on wall shear stress from its mean direction) was higher close to the sinotubular junction (STJ), near the origin of innominate artery, and on the lesser curvature of proximal descending aorta. All these areas are predilection points for intimal tears (143). Clinical evidences are limited, but suggest that different patterns of aortic segment dilatation and blood flow properties across the aortic valve can promote development of intimal tear in different areas of proximal aorta; with major involvement of the lesser curvature of ascending aorta in patients with preserved or not extremely dilated STJ; the right lateral side of the aorta in case of diffusely dilated proximal aorta; and the sinus(es) of Valsalva/STJ in presence of a dilated aortic root (143) (144).

Different pathologic and pathogenetic substrates between young and elderly patients - the latter are affected by long-standing hypertension and a progressive atherosclerotic process - require a significantly different approach in proximal repair of aortic dissection. We found

that full root replacement was regularly performed in younger patients, while elderly patients underwent a more conservative proximal repair. The literature reports an average rate of 23%-25% full root replacement in the overall population of patients undergoing TAAD repair, around 40%-60% in people under the age of 50 (130) (145) (133), 10%-20% in septua- and 5%-10% in octogenarians. Isolated aortic valve associated with interposition graft replacement of the ascending aorta is nowadays reserved in case of valve leaflets degeneration or calcification, and reported in about 5% of cases; mostly in people aged over 70 years. There is no doubt that younger people deserve more radical aortic resection, but besides clinical and prognostic reasons we should recognize the importance of pathologic background and anatomic features in determining the surgical strategy for proximal repair. Nevertheless, recommendation for a full root replacement in case of connective tissue disorders, dilated or severely dissected aortic root, and in presence of an intimal tear in the aortic root, is nowadays widely accepted aiming a safe procedure in an acute setting and reduction of risk of reoperation in mid- and long-term. Evaluation of anatomical characteristics can also explain similar prevalence of arch procedures in young and elderly patients in the literature (130); more extensive distal repair is usually reserved in case of an intimal tear situated in the aortic arch or in presence of an aortic arch aneurysm. We were not able to report aortic dimensions, but we found no difference in patients' age regarding presence of an intimal tear involving the aortic arch.

Clinical presentation and occurrence of dissection related malperfusion syndrome were not associated, apart from presence of signs of myocardial ischaemia and syndromic connective disorders, with the age of patients presenting with TAAD. More extensive involvement of the proximal and distal aorta characterized the younger patients. Different pathologic background triggering the onset of TAAD in young and elderly could explain this finding. Higher rate of connective tissue disorders and wide prevalence of undiagnosed intrinsic underlying disease of the proximal aortic wall might be accountable for this peculiar presentation in the young. Intimal tear in the aortic root is also more common at lower age of presentation. This finding associated with prognostic reasons is strongly supports a higher prevalence of full root replacement in younger patients.

Summary of new findings

1. Minimal invasive central cannulation by Seldinger method on concavity of the aortic arch is technically feasible and safe. It may avoid cerebral embolization and organ malperfusion; therefore, may reduce the rate of neurological and malperfusion complications. This alternative arterial inflow technique can be applied for prompt establishment of CPB in type A dissections or other aortic emergencies, especially during haemodynamic instability. SACP provides more homogenous perfusion to both haemispheres than UACP, reducing the risk of overperfusion of the right, and relative hypoperfusion on the contralateral side.

2. We have proven that tympanic temperature monitoring is highly reliable as a guide to temperature changes of the brain during HCA and rewarming, as best correlating with arterial and brain temperatures. We recommend multiple temperature measurement sites - additional bladder or rectal - during aortic surgery applying HCA and SACP to be able to assess homogenous cooling and rewarming of the patient.

3. Early diagnosis and aggressive surgical approach without delay is a key factor in effective treatment for AOF. TEVAR treatment is essential to save the patient, but as the process is usually situated in an infected environment due to communication with the inner body surface; TEVAR as a stand-alone procedure would often end-up with life threatening mid-term graft infection. Therefore, following short-term vital stabilization, the oesophagus should be removed, and the infected posterior mediastinal area cleared. After sufficient recovery period, a second stage interval gastrooesophageal reconstruction may lead to the most optimal long-term results.

4. We have demonstrated that more extensive involvement of proximal and distal aorta, myocardial ischaemia and syndromic connective disorders characterize younger patients. Different pathologic background promoting onset of TAAD in young and elderly patients could explain this finding. Intimal tear localized in the aortic root is also more common at lower age of presentation. These findings associated with prognostic reasons support the necessity for radical surgical approach in younger patients.

Acknowledgements

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Appendix

I

Proposal for bail-out procedures - Vascular thoracic

Surgical management for Stanford type A aortic dissection: direct cannulation of real lumen at the level of the Botallo's ligament by Seldinger technique

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Abstract

A 50-year-old man was diagnosed with Stanford type A acute aortic dissection with cerebral malperfusion and unconsciousness. This clinical presentation was investigated by computed tomography which revealed a severe type A dissection involving all limb arteries. Successful operative treatment based on the direct arterial cannulation of the real lumen of dissected aorta at the level of Botallo's ligament by Seldinger technique achieves an appropriate perfusion and rapid cooling of the instable patient. To our knowledge this is the first reported case in the literature.

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1. Introduction

Acute Stanford type A dissection, with or without involvement of the aortic arch, represents an emergency situation that requires immediate surgical intervention. Surgical therapy consists mainly in replacing the ascending aorta, and as extended procedure also removing the arch up to the proximal descending region as well, regardless of the extent of the pathological process. Acute aortic insufficiency, when present, is generally treated by valve resuspension or replacement. Mortality rates from these operations have dramatically improved as the result of recent advances in preoperative recognition, intraoperative techniques, and postoperative care [1]. Nevertheless, operations for acute type A dissections is still associated with high mortality rates [2]. Cannulation of an extended lesion presents often an enormous challenge either through subclavian or lower limb arteries [3–5]. We prefer an innovative cannulation method through the dissection membrane at the level of Botallo's ligament by Seldinger manner.

2. Case

A 50-year-old man complained of sudden chest pain, was admitted unconscious with anisochoria to our hospital. A computed tomography scan showed a Stanford type A aortic dissection. The dissection began directly over the aortic valve; the maximal aortic diameter of 6.0×5.5 cm was detected on the ascending part. A connection of real lumen

with the adjacent wall elements could be observed at the level of the Botallo's ligament (Fig. 1). The dissection involved both brachiocephalic trunk, left carotid and subclavian artery. The visceral arteries originated from the real lumen except the left renal artery. Wall destruction showed in the iliac arteries too.

Because of rapid worsening of general status and cardiovascular instability, the ascending aorta and aortic arch were exposed through a median sternotomy. The punction of the aorta adjacent to the pulmonary trunk at the level of Botallo's ligament was followed by a minimal invasive cannulation with dilation steps by Seldinger technique (Fem-Flex Femoral Arterial Cannula®, 24 Fr TFA 02425H Edwards Lifesciences LLC, Irvine, USA; Joline Special Dilatatorset®, Hechingen, Germany) (Fig. 2). Correct position of the guidewire and cannula was confirmed by TEE in the descending aorta. Cardiopulmonary bypass was instituted between the arterial cannulation site and right atrium. The patient was cooled down to a tympanic temperature of 23.5 °C (Mon-a-therm® Thermistor YSI 400 Series tympanic temperature probe, Mallinckrodt Inc, St Louis, USA), rectal temperature measured 25.3 °C, bladder temperature reached 20.7 °C. After cross-clamping an ascending aortic incision was made, antegrade crystalloid cardioplegic solution (2000 ml Custodiol® HTK-Solution by Brettschneider, Dr F. Köhler Chemie, Hähnlein, Germany) was administered through both coronary orifices. Hypothermic cerebral perfusion was maintained through selective cannulation of both carotids (DLP Retrograde Coronary Sinus Perfusion Cannula with manual Inflating Cuff®, Medtronic Inc, Minneapolis, USA) at a flow rate of 190–200 ml/min each side

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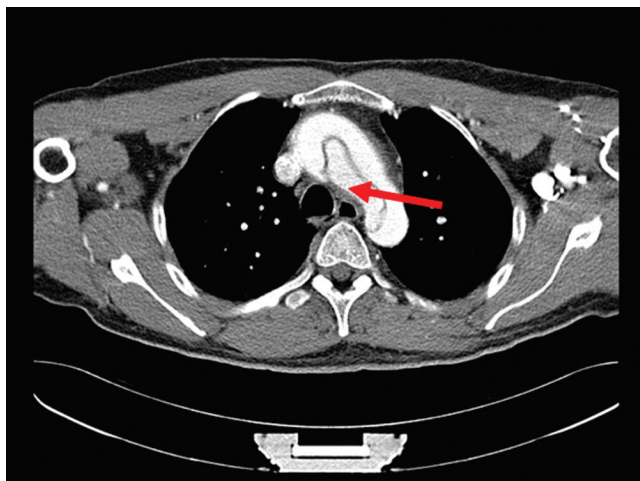 E-mail address: isartor@hotmail.com (L. Göbölös).

Fig. 1. Real lumen attachment to further aortic wall elements at Botallo's ligament.
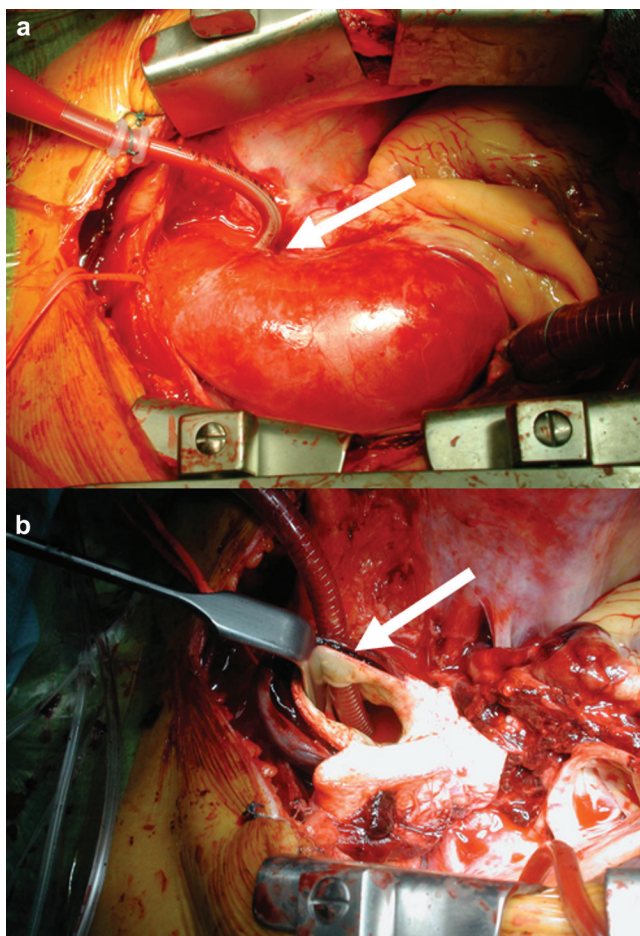

Fig. 2. Direct cannulation by Seldinger technique (a – mediastinal situs; b – intraluminal position).

and a perfusion pressure of 25–30 mmHg. Cerebral monitoring was performed with near infrared spectroscopy (INVOS® cerebral oxymeter, Somanetics Inc, Troy, USA), brain tissue oxygen saturation measured 60–65% continuously during perfusion.

Under systemic circulatory arrest, a complete reconstruction of the aorta up to proximal descending section was performed by a 30-mm vascular prosthesis (Hemashield Platinum Woven Double Velour Vascular Graft®, Boston Scientific Inc, Wayne, USA) including the island type reinsertion of all supraaortic vessels. The false lumen was eradicated with 45% bovine serum albumin-10% glutaraldehyde glue (BioGlue®, CryoLife International Inc, Kennesaw, USA); aortic valve commissures were refixed with the resuspension suture technique. Systemic reperfusion and rewarming were started through a graft side-branch. ECC time measured 156 min, circulatory arrest 63 min, antegrade selective cerebral perfusion time 50 min.

Pathological study of the aortic wall showed a degenerative atherosclerosis in combination with adventitial hemorrhage. A computed tomographic scan undertaken 12 days after the operation showed consolidation of the complete vascular situation and proper perfusion of both supraaortic and visceral branches. The postoperative course was uneventful except for a reversible left upper limb palsy. The patient was discharged after 22 days, and event free at six-month outpatient visit with consolidated vascular status.

3. Discussion

A Stanford type A dissection should always be treated surgically consisting of at least an ascending aortic grafting, although ascending aorta and total aortic arch grafting is appropriate for some of the complicated cases. The cannulation is a crucial point in dissection patients, if medial tear involves all great limb arteries. Establishing an access point at the level of the Botallo's ligament by Seldinger technique could provide a useful alternative to achieve a quick arterial entry. At this portion of aorta the pulmonary trunk is firmly bound by a massive connective tissue, which usually prevents complete dissection in this area. Through the rapid and atraumatic cannulation method ECC is introduced, thereby reducing the likelihood of peroperative shock leading to an increased mortality [6]. With increasing experience in arch reconstructions and improvement in outcome, the indications of minimal invasive direct cannulation could be expanded to include all type A aortic dissections with or without limb artery involvement. Concomitant replacement of aortic arch in ascending aorta surgery recently has been recommended for event-free long-term survival [7, 8]. It is mandatory to protect the central nervous system; a successful cerebral protection contributes to lower hospital mortality rate to 28% [9]. Reversible unilateral limb palsy is a rare complication of the procedure, in 3.8% observed according to some studies [10]. To our knowledge this is the first reported case of direct Seldinger cannulation of a Stanford A aortic dissection in the literature.

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eComment: Perfusion of the true lumen during surgery for aortic dissection

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We read with interest the paper of Gobolos and co-workers [1], and we congratulate the authors for this precise technique.

Retrograde perfusion via the femoral artery has been the perfusion mode of choice in aortic dissection surgery. However, many groups have moved to routine axillary artery cannulation to avoid potential malperfusion and atheroembolic complications associated with retrograde perfusion. However, in cases of hemodynamic instability, the axillary approach is time-consuming. We also have to consider that sometimes the dissection may extend to the innominate artery, with difficulties in the cannulation. Furthermore, even with axillary cannulation and antegrade perfusion, due to the presence of internal flap, there may be a malperfusion syndrome during cardiopulmonary bypass (CPB). This is usually due to the presence of multiple flaps inside the dissected aorta. Alternately, Wada and colleagues [2] reported good results with transapical left ventricular cannulation across the aortic valve into the true lumen guided by transesophageal echocardiography. Jakob and coworkers [3] reported the use of an open direct cannulation of the ascending aorta after exanguination of the patient through the venous line.

All those techniques share together an important point: the importance of true lumen perfusion. We should consider that aortic dissection is an acute disease with often rapid progression. Areas of intact aorta during the diagnosis by CT scan may result dissected at the time of surgery. The dissection may progress, and new intimal tears with new flaps may be present. Cannulation sites thought to be appropriate at the moment of diagnosis may later result insufficient to give an appropriate perfusion for the presence of new flaps. Malperfusion with low flow during CPB will prolong the time to reach the temperature chosen for the circulatory arrest and will predispose to malperfusion of vital organs and incidence of acidosis. The cannulation and perfusion of the true lumen appear then of vital importance.

We had a case where we used a technique similar to the one used by Gobolo. We would add that really, in our case, there was no need to cannulate near the Botallos ligament, and that the ascending aorta or the arch, even if dissected, may be cannulated using the Seldinger technique and ultrasound control.

In conclusion, we congratulate again the authors and we look forward to using this technique in particular clinical settings to further improve it.

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II

Central Cannulation by Seldinger Technique: A Reliable Method in Type A Aortic Dissection Repairs

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Data Collection B
Statistical Analysis C
Data Interpretation D
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Background: Extensive type A aortic dissections that involve peripheral great vessels can complicate the choice of a cannulation site for cardiopulmonary bypass. We started to employ direct cannulation of the true lumen on the concavity of the aortic arch by Seldinger technique and evaluated the efficacy of this access technique as an alternative arterial inflow target in aortic surgery.

Material/Methods: Twenty-four consecutive patients (mean age: 59±14 years) underwent type A aortic dissection repair using selective antegrade cerebral perfusion. Direct aortic cannulation was used in 14 cases, subclavian access in 6 patients, and femoral entry in 4 patients. Perioperative factors were evaluated to identify the reliability and eventual benefits of direct cannulation method at the aortic arch.

Results: There were no operative deaths and cumulative 30-day mortality rate was 25% (6). Permanent neurological deficits were not observed; in 1 patient transient changes occurred (4%). Time to reach circulatory arrest was the shortest in the direct access group, with mean 27±11 (CI: 20.6–33.3) min *vs.* 43±22 (28.0–78.0) min (p=0.058) and 32±8 (23.6–40.4) min (p=0.34) by femoral cannulation and subclavian entry, respectively. Direct arch cannulation resulted in the best renal function in the first 72 h after surgery and similar characteristics were observed in lactic acid levels.

Conclusions: Ultrasound-guided direct cannulation on the concavity of the aortic arch using a Seldinger technique is a reliable method in dissection repairs. Prompt antegrade perfusion provides not only cerebral but also peripheral organ and tissue protection, which is an advantage in this high-risk group of patients.

MeSH Keywords: Aortic Aneurysm • Aortic Diseases • Hemodynamics • Tissue Preservation

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Background

Acute Stanford type A dissection, with or without involvement of the aortic arch, is a clinical emergency that requires immediate surgical intervention. Despite remarkable achievements by Cooley [1], DeBakey [2], Alley [3], and Bahnson [4], surgery of the aortic arch remains a high-risk intervention. Surgical therapy today consists mainly of an interposition graft replacement of the ascending aorta. When indicated, this may be extended to include aortic arch replacement; usually as a hemiarch replacement or, when required, total arch replacement. Acute aortic valve insufficiency, when present, is generally treated by valve resuspension or replacement. Mortality rates of these operations have dramatically improved as the result of recent advances in preoperative preparation, intraoperative techniques, and postoperative care [5]. Nevertheless, operations for acute type A dissections are still associated with a relatively high rate of mortality and postoperative morbidity compared to routine heart surgery [6].

In patients undergoing aortic surgery, especially with involvement of the aortic arch, perioperative stroke and death can be precipitated by either dislodgement of atherosclerotic debris from the aortic wall or organic malperfusion. Cardiopulmonary bypass (CPB) via axillary/subclavian artery has become popular as an alternative perfusion site in recent years, predominantly for acute aortic dissections and patients with severe aortic atherosclerosis [7–13]. Despite several advantages of axillary/subclavian artery cannulation (e.g., antegrade perfusion of the aorta), problems and complications of this technique are becoming increasingly recognized with more frequent use of this approach. Axillary/subclavian artery inflow may not be suitable for rapid establishment of antegrade perfusion in cases with hemodynamic instability, because it requires more time for preparation prior to cardiopulmonary bypass. In patients with a small body surface area, limitation of pump flow due to a narrow axillary artery may be a concern [14,15].

However, cannulation for extensive aortic lesion in type A aortic dissection can present an enormous challenge, either through axillary/subclavian or lower limb arteries, if they are involved in the pathological process [12,16,17]. In light of problems associated with the above cannulation techniques, we started to use an innovative ultrasound-guided entry method on the usually uninvolved aortic wall segment on the concavity of the aortic arch via Seldinger technique. This aortic wall segment at the ligamentum arteriosum is not completely identical to the vast majority of the aorta, because it contains more connective tissue as a remnant of the ductus arteriosus; also, coarctations are located here due to this exclusive histological background. This relative rigidity can play a role in preventing dissections in the area and therefore providing an ideal point for arterial cannulation without purse-string stitches. As this aortic area allows easy landing into the true lumen at cannulation, the rest of the configuration of the aortic dissection is not important for perfusion. With the aid of preoperative CT scan for planning the cannulation spot and continuous intraoperative transesophageal ultrasound (TEE) guidance throughout the direct cannulation procedure of the diseased aorta, we achieved prompt antegrade perfusion to repair the involved ascending aorta and aortic arch, and subsequently evaluated its safety and efficacy.

Material and Methods

Within a period of 2.5 years, 24 consecutive patients (mean age: 59±14 years, CI: 53.0–64.8, 17 men and 7 women) underwent operations on the thoracic aorta. In all patients, a standard operative technique for acute aortic dissection was used and the only difference in surgical strategy was the choice of site for arterial cannulation. Direct cannulation by Seldinger technique was used in 14 patients (57%), subclavian access in 6 patients (25%), and femoral entry in 4 patients (17%). Further preoperative data is provided in Table 1.

The preoperative diagnosis was established on the basis of emergency computed tomography with additional intraoperative transesophageal echocardiography in all patients. Aortography or coronary angiography was not performed for preoperative evaluation.

Table 1. Demographic and preoperative data. Significance calculations are given as comparisons to the group with direct cannulation.

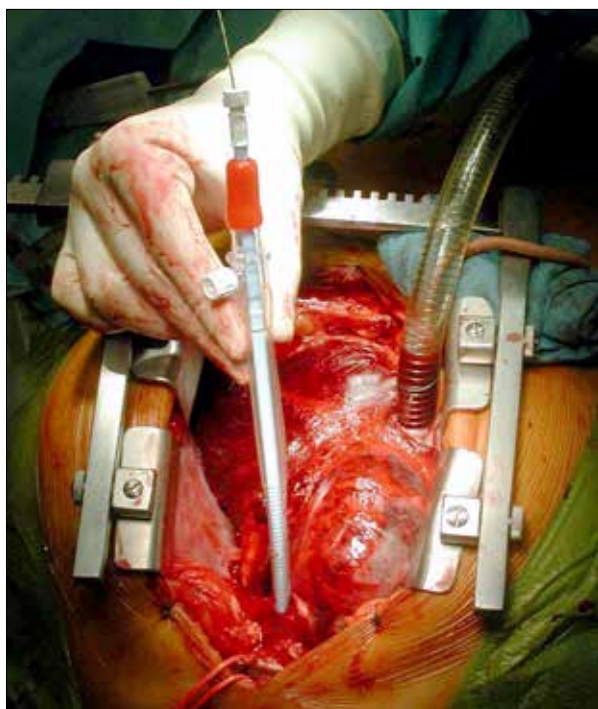| Characteristics	Direct	Subclavian	Femoral
No. of patients	14	6	4
Male	8	6	3
Female	6	0	1
Age (years (median))	65±10 (66)	51±17 (49) [N.S. p=0.11]	51±13 (46) [N.S. p=0.13]
Hypertension	13	5	3
Preoperative ventilated	4	4	3
Preoperative renal insufficiency	2	2	0

Figure 1. Direct aortic cannulation via Seldinger technique.

The standard operative technique for aortic dissection repair at our institution has been graft replacement of the ascending aorta and proximal aortic arch. Inspection of the supraaortic vessels was always carried out to decide whether to perform a concomitant island transposition, depending on the supraaortic status. The patient was placed in the standard supine position. The arms were horizontal beside the body as for the usual cardiac procedure. Monitoring of arterial pressure was performed by placing 3 lines routinely in both radials and the right femoral artery.

The ascending aorta and aortic arch were exposed through a median sternotomy. The approach of concavity of the aortic arch at level of Botallo's ligament (ligamentum arteriosum) was followed by a minimally invasive cannulation with dilation steps by Seldinger technique (Fem-Flex Femoral Arterial Cannula®, 24 Fr TFA 02425H Edwards Lifesciences LLC, Irvine, USA; Joline Special Dilatatorset®, Hechingen, Germany) (Figure 1). As previously described, no purse-string sutures are required in this area; the arterial line is fixed with a stitch to the cranial sternotomy skin incision corner to avoid accidental dislocation. Correct position of the guide wire and cannula in the aorta was routinely confirmed by TEE, or by epiaortic ultrasound in rare cases of technical difficulty with TEE. The same type of cannula was inserted in both peripheral access sites. CPB was instituted between the arterial cannulation site and right atrium. The patient was cooled to a tympanic temperature of 19–20°C (Mon-a-therm® Thermistor YSI 400 Series tympanic temperature probe, Mallinckrodt Inc., St. Louis, USA). Rectal (Thermocouple probe, Mallinckrodt Medical, USA) and bladder

(Curity®, Degania, Israel) temperatures were also followed-up simultaneously throughout the procedures. After cross-clamping, an ascending aortic incision was made and antegrade crystalloid cardioplegic solution (2000 ml Custodiol® HTK-Solution by Brettschneider, Dr. F. Köhler Chemie, Hähnlein, Germany) was administered proportionally through both coronary orifices. During deep hypothermic circulatory arrest (HCA), selective antegrade cerebral perfusion (SACP) was applied via the carotid arteries (DLP Retrograde Coronary Sinus Perfusion Cannula with manual Inflating Cuff®, Medtronic Inc., Minneapolis, USA) at a flow rate adapted to keep a constant cerebral O_2 saturation on each side, providing a perfusion pressure of 35–40 mmHg. Cerebral monitoring was performed with near infrared spectroscopy (INVOS® cerebral oximeter, Somanetics Inc., Troy, USA), and brain tissue oxygen saturation measured 65–70% continuously during perfusion, which corresponded to the induction values.

Reconstruction of the aorta was done with a woven Dacron side-branched vascular prosthesis (Hemashield Platinum Woven Double Velour Vascular Graft®, Boston Scientific Inc., Wayne, USA) including the island-type reinsertion of all supraaortic vessels, if applicable. The false lumen was eradicated with 45% bovine serum albumin-10% glutaraldehyde glue (BioGlue®, CryoLife International Inc., Kennesaw, USA); aortic valve commissures were refixed with the resuspension suture technique. The valve was replaced if it appeared diseased. Composite valve graft replacement was applied in patients with Marfan syndrome or if intraoperatively severe local involvement of the aortic wall could be observed. The decision whether to implant a composite graft did not depend on the maximal diameter of the aortic root, but rather was based on the presence of Marfan syndrome or the severity of wall destruction. Systemic reperfusion and rewarming was started through the graft side-branch. The summary of performed surgical procedures is presented in Table 2.

Statistical analysis

Statistical analysis was performed using SPSS v15.0 software (IBM Corporation, Armonk, New York, USA). For graphic demonstration, Microsoft Excel 2007® (Microsoft Corporation, Redmond, Washington, USA) was used.

For statistical comparisons of the groups, the Mann-Whitney U test and chi-square test. Although the number of cases in 2 groups (femoral cannulation and subclavian approach) was relatively low (4 and 6 cases, respectively), we considered a p-value <0.05 to be significant to enhance the statistical power of the comparisons. Where appropriate, confidence interval (CI) was calculated with a confidence level of 95%. Data are presented as mean values ±SD and, where applicable, the corresponding CI is in parentheses.

Table 2. Surgical procedures.

Surgical procedure	Direct	Subclavian	Femoral
Ascending aorta + hemi arch	13	6	4
Ascending aorta + total arch	1	*	*
° David reconstruction	1	*	*
° Yacoub reconstruction	2	1	1
° Bentall procedure	3	1	*
° Coronary bypass grafting	2	1	*

° Marks an additional procedure of aortic graft implantation.

Table 3. Intraoperative data. Significance calculations are given as comparisons to the group with direct cannulation.

Intraoperative data	Direct		Subclavian		Femoral	
	Mean ±SD (median)					
Time to HCA (min)	27±11	(26)	32±8	(31)	43±22	(48)
CPB time (min)	181±77	(149)	188±32	(193)	180±52	(200)
HCA time (min)	51±20	(52)	51±22	(50)	53±31	(48)
SACP time (min)	39±18	(39)	36±24	(25)	41±29	(31)
SACP flow right start (ml/min)	201±41	(200)	218±52	(200)	258±59	(250)
SACP flow right end (ml/min)	196±37	(185)	282±56	(300)	350±54	(330)
SACP flow left start (ml/min)	216±54	(205)	243±99	(275)	240±37	(240)
SACP flow left end (ml/min)	227±68	(220)	283±49	(300)	275±64	(275)
Tympanic temperature minimum	20.8±0.9	(20.8)	19.5±1.0	(19.7)	20.8±0.3	(20.9)
Rectal temperature minimum	26.9±3.3	(27.3)	26.8±4.3	(27.6)	26.0±2.3	(26.0)
Urinary bladder temperature minimum	26.0±4.8	(25.6)	24.8±3.4	(24.8)	23.8±2.3	(23.7)

HCA – hypothermic circulatory arrest; CBP – cardiopulmonary bypass; SACP – selective antegrade cerebral perfusion.

Results

There were no intraoperative deaths; cumulative 30-day mortality rate was 25% (6) for the entire patient population; 3 of 14 (21%) in the direct group, 2 of 6 (33%) in the subclavian group, and 1 of 4 (25%) in the femoral cannulated group (p=0.24 and p=0.46, respectively), all due to multiorgan failure. Direct aortic cannulation was safely performed in all cases and there was no need to switch to an alternative cannulation site. The adventitia of the dissected aorta was firm enough to support the cannula inserted by Seldinger technique with staged dilatators, and there was no case of complicated local massive hemorrhage at the cannulation site. No malperfusion or apparent thromboembolism due to cannulation was observed. Malperfusion would have been anticipated if a cerebral saturation difference of 10% occurred compared to preoperative values and/or if there was a pressure difference between the

peripheral arteries greater than 20 mmHg. Permanent neurological deficits were not present. Transient changes occurred in 1 patient (4%) in the direct group. Because the Seldinger technique was easier and quicker to apply than the peripheral approaches (Table 3) and it showed certain advantages in the preliminary results, we permanently changed our cannulation method to the direct aortic entry in all patients. The transesophageal echo guidance was useful for aortic cannulation along with color Doppler imaging, which provided real-time information about the true lumen antegrade perfusion.

Mean extracorporeal perfusion duration was 183±63 min (156.4–209.6) and mean time to reach circulatory arrest was 28±14 (23.1–34.9) min in the entire cohort, with no significant differences between groups (Table 3). Initial SACP flow was comparable in all 3 groups, but we observed a significant difference between the SACP flow required to maintain
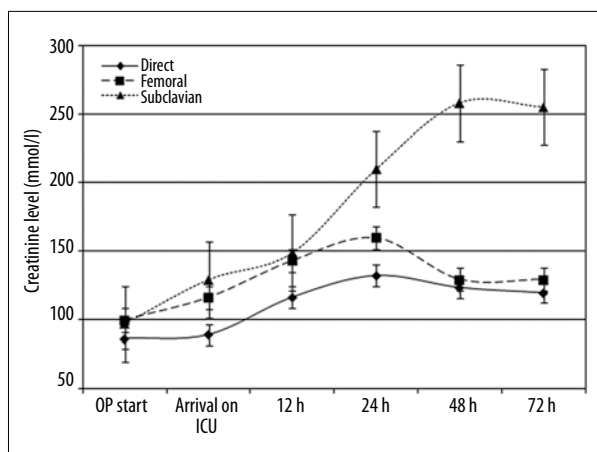
Figure 2. Changes in creatinine levels with different cannulation methods.

Figure 3. Lactate mirror of the 3 perfusion groups.

the initial cerebral saturation at constant blood pressure at the end of the perfusion period between the direct cannulation group (right: 196±37 ml/min [177.3–227.4]; left: 227±68 ml/min [184.8–247.2]) and both the femoral entry group (right: 350±54 ml/min [264.1–435.9] [p=0.006]; left: 275±64 ml/min [173.2–376.8] [p=0.24]) and the subclavian access group (right: 282±56 ml/min [223.2–340.8] [p=0.02]; left: 283±49 ml/min [231.6–334.4] [p=0.05]) in favor of the direct cannulation. Further intraoperative data were evaluated to identify the reliability and benefits of direct cannulation method (Table 3).

Time required to reach circulatory arrest was the shortest in the direct access group, with mean 27±11 (20.6–33.3) min; in the femoral cannulation group it was 43±22 (28.0–78.0) min (p=0.058); and in the subclavian entry group it was 32±8 (23.6–40.4) min (p=0.34).

Direct arch cannulation resulted in the best renal function on the first postoperative day, with a creatinine level of mean 140±48 mmol/L (112.3–167.7); the femoral entry showed 179±79 mmol/L (53.4–304.6; p=0.08); at subclavian access 199±69 mmol/L (89.3–308.7; p=0.25). Although comparison of creatinine levels in the direct cannulation group and the other 2 approaches shows the clear superiority of the direct cannulation technique, the differences did not reach the level of significance due to a relatively low number of patients in the subclavian access and femoral entry groups. Figure 2 demonstrates the plasma creatinine levels during the first postoperative 72 hours. Two of the direct and 2 of the subclavian cannulated patients were excluded from the statistical analysis due to preoperative renal impairment. Similar characteristics could be observed in lactic acid levels in the intensive care unit as a marker of preoperative global ischemia (Figure 3). Four of the direct, 1 of the femoral, and 2 of the subclavian perfused patients were not considered for statistical analysis due to an initial lactic acid level over 2 mmol/l.
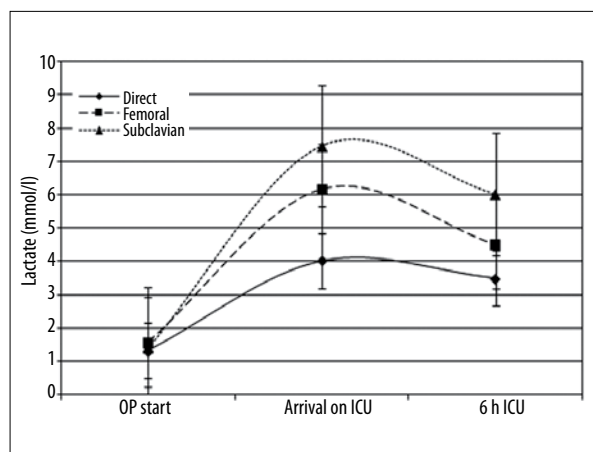
Treatment duration in the intensive care unit (ICU) of over 5 days occurred in 5 of 14 (36%) patients in the direct group, 4 of 6 (66%; p=0.21) in the subclavian group, and 2 of 4 (50%; p=0.51) in the femoral cannulated patients.

Discussion

Our study demonstrates that direct cannulation on the concavity of the aortic arch instead of the femoral or right subclavian artery may improve the results of ascending aorta and aortic arch replacement. However, this was an observational study because the 3 groups were not balanced.

Although the idea of cannulating ascending aorta in type A aortic dissection was described decades ago [18,19], direct cannulation to the ascending aorta has only been performed occasionally as an emergency technique to avoid retrograde malperfusion [20]. Recently, successful attempts have been made to establish antegrade perfusion via the ascending aorta primarily for type A dissections [21–23]. Ascending aorta or arch cannulation may have the great advantage of technical simplicity, especially when there is hemodynamic instability or at dissected limb arteries [24–27]. According to these reports, this technique can be performed safely under ultrasound guidance. Establishing an access point at the level of Botallo's ligament by Seldinger technique could provide a useful alternative to establish rapid arterial entry. At this section of the aorta the pulmonary bifurcation is firmly connected by massive connective tissue, which usually prevents complete dissection in this area. With the aid of this rapid and atraumatic cannulation method, CPB can be established, thereby reducing the likelihood of perioperative shock, which would lead to an increased mortality [28]. Although the time to reach circulatory arrest was remarkably lower using the direct cannulation technique compared to the other 2 accession methods, the level of significance was not reached because of the

relatively low number of patients in the other 2 groups and greater standard deviation values.

Rapid establishment of arterial access facilitates quicker initiation of antegrade systemic perfusion and core cooling, which also reduces the duration of the surgical procedure. This may also contribute to lower morbidity through enhanced organ perfusion and reducing the probability of coagulation disorders. Our method of aortic cannulation has additional advantages. The benefit of this type of arch cannulation is combined with having the tip of the cannula located in the proximal descending aorta. Consequently, the turbulence at the tip of the cannula occurs in the descending aorta, thereby reducing the risk of embolization of debris into the carotid arteries. A further advantage of proximal descending aortic perfusion is the reduction of the fluid jet stream – Coanda's effect – which can be associated with relative carotid hypoperfusion in patients undergoing perfusion with a short cannula from the ascending aorta [29]. Most patients who have a type A aortic dissection undergo at least a hemiarch replacement in our practice, so the cannulations site is removed with the affected aortic wall segment, and the repositioned cannula fits perfectly into the side-branched prosthesis.

In addition, transesophageal or epiaortic ultrasonographic guidance may also be indispensable for reliable real lumen cannulation, examinations of which are simple methods to obtain imaging information of the ascending aorta and proximal arch. Although preoperative CT scan is mandatory to obtain correct operative planning, the ultrasonographic control provides real-time information on the location of intimal tear, intimal flap, true and false lumen, because this intraluminal situation can change progressively following the CT scan. Moreover, the guide wire and the correct position of the cannula can be checked continuously, avoiding false lumen perfusion, which is not the case with the peripheral approaches. The simultaneous application of ultrasonographic control and cerebral monitoring by near infrared spectroscopy reduces the likelihood of malperfusion, thromboembolism, and subsequent extension of the false lumen. We have observed no local complications with the Seldinger technique, but were always prepared to perform an apical cannulation described by Wada et al. [30] as a bail-out procedure.

The problem of neurological injury resulting from embolic events and cerebral malperfusion in aortic dissections should be discussed because there are a number of different cannulation approaches. Femoral cannulation is associated with a higher risk of retrograde embolization and potential perfusion of the false lumen via the distal re-entry point; although in our cohort there were no perfusion complications in this group. In this respect, techniques providing antegrade flow may offer a better option, especially in patients with Stanford A dissections [5].

In our practice, Seldinger cannulation on the concavity of the aortic arch has become the standard approach for arterial access in both elective and emergency cases as by the Hannover group [22,31]. This cannulation technique is fast and simple, which can be important, especially in hemodynamically unstable patients. It avoids additional time-consuming incisions, thereby avoiding additional surgical trauma and possible local complications at peripheral cannulation sites. In combination with cold selective antegrade cerebral perfusion and deep/moderate hypothermic circulatory arrest, this technique allows adequate protection for the body and is not associated with higher risk of cerebral microemboli [32,33]. The effectiveness of selective antegrade cerebral perfusion as an adjunct to hypothermic arrest has been proven in numerous studies [34,35].

As with other surgical approaches, there are some disadvantages that need to be recognized. This includes cannulation of the false lumen with potential malperfusion or even complete rupture of the cannulated aorta. For those emergency situations, alternative strategies have to be available. In the above-mentioned cases there are basically 3 major goals to be achieved: cerebral protection, myocardium conservation, and proper perfusion of the lower body. This stepwise approach necessitates the cooperation of the anesthesiologist, perfusionist, and surgeon to obtain optimal results.

Reece et al. applied the Seldinger technique for cannulation in 24 patients, resulting in no misplacement [36], but the study was not randomized and various aortic pathologies were excluded, leading to potential selection bias. Furthermore, the cannula is held in position manually during the cooling phase, preventing further surgical activity during this period; the authors are not convinced that sutures in the dissected aorta remain stable. With our technique there is no need for sutures in the aorta; the cannula is fixed to the cranial skin incision corner by a suture and situated deep enough in the proximal descending aorta to not require any further support. Inoue et al. report on 32 cases using the Seldinger technique, controlled by epiaortic ultrasound. Prior to ascending aortic cannulation, they cannulated the femoral artery to be able to regulate the aortic pressure [26]. Although no malperfusion occurred in their series, the double arterial approach is questionable in the context of avoiding time-consuming preparations and potential retrograde embolism or further dissection [37].

Transapical cannulation is another elegant method for achieving reliable antegrade access, as described by Wada et al. [30]. In a large cohort of 138 patients, the cannula was inserted through a 1-cm apical incision directly into the true lumen via the aortic valve under TEE guidance. The impact of causing an acute aortic insufficiency in this context has not been discussed in detail. Both Wada's technique and Reece's method have the disadvantages of resulting in prolonged cardiopulmonary

bypass times because no additional procedures can be performed during cooling, such as inspection and preparation of the aortic root.

Axillary/subclavian cannulation is also an elegant, widely used method for arterial access during aortic arch surgery [16]. However, it is presumably more time consuming, and carries the possibility of failure rates up to 4.2%. Nevertheless, it provides the possibility of continuous unilateral blood flow without interruption [38]. Applying the standard technique, however, only the right hemisphere is continuously perfused, which can result in malperfusion of the contralateral hemisphere; Merkkola et al. demonstrated that up to 17% of the patients have an incomplete circle of Willis [39]. Even in the presence of a complete circle of Willis, it is still unclear if the exclusively right-sided perfusion can sufficiently supply the left hemisphere. Our results with SACP also demonstrate that the lowest perfusion volume is necessary to maintain the proper bilateral cerebral oxygenation in the direct cannulated group. Since the brachiocephalic trunk divides anatomically into 2 nearly equivalent branches – the right carotid and subclavian artery – the provided flow through the latter vessel on CPB can lead to a relative hyperperfusion of the right carotid parallel to a relative hypoperfusion of the aorta. This could explain our findings regarding SACP flow values and peripheral organic perfusion monitored by the renal function and lactate level. The Seldinger technique delivers rapid arterial access, which results in a shorter cerebral and peripheral ischemic periods. Subclavian perfusion provides sufficient oxygenation for the right hemisphere but may not for the contralateral side, so the required initial right SACP flow is similar to the direct group, but the left shows values similar to the femoral group. Additionally, the constant relative hyperperfusion of the right hemisphere most probably leads to an intracerebral edema, which elevates the SACP flow requirements to maintain a proper cerebral saturation at the end of HCA. The relative hypoperfusion of the body is characterized by diminished renal function at subclavian cannulation. In the subclavian approach, smaller cannulas can usually be applied due to the anatomical situation. The femoral access takes more time to establish, resulting in relative cerebral hypoperfusion/longer ischemic period shown by the higher initial SACP flow requirements in this group. The femoral perfusion, in case of no malperfusion, provides a good

renal blood supply, thus the renal function is better preserved than with subclavian access, but the initial hypoxia due to delayed establishment of perfusion is clear when comparing the creatinine levels in this group to the direct cohort.

Moizumi et al. could not use axillary artery access in 5.5% of their aortic dissection cohort, because the pathological changes extended into the axillary artery [40]. Our first experience with Seldinger technique was in a patient with dissection in all limb arteries [25]. Carotid artery cannulation, performed by Urbanski in 100 patients, including 27 with Stanford A dissections, seems to be another alternative method, but also carries the risk of brain malperfusion and later complications in the vessel [41]. The report on innominate artery cannulation by Di Eusanio et al. included 55 patients, with only 2 in acute aortic dissections [42]. Fusco at al presented their results in femoral artery cannulation in 2004 [43]. With a conversion rate of 2.5% to ascending aortic cannulation, they conclude that femoral cannulation is appropriate and yields excellent clinical results, but they did not consider the problem of retrograde embolism from the downstream aorta, probably because in their experience arteriosclerosis is less common in dissection patients.

Conclusions

Our study has some important limitations. It was an observational study without randomization and presents preliminary experience with a small number of patients. These good preliminary results have to be confirmed by further studies in a larger group of patients.

In conclusion, arterial access for establishing CPB, especially in patients requiring repair of acute type A aortic dissection, is a controversial subject in the current literature [44]. Minimal invasive central cannulation by Seldinger on the concavity of the aortic arch is technically feasible and safe. It may avoid cerebral embolization and organ malperfusion, and thus may reduce the rate of neurological and malperfusion complications. This alternative arterial inflow technique can be applied for prompt establishment of CPB in type A dissections, especially during hemodynamic instability.

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III

Reliability of different body temperature measurement sites during aortic surgery

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Abstract

Objective: We retrospectively performed a comparative analysis of temperature measurement sites during surgical repair of the thoracic aorta.

Methods: Between January 2004 and May 2006, 22 patients (mean age: 63±12 years) underwent operations on the thoracic aorta with arterial cannulation of the aortic arch concavity and selective antegrade cerebral perfusion (ACP) during deep hypothermic circulatory arrest (HCA). Indications for surgical intervention were acute type A dissection in 14 (64%) patients, degenerative aneurysm in 6 (27%), aortic infiltration of thymic carcinoma in 1 (4.5%) and intra-aortic stent refixation in 1 (4.5%). Rectal, tympanic and bladder temperatures were evaluated to identify the best reference to arterial blood temperature during HCA and ACP.

Results: There were no operative deaths and the 30-day mortality rate was 13% (three patients). Permanent neurological deficits were not observed and transient changes occurred in two patients (9%). During re-warming, there was strong correlation between tympanic and arterial blood temperatures (r= 0.9541, p<0.001), in contrast to the rectal and bladder temperature (r=0.7654, p= n.s; r=0.7939, p= n.s., respectively).

Conclusion: We conclude that tympanic temperature measurements correlate with arterial blood temperature monitoring during aortic surgery with HCA and ACP and, therefore, should replace bladder and rectal measurements.

Keywords

aortic surgery; temperature monitoring; antegrade cerebral perfusion; hypothermia; circulatory arrest; tympanic; rectal; bladder

Introduction

Accurate monitoring of the core temperature during aortic surgery, especially with the application of deep hypothermic circulatory arrest (HCA), is an important component of routine perioperative care. Preservation of neurological function is one of the main goals in such patients. Increasing the tolerance of the brain to ischaemia by the application of systemic hypothermia allows for a safe period of circulatory arrest and has remained the mainstay of neuroprotection for decades[1,2] The safety of this procedure relies on adequate systemic cooling under strict control. If this control is incomplete or fails, neurological injury may occur during HCA.

Whereas hypothermia is neuroprotective, even mild hyperthermia is hazardous during cerebral ischaemia since it accelerates neuronal death.[3-7] This results from oxygen free radical production,[8] destabilization of the cytoskeleton,[9] intracellular acidosis[10] and increased blood-brain barrier permeability.[11] Thus, to estimate the actual brain temperature, different sites are used for

perioperative temperature measurements, e.g., urinary bladder, oesophagus, rectum and tympanic membrane. Body temperatures measured on these alternative sites may, however, substantially deviate from the actual cer-

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Table 1. Preoperative patient characteristics.

Characteristics	
No. of patients	22
Male	12
Female	10
Mean age in years±standard deviation	63±12
Emergency operations	15
Indications	
Type A dissection	14
Degenerative aneurysm	6
Aortic infiltration of thymic carcinoma	1
Intra-aortic stent refixation	1
Hypertension	16
Preoperative ventilation	4
Preoperative renal insufficiency	3

ebral temperature. Adequate neuroprotection requires meticulous temperature management to avoid too low or too high temperatures leading to overcooling or overheating the patient due to inappropriate "slow responding" temperature monitoring. The aim of our study was to evaluate the reliability of the commonly used core body temperature measurement sites in contemporary aortic surgery performed with the aid of HCA and selective antegrade cerebral perfusion.

Patients and methods

Between January 2004 and May 2006, 22 patients (mean age: 63±12 years, 12 men and 10 women) underwent operations on the thoracic aorta. In all patients, a standard operative technique for acute aortic dissection or aneurysm resection was used at our institution. Cardiopulmonary bypass (CPB) was established via arterial cannulation performed on the concavity of the aortic arch and, during HCA, selective bilateral antegrade carotid perfusion was used. Indications for surgery included: acute type A dissection (n=14, 64%), degenerative aneurysm (n=6, 27%), aortic infiltration of thymic carcinoma (n=1, 4.5%) and intra-aortic stent refixation (n=1, 4.5%). Fifteen patients (68%) underwent emergency operations. Preoperative patient characteristics are given in Table 1.

Diagnosis was confirmed by contrast-enhanced computed tomography and intraoperative transoesophageal echocardiography (TOE) in all patients. Aortography or coronary angiography was not performed in emergency cases.

The standard operative technique for aortic dissection or aortic aneurysm at our institution is Dacron graft replacement of the ascending aorta and proximal aortic arch combined with inspection of the supra-aortic
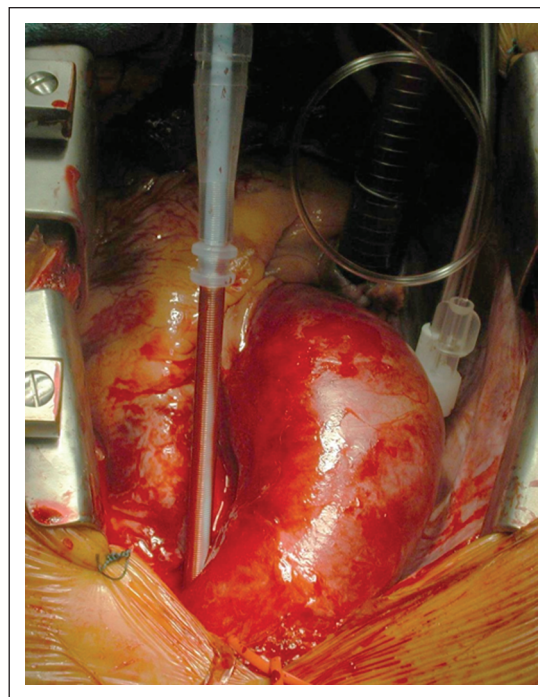

Figure 1. Showing direct aortic cannulation over arch concavity with the Seldinger technique.

vessels ± concomitant island transposition, depending on the supra-aortic status. The patients were placed in the standard supine position. Monitoring of arterial pressure was performed by routinely placing three lines in both radial and right femoral arteries. A median sternotomy was performed in all patients. Puncture of the proximal aortic arch concavity at the level of Botallo's ligament was followed by a minimal invasive cannulation, with dilation steps by the Seldinger technique (Fem-Flex Femoral Arterial Cannula®, 24 Fr TFA 02425H Edwards Lifesciences LLC, Irvine, CA, USA; Joline Special Dilatatorset®, Hechingen, Germany) (Figure 1). Correct position of the guide wire and cannula was confirmed by TOE of the aorta. CPB was instituted between this and a single, two-stage, right atrial venous cannula.

Patients were cooled down to a tympanic temperature of 19-20°C (Mon-a-therm® Thermistor YSI 400 Series tympanic temperature probe, Mallinckrodt Inc., St. Louis, MO, USA). Rectal (Thermocouple probe, Mallinckrodt Medical) and urinary bladder (Curity®, Degania, Israel) temperatures were simultaneously recorded throughout the procedures. Tympanic, rectal and bladder probes were connected to Mallinckrodt Model 6510 electronic thermometers which require no previous calibration and have an accuracy of around 0.1°C with disposable thermocouples, according to the user's manual. Prior to insertion of the tympanic probe, the cerumen-free status of the auditory channel was always controlled by otoscopic examination. The auditory channel was always

Table 2. Surgical procedures performed.

Surgical procedure	n
Ascending aorta + hemi arch	20
Ascending aorta + total arch	2
° David reconstruction	3
° Yacoub reconstruction	4
° Bentall procedure	4
° Coronary bypass grafting	4

° marks an additional procedure of aortic graft implantation.

Table 3. Intraoperative data.

Intraoperative data	Mean±SD (Median)
Time to HCA (min)	25±12 (21)
CPB time (min)	176±63 (158)
HCA time (min)	46±21 (45)
ACP time (min)	36±18 (34)
ACP flow right start (ml/min)	216±55 (200)
ACP flow right end (ml/min)	199±40 (190)
ACP flow left start (ml/min)	224±55 (210)
ACP flow left end (ml/min)	230±61 (220)

CPB: cardiopulmonary bypass; HCA: deep hypothermic circulatory arrest; ACP: selective antegrade cerebral perfusion.

insulated by a cotton swab, the probe securely fixed by a tape and a gauze bandage was additionally positioned over the external ear. Theatre temperature was continuously kept at 20-22°C throughout the operative procedures.

After cross-clamping, an ascending aortic incision was made and antegrade crystalloid cardioplegic solution (2000 ml Custodiol° HTK-Solution by Brettschneider, Dr. F. Köhler Chemie, Hähnlein, Germany) was administered through both coronary ostia. During HCA, selective ACP was provided through both carotid arteries (DLP Retrograde Coronary Sinus Perfusion Cannula with manual Inflating Cuff°, Medtronic Inc., Minneapolis, MN, USA) at a flow rate adapted to keep a constant cerebral O_2 saturation on each side with a perfusion pressure of 35-40 mmHg. Cerebral monitoring was performed with near infrared spectroscopy (INVOS° cerebral oxymeter, Somanetics Inc., Troy, MI, USA) and brain tissue oxygen saturation measured at 65-70% continuously during perfusion, which corresponded to the induction values.

Reconstruction of the aorta was performed with a woven Dacron side-branch vascular prosthesis (Hemashield Platinum Woven Double Velour Vascular Graft°, Boston Scientific Inc., Wayne, NJ, USA), including the island type reinsertion of all supra-aortic vessels, if applicable. The false lumen was eradicated with 45% bovine serum albumin-10% glutaraldehyde glue (BioGlue°, CryoLife International Inc., Kennesaw, GA, USA); aortic valve commissures were refixed with the resuspension suture technique. The valve was replaced if it was severely diseased. Composite valve graft replacement was applied in patients with Marfan syndrome or if severe local injury with aortic wall destruction was found intraoperatively. The decision whether or not a composite graft was implanted did not depend on the maximal diameter of the aortic root, but was based on the presence of Marfan syndrome or the severity of the wall destruction. Systemic reperfusion and re-warming were started through the graft side-branch. A summary of performed surgical procedures is presented in Table 2.

Statistical analysis

Statistical analysis for body temperature measurement sites was done using univariate analyses (Pearson's correlation and Student's t-test) with SPSS v17.0 (SPSS Inc., Chicago, IL, USA) to identify the best reference to arterial blood temperature during HCA and ACP. A p-value <0.05 was considered as significant.

Results

Perioperative data

There were no operative deaths; cumulative 30-day mortality rated 13% (n=3). The cause of death was multiorgan failure in all three patients. Eight patients (36%) stayed in the intensive care unit >5 days.

Direct aortic cannulation was safely performed in all cases; there was no need to switch to an alternative cannulation site. The adventitia of the dissected aorta was firm enough to support the cannula inserted by the Seldinger technique with staged dilatators and there was no case of complicated local massive haemorrhage at the cannulation site. TOE guidance was useful for aortic cannulation along with colour Doppler imaging, which provided information about the true lumen antegrade perfusion. No malperfusion or apparent thrombo-embolism due to the cannulation was observed. Malperfusion was defined by a cerebral saturation difference of 10% compared to preoperative values and/or pressure difference between the peripheral arteries >20 mmHg. There were no permanent neurological deficits, but two patients (9%) suffered from transient neurological dysfunction.

Mean CPB time was 176±63 minutes (median: 158), mean time to reach HCA was 25±12 minutes (median: 21), mean HCA time was 46±21 minutes (median: 45) and mean selective antegrade carotid perfusion time was 36±18 minutes (median: 34). Intraoperative patient data is shown in Table 3.
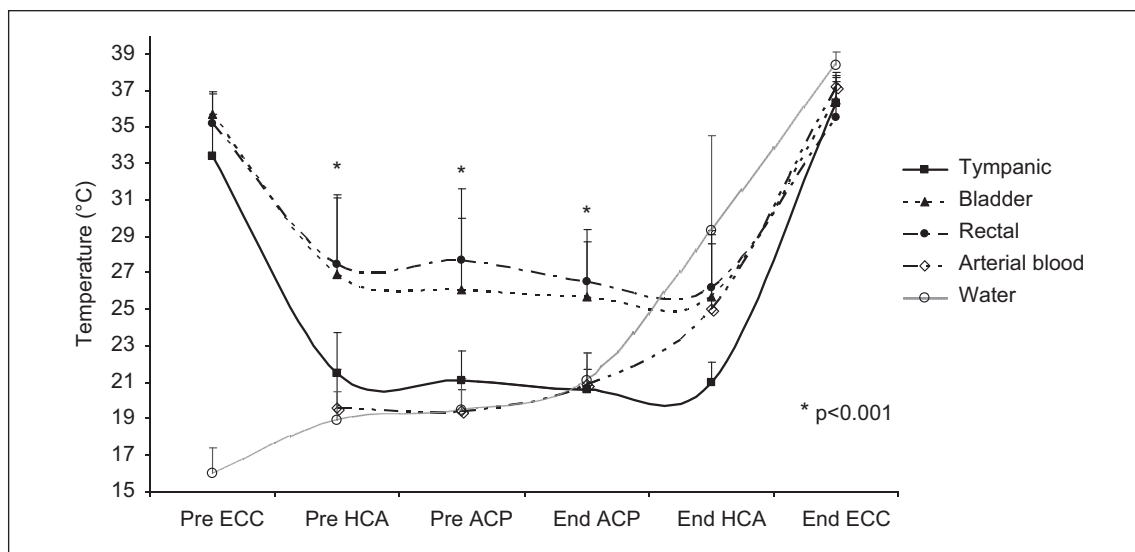
Figure 2. Temperature changes at different measurement sites during extracorporeal circulation (ECC), deep hypothermic circulatory arrest (HCA) and selective antegrade cerebral perfusion (ACP).

Temperature evaluation

Statistical analysis revealed a strong association between the tympanic temperature and the arterial blood temperature during HCA, while rectal and bladder values did not represent the core temperature adequately. The difference between rectal and arterial blood temperatures was significantly greater than the difference between tympanic and arterial blood temperatures [average temperature difference (rectal minus arterial): 7.9 (pre HCA), 8.3 (pre ACP), 5.6°C (end ACP); average temperature difference (tympanic minus arterial): 1.9, 1.7, 0.3°C, respectively; (p<0.001)]. There was a similar relationship between the bladder and tympanic temperatures (average temperature difference (bladder minus arterial): 7.3, 6.7, 4.8°C, respectively; average temperature difference (tympanic minus arterial): 1.9, 1.7, 0.3°C, respectively; (p<0.001)]. Figure 2 shows the temperature detected at the different sites during the course of the operation.

Analysis of the rewarming phase revealed strong correlation between tympanic and arterial blood temperatures (r= 0.9541; p<0.001) as well as between the arterial blood and heat exchanger water temperatures (r=0.9879; p<0.001). The urinary bladder and rectal values showed less correlation with the arterial blood (r=0.7939, p= n.s.; r=0.7654, p= n.s., respectively). Figure 3 shows the temperature detected at different sites during the re-warming phase.

Discussion

Our study demonstrates that tympanic measurements are reliable for intraoperative temperature estimation during aortic surgery performed under HCA. This may aid in improved postoperative outcomes due to a reduced cooling phase and adequate rewarming. Although the application of hypothermia has been an important contribution to patient management as a neuroprotective method from the dawn of cardiac surgery,[12,13] proper body temperature management relies on the accurate measurement of the temperature to enable adequate monitoring of changes during CPB and HCA. Oxygen consumption drops with lower body temperatures so that ischaemic tolerance is increased by cooling. Cerebral oxygen requirement decreases to approximately one-fifth of normothermic needs at 20°C,[14] allowing a safe period of 45-50 minutes for HCA. In addition, hypothermia may contribute to neuroprotection by a variety of complex mechanisms, including decreased vascular permeability, reduced ion influx and decreased excitatory transmitter release.[15] During the rewarming phase of CPB, conventional temperature monitoring sites may not reflect true brain temperature, so cerebral hyperthermia may not be detected if conventional temperature monitoring underestimates the brain temperature or there is a delay with the arterial heat exchange.[16,17]

Monitoring rectal or urinary bladder temperature to control intraoperative core temperature is standard in many institutions all over the world. Rewarming, which aims to normalise the temperature after HCA, relies on measured data from the above sites. We have shown that temperature measurement at these sites could be misleading, possibly due to latency in the heat exchange process at these points. Clinicians are often concerned about the risks of postoperative hypothermia, such as shivering leading to increased myocardial oxygen
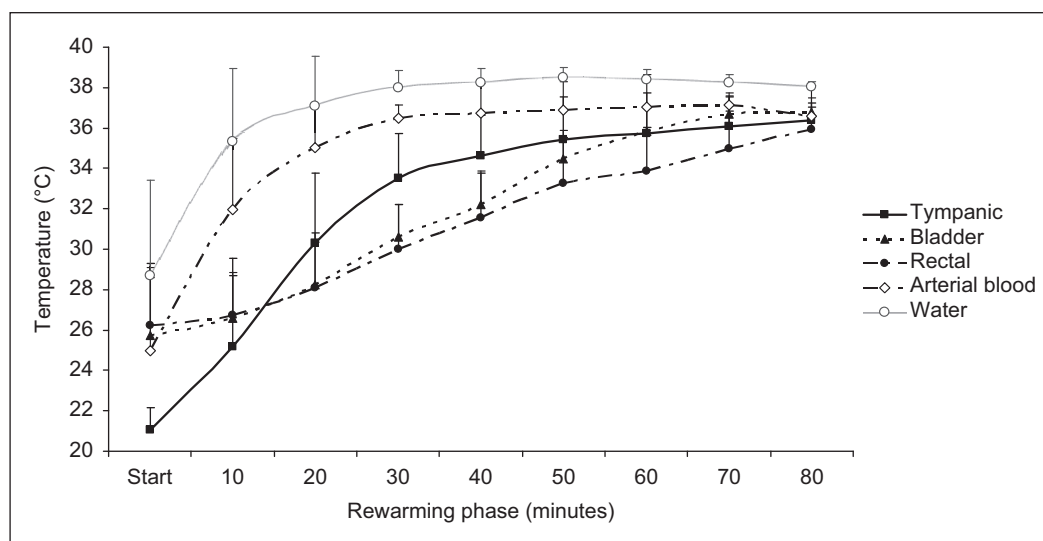
Figure 3. The temperature at various intervals during re-warming, following deep hypothermic circulatory arrest.

consumption, arrhythmias, coagulopathy, greater risk of wound infections and elongated hospital stay,[18-21] but the possible side effects of cerebral hyperthermia are rarely taken into account. Thus, the rewarming phase must be carefully monitored and managed to avoid cerebral hyperthermia, since it elevates the risk of post-ischaemic tissue injury[22,23] and intraoperative hyperthermia is well known to be associated with postoperative neurological impairment.[24,25]

Arterial blood temperature is considered to be the most accurate indicator of cerebral temperature.[26] This is not surprising as this is the medium for heat exchange for the brain during HCA and ACP. According to our results, tympanic temperatures correlate well with arterial blood temperatures and, hence, with cerebral temperatures, not only during HCA, but also during the rewarming phase of the operation. Urinary bladder and rectal temperatures lag behind arterial blood temperatures, therefore, these measurement sites cannot be relied upon to provide an accurate estimation of temperature change. This affects the management of these patients at various phases of cooling and rewarming.

The tympanic membrane is situated in the immediate vicinity of the internal carotid artery and is supplied by its branches. Thus, the tympanic temperature is well-placed to closely represent the cerebral thermal state. Although some authors consider tympanic temperature as a good standard for cerebral temperature monitoring by reflecting the hypothalamic status,[27,28] others have suggested that the tympanic temperature can be influenced by changes in ambient temperature.[29,30] If, prior to insertion of the tympanic probe, the debris-free status of the auditory channel is confirmed via otoscopic examination along with careful insulation by cotton

swab and the probe is securely fixed by tape and a gauze bandage over the external ear, the ambient temperature influence on tympanic measurement can be effectively diminished. Variations in urinary flow, which is a normal phenomenon during CPB and, especially with HCA, may affect the bladder temperature sensors.[31] On the other hand, rectal probes can become lodged in faecal matter, which insulates them from the surrounding tissues.[32] The above factors contribute to the weak correlation of these temperature measurements with those of the arterial blood.

In our institute, we do not use nasopharyngeal/oesophageal temperature monitoring in HCA as standard measurement sites, as it has been shown in several studies to modestly, but significantly, over- and underestimating brain temperatures during the cooling and rewarming phases, respectively.[33-35] It is probable that this is a result of the suboptimal heat exchange environment as these probes are situated in larger, air-containing cavities. Although oesophageal probes are placed relatively close to the descending aorta, the open chest or eventually applied topical cooling in the pericardium could also influence measurement accuracy. Akata, et al. have, furthermore, demonstrated that pulmonary artery temperatures closely reflect changes in brain temperatures, but nasopharyngeal/oesophageal measurements could not be considered as a reliable index of brain temperature, at all, during rapid induction of moderate/deep hypothermia.[36]

Our study has some important limitations. It is an observational, retrospective study without randomisation and presents preliminary experience with a small number of patients. The good preliminary results have to be confirmed by further studies on larger patient groups.

Conclusion

We recommend multiple temperature measurement sites during aortic surgery with HCA and ACP to be able to assess homogenous cooling and rewarming of the patient. To achieve good postoperative neurological outcome, we believe that tympanic values are highly reliable as a guide to temperature changes of the brain during HCA and re-warming.

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IV

Management options for aorto-oesophageal fistula: case histories and review of the literature

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Abstract

Objective: An aorto-oesophageal fistula is a rare clinical entity, leading to life-threatening gastrointestinal bleeding. Thoracic aortic aneurysms are the most common cause of aorto-oesophageal fistulae; further causes involve foreign body ingestion, trauma (in most cases iatrogenic), carcinoma or, very rarely, aortitis tuberculotica.

Methods: Due to its rarity, there are no large multicentre studies present to evaluate the efficacy of different therapeutic management options. Since it is associated with significant morbidity and mortality, we give a short summary of various treatment approaches performed in our clinical practice in the past three years. The most straightforward therapeutic option may be an endovascular aortic repair and subtotal oesophageal resection followed by gastro-oesophageal reconstruction, but other alternative treatment possibilities are also present, although with probable higher morbidity.

Conclusions: Eliminating the source of bleeding as an emergency, resecting the oesophagus urgently to prevent sepsis and reconstructing the gastrointestinal continuity as an elective case after having the inflammatory processes settled seems to justify the endovascular aortic repair and subtotal oesophageal resection, followed by a gastro-oesophageal reconstruction, as an effective surgical approach.

Keywords

aorto-oesophageal fistula; endovascular aortic repair; gastro-oesophageal reconstruction; surgical approach; conservative management

Introduction

An aorto-oesophageal fistula (AEF) is a rare cause of gastrointestinal bleeding, but is a highly lethal condition, even when promptly diagnosed and treated. The main causes of an AEF are lesions of the oesophageal wall resulting from a thoracic aortic aneurysm (in up to 54% of cases) and ingestion of foreign bodies (in 19% of cases).[1] Conservative treatment of an AEF results in a high in-hospital mortality rate and the conventional surgical procedure has a reported in-hospital mortality rate of nearly 40%.[2] Thoracic endovascular aortic repair (EVAR) as a stand-alone procedure has recently gained recognition as a possible technique for the emergency treatment of AEF, despite a considerable risk of infection,[3] in contrast to the conventional solution of open thoracic surgery with higher mortality and morbidity. However, relatively little is known about long-term results of EVAR for AEF due to its rarity and the lack of large clinical experience.

Methods

We retrospectively analysed all our patients with an AEF between 2009 and 2010 undergoing different management approaches by separate surgeons. We demonstrate

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the pros and cons of different strategies since each of them presents a possible management pathway in this group of patients, with different advantages and disadvantages.

Management by EVAR and subtotal oesophageal resection followed by gastro-oesophageal reconstruction

A 69-year-old man presented with 3 days of central chest pain, coughing and haematemesis. His past medical history included hypertension, hyperlipidaemia and gastro-oesophageal reflux disease. Laboratory findings showed increased inflammatory markers. Computed tomography (CT) revealed a saccular mycotic aneurysm of the mid-descending thoracic aorta in a close relationship to the thickened wall of the oesophagus anteriorly. Air inclusions were visible within the aneurysm thrombus. No pathological lymph nodes were present. A communication between the descending aorta and the oesophagus was demonstrated on the computed tomography (Figure 1). Urgent EVAR was performed, which successfully isolated the aneurysm (Figure 2).

Total oesophageal resection, evacuation of the infected thrombus and a tunnelled feeding jejunostomy was undertaken, thereafter, to prevent sepsis. Surprisingly, histology of the resected specimen showed a clearly defined fistula tract on the basis of moderately differentiated squamous cell carcinoma colonised by E. coli, suggesting that this, rather than pressure, was the aetiology of the AEF.

The patient's prolonged postoperative course was complicated by respiratory distress syndrome and acute renal failure, which were both successfully managed. The patient was discharged well after 71 days, with normal inflammatory markers. Outpatient rehabilitation was undertaken

Figure 1. 3D reconstruction of the aorto-oesophageal relationship at the AEF: contrast enhancement outlines the oesophageal silhouette.

prior to gastro-oesophageal reconstruction which was scheduled six months following EVAR.

Management by open thoracic surgery

A 30-year-old patient was admitted as an emergency after having an electromechanical dissociation arrest during oesophago-gastroscopy (OGD) for gastrointestinal bleeding. The OGD showed an oesophageal ulcer. Computed tomography demonstrated a communication with the descending aorta where an aneurysm was situated.

An aortic repair was performed with a 30-mm diameter, gelatin-coated, woven polyester, interposition tube graft (Gelwave; Vascutek, Inchinnan, UK) followed by a McKeown oesophagectomy and a gastro-oesophageal reconstruction with orthotopic gastric interposition at the same operation. Postoperatively, he became septic with *Pseudomonas* in the blood cultures and developed a left upper lobe infarction. A redo-thoracotomy was undertaken; the necrotic left upper lobe was removed followed by a pleurectomy.

During the patient`s regular follow-up, a repeat CT scan after six months showed a fluid collection around the graft anastomosis, with some inflammatory signs. The graft was replaced by a homograft as an urgent procedure. After this surgical intervention, the patient was discharged after 15 days in a good general condition.

Conservative management of postoperative graft infection

A 62-year-old male patient presented with back pain and severe shortness of breath. He had no significant past medical history. A computed tomography angiogram showed a Crawford type I descending aortic aneurysm, extending from the left subclavian artery and ending at the renal arteries. The diameter of the descending aorta was 6-7 cm at the beginning; the maximum diameter reached 10 cm at the level of the tracheal bifurcation, with an obvious rupture and a large haematoma compressing both trachea and oesophagus. There was an oesophageal communication also demonstrated.

The aneurysm was replaced by an interpositional Dacron tube graft and the oesophageal rupture orifice was closed with a bovine pericardial patch so that the Dacron graft could be separated from the trachea and the oesophagus.

After a couple of days, a recurrent oesophageal leakage was demonstrated on per oral feeding. The patient refused radical oesophageal surgery, so he was further treated conservatively with the aid of antibiotics. In the following weeks, his general condition was stabilized and he was discharged on a six-months' course of antibiotics. The patient was reluctant to carry on with the prescribed treatment after one month; later on, he was
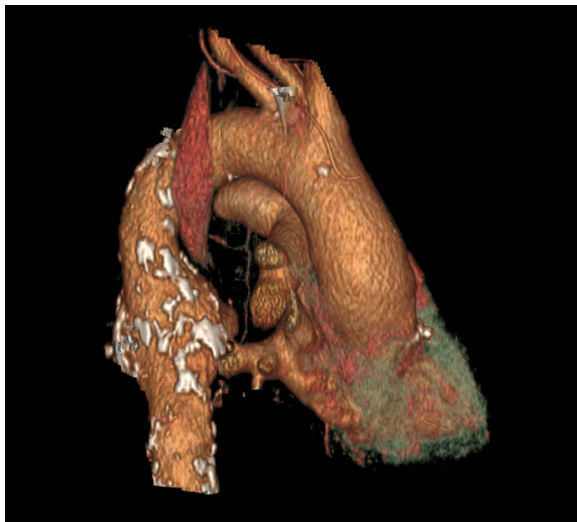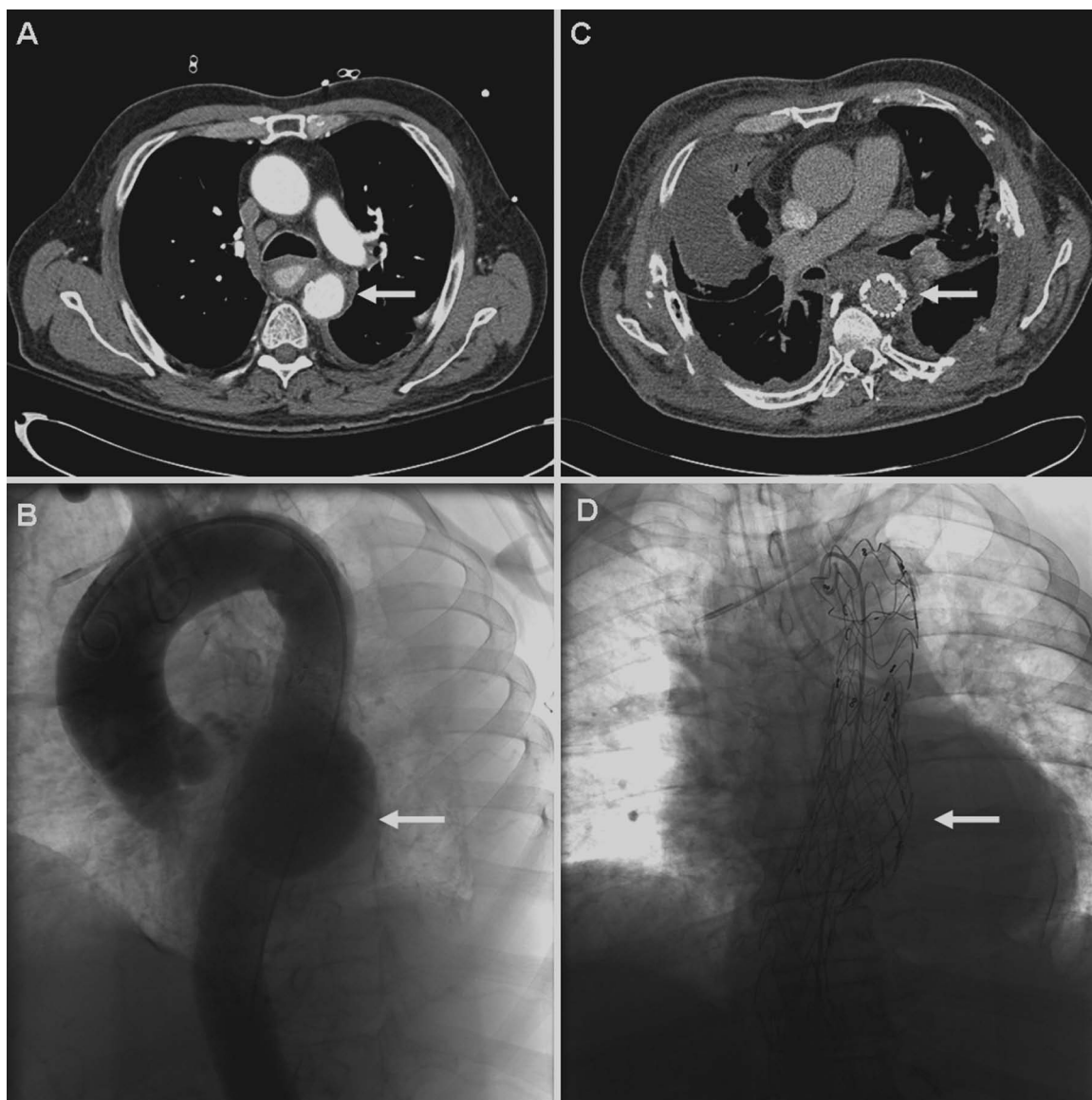
Figure 2. Pre- and postoperative diagnostic images of EVAR treatment in the AEF.
Panel A – Arrow marks the level of the AEF: note the contrast enhancement inside the oesophagus.
Panel B – Saccular aneurysm of the mid-descending thoracic aorta on fluoroscopic image.
Panel C – Arrow shows the EVAR in position: note the absence of the oesophagus.
Panel D – Fluoroscopic image of the endovascular stent graft in situ.

readmitted with recurrent graft infection. This time he also refused further surgical intervention; under long-term (one year) antibiotic therapy, he could be discharged following prolonged in-patient care.

Discussion

An aorto-oesophageal fistula is a rare cause of gastrointestinal bleeding, characterized by significant morbidity and mortality, even with early diagnosis and intervention. Thoracic aortic aneurysms are the most common cause of an AEF; further causes include foreign body ingestion, trauma (usually iatrogenic), carcinoma or,

rarely, aortitis tuberculotica. Several therapeutic management options have been reported in the literature, although all rely on the same principle: urgent management of the aortic tear with immediate or delayed repair of the oesophageal lesion.

Although there are many approaches to treat an AEF, the treatment has to be adapted to the patient's wish in some cases. Our most straightforward therapeutic option was EVAR and subtotal oesophageal resection followed by a gastro-oesophageal reconstruction. Securing the bleeding source as an emergency, removing the oesophagus urgently to prevent sepsis and subsequent elective reconstruction of gastrointestinal continuity appears to

be a justified surgical approach, as the currently available literature also states, although there are no large studies available.

EVAR is a new, lower-risk, emergency alternative, although EVAR alone leaves the oesophageal defect untreated, contributing to a higher risk of mediastinitis and increased mortality and morbidity.[3] A similar conclusion resulted from the Regensburg experience; EVAR is an effective emergency alternative to prevent early fatal exsanguinations, however, it can rarely be utilized as a stand-alone procedure.[4] A nationwide, multicentre, Italian study provided information on 25 aorto-oesophageal and aortobronchial fistulae that were treated with EVAR. The results demonstrated that patients who underwent combined EVAR and tracheobronchial/oesophageal intervention had lower graft infection rates and better survival than patients receiving EVAR treatment exclusively.[5] Most probably, the long-term prognosis is affected by a concomitant mediastinal infection and graft contamination.

The surgical approach to the oesophageal lesion is controversial in the literature. Snyder et al. reported a primary suture of the oesophageal defect, with minimal mediastinal contamination, although it was associated with a higher risk of dehiscence and fistula recurrence, probably due to local ischaemia.[6] Instant oesophago-gastric anastomosis after subtotal oesophagectomy may be another alternative,[7] although associated with an increased risk of perioperative death, but this risk could be reduced by omentopexy around the tube graft. Subtotal oesophageal resection followed by gastric or jejunal interposition as a second-stage surgical intervention could minimize the hazard of graft infection.[8,9] For feeding, transdiaphragmatic or transthoracic gastrostomy are reliable solutions that both avoid further opening of the abdomen for a separate gastrostomy or jejunostomy and minimize damage to the stomach, but maintain patency of the upper gastrointestinal tract.

Another interesting complex solution to prevent late thoracic interposition graft infections has been described by Aleksic et al. and Aizawa et al. Although with different aetiologies, they both demonstrated reasonable long-term results after implantation of an extra-anatomic, ascending-descending, aortic, interposition tube-graft bypass with stump closure of the affected descending aorta, with or without omentopexy around the descending stump.[10,11] Our personal experience with extra-anatomical bypasses is limited to extensive chronic Type B aortic dissections, in which cases the distal abdominal and lower limb perfusion was severely compromised. The operative solution of bilateral subclaviofemoral bypasses provided acceptable perfusion results, although the long-term patency was significantly influenced by the effectiveness of the

anticoagulation. Müller et al. have investigated 33 patients with anatomic and extra-anatomic repair following mycotic aneurysms of the thoracic and the abdominal aorta.[12] Their conclusion shows that the in situ reconstructions did not carry a higher risk of morbidity and mortality than the extra-anatomic reconstructions.

In conclusion, early diagnosis and aggressive surgical approach without delay is the only option for effective treatment for an AEF. Second-stage interval gastro-oesophageal reconstruction may lead to the most optimal long-term results. Imaging examination is essential in the primary diagnosis; computerized tomography is a safe, reliable, non-invasive method in the early recognition of this highly lethal entity. We have to emphasise the importance of the multidisciplinary character of the treatment, involving radiologists, gastroenterologists and upper-gastrointestinal and cardiothoracic surgeons to obtain the most favourable results in the management of an AEF.

Conflict of interest statement

Funding

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V

Age-related presentation of acute type A aortic dissection

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Abstract

Background: We evaluated the clinical and anatomic presentations of acute type A aortic dissection according to patient age.

Methods: We retrospectively reviewed 235 consecutive patients who underwent acute type A dissection repair between January 2000 and December 2014. The influence of age on anatomical and clinical presentation, surgical management in the entire cohort and also after exclusion of patients with known connective tissue disorders was assessed using logistic regression.

Results: Males presented with type A acute aortic dissection at a younger age than females. Acute onset with signs of myocardial ischemia, connective tissue disorders, or bicuspid aortic valve characterized the younger population. Extension to the coronary sinus(es) ($p = 0.0003$), descending thoracic aorta ($p = 0.016$), and abdominal aorta ($p = 0.029$), and an intimal tear at the level of the aortic root ($p = 0.0017$) correlated inversely with patient age. Similar findings were obtained after exclusion of patients with connective tissue disorders or a bicuspid aortic valve.

Conclusions: More frequent proximal and distal progression of the dissection flap occurs in younger patients with acute type A aortic dissection. Older age is associated with a lower probability of an intimal tear at the level of the sinus of Valsalva. These findings, associated with prognostic implications, account for the choice of more radical proximal procedures for repair of aortic dissection in younger patients.

Keywords

Age factors, Aorta, Aneurysm, dissecting, Aortic root, Genetic predisposition to disease, Vascular surgical procedures

Introduction

The incidence of acute type A aortic dissection (ATAAD) is higher in the seventh and eighth decades of life.[1] This event is less frequent but not uncommon in younger people, accounting for approximately 7% of surgical cases involving patients younger than 40 years and 18%–22% of patients younger than 50 years.[1,2] Surgical mortality in the younger age group is not negligible and not significantly lower than that in advanced age.[1–3] In younger patients, more frequent involvement of the distal aorta and supraaortic vessels has been described,[2,4] as well as a higher prevalence of connective tissue disorders.[2,4–6] These features can also explain the necessity for more radical and extensive surgical procedures in patients with inherited vascular wall disorders. A limited number of reports have focused on the preoperative features and their correlation with age in patients presenting with ATAAD.[2,4] Therefore, we studied the clinical and anatomic presentations of ATAAD, characterized their relationships with patient age, and considered the implications in terms of pathologic background and surgical management.

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Patients and methods

The departmental database of Wessex Cardiothoracic Centre at the University Hospital Southampton was interrogated to retrieve data of patients treated for spontaneous ATAAD between January 2000 and December 2014. We identified 235 patients who underwent repair of spontaneous acute type A aortic dissection during the study period. In this retrospective cohort study, we analyzed data on clinical presentation, anatomic features of ATAAD, and operative techniques for aortic repair, according to patient age. Particularly, anatomic details from preoperative imaging and intraoperative findings were available to characterize extension of the dissection flap beyond the ascending aorta, thus involving the aortic arch, descending thoracic aorta, and abdominal aorta. The site of the intimal tear was coded according to its intraoperative description as located at the level of the aortic root (intimal tear at the level of the sinus of Valsalva), ascending aorta, or aortic arch. Because of relevant implications in surgical strategy, an intimal tear extending from the ascending aorta to the aortic root or aortic arch was coded as a tear of the aortic root or aortic arch, respectively. Our institutional surgical protocols in cases of acute aortic dissection repair have been described previously.[7,8]

Patients were consented prior to procedures, according to British legislation: Section 14U of the National Health Service Act 2006 (as amended by the Health and Social Care Act 2012) with the aid of NHS Standard Consent Forms. Everyone aged 16 or more is presumed to have the capacity to give consent, unless the opposite is demonstrated. The consent form acts as an aide-memoire to patients and health professionals by providing a checklist of information that should be offered, and giving the patient a written record of the main points discussed (NHS Standard Consent Form

Nr 1). The Mental Capacity Act 2005 states that people who lack capacity to make decisions about their care and treatment should be involved in such decisions "so far as practicable" (www.england.nhs.uk/shared-decision-making/why-is-shared-decision-making-important/shared-decision-making-to-comply-with-national-legislation-and-policy). If this is not possible, NHS Standard Consent Form Nr 4 is applicable for adults who are unable to consent to investigation or treatment. In this case, two medical professionals act on behalf and in the best interest of the patient if treatment cannot be delayed until the patient recovers capacity. Next-of-kin may receive information either personally or via telephone as part of "good clinical practice", but final responsibility for determining whether a procedure is in an incapacitated patient's best interests lies with the health professionals performing the procedure.

Continuous data are presented as mean ± standard deviation, categorical variables are provided as counts and percentages. Student's t test was applied to compare age between groups defined by clinical presentation, etiology, anatomical details of aortic involvement, and surgical procedures. The influence of age on the probability of an anatomical presentation was assessed by logistic regression considering the overall population and patients without connective tissue disorders or bicuspid aortic valve (BAV). Statistical analyses were performed by Stat-View Statistical Software Package version 5.0 (SAS Institute, Inc., Cary, NC, USA) and NCSS 2001 (Number Cruncher Statistical System, Kaysville, UT, USA).

Results

Figure 1 shows the age distribution among the 235 patients who underwent repair of spontaneous acute type A aortic dissection. Patients younger than 40 years represented 6% of the total, 18% were younger
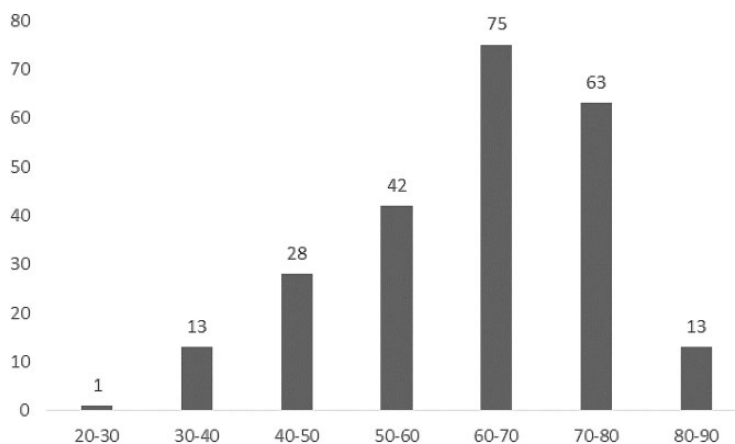

Figure 1. Age distribution in patients undergoing acute type A aortic dissection (ATAAD) repair.

Table 1. Patient age in emergency acute type A aortic dissection repair with (variable = yes) or without (variable = no) the listed preoperative characteristics according to etiology and clinical presentation.

Variable	No. of patients	Mean age (years)		p value
		Variable = yes	Variable = no	
Male	154 (66%)	61.4 ± 12.6	68.0 ± 12.1	<0.0001
Presentation				
Myocardial ischemia	36 (15%)	60.0 ± 14.8	64.9 ± 13.5	0.04
Tamponade	39 (17%)	66.2 ± 18.3	63.6 ± 13.5	0.24
New onset of cerebral stroke	18 (8%)	65.6 ± 22.9	63.9 ± 13.4	0.59
Mechanical ventilation	16 (7%)	61.6 ± 22.1	64.2 ± 13.4	0.41
Acute renal failure	12 (5%)	64.9 ± 25.2	64.1 ± 13.4	0.82
Limb ischemia	12 (5%)	62.7 ± 25.2	64.0 ± 14.0	0.72
Abdominal ischemia	2 (1%)			
Cardiopulmonary resuscitation	10 (4%)	67.3 ± 27.5	63.9 ± 13.4	0.41
Connective tissue disorders/BAV	22 (9%)	50.1 ± 17.2	64.5 ± 12.6	0.004
Marfan syndrome	6 (3%)	45.5 ± 22.4	64.3 ± 13.3	<0.0001
Previous cardiac surgery	14 (6%)	62.6 ± 25.4	64.2 ± 13.1	0.65

BAV: bicuspid aortic valve.

than 50 years, and 32% were older than 70. Male patients experienced acute dissection earlier in life. Patients with a known connective tissue disorder or BAV ($n = 22$) were significantly younger than patients with no syndromic features and tricuspid aortic valves ($n = 213$). Patient age was not different regarding the featured characteristic of preoperative clinical presentation; however, we found that signs of myocardial ischemia in acute aortic dissection were associated with younger age. Table 1 lists the preoperative clinical characteristics. Aortic dissection involved the ascending aorta in all patients (Stanford type A); according to the DeBakey classification, 205 patients had type I and 30 had type II aortic dissection. Patients presenting with progression of the dissection flap into the coronary sinus(es), descending thoracic aorta, and abdominal aorta were significantly younger than those who had exclusively ascending aorta and/or arch involvement. The distribution of primary tear sites showed that younger age was associated with an intimal tear at the level of the aortic root (Table 2). We found similar results regarding proximal and distal aortic involvement after exclusion of syndromic disorders and BAV. In the entire cohort, the probability of aortic dissection extending into the coronary sinus (es), descending thoracic aorta, and abdominal aorta decreased with patient age: odds ratio (OR) = 0.96, 95% confidence interval (CI): 0.933–0.980; OR = 0.97, 95%CI: 0.95–0.99; OR = 0.97, 95%CI: 0.95–0.99, respectively. Older age was characterized by a lower probability of an intimal tear in the aortic root (OR = 0.95, 95%CI: 0.93–0.98; Figure 2). In patients having no known connective tissue disorder, the probability of aortic dissection extending into the coronary sinus(es), descending thoracic aorta, and abdominal

aorta decreased with age (OR = 0.96, 95%CI: 0.935–0.985; OR = 0.98, 95%CI: 0.96–1.02; OR = 0.98, 95% CI: 0.96–1.003, respectively). Advanced age was characterized by a lower probability of an intimal tear in the aortic root (OR = 0.95, 95%CI: 0.92–0.98; Figure 3). All patients underwent replacement of the ascending aorta. No difference in patient age was identified regarding the distal repair strategy, considering total arch replacement and proximal arch replacement (including resection limited to two-thirds of the lesser curvature of arch; "hemiarch technique"). Advanced age characterized patients who underwent associated aortic valve replacement due to degenerative changes in the valve; the younger population received full root replacement because the dissection involved the aortic root (Table 3).

Discussion

ATAAD is more common from the seventh decade of the life. It is an unexpected finding in healthy subjects, and represents one of the well-recognized causes of sudden death in young people.[9,10] Our data entirely support previous reports that among patients undergoing ATAAD repair, approximately 6% are younger than 40 years, and nearly 20% are less than 50-years old.[1,2] An underlying connective tissue disorder has been widely recognized as the fundamental predisposing factor strongly characterizing this population.[2,4] Furthermore, several contributors including hypertension, smoking, cocaine and amphetamine abuse have been associated with the occurrence of this catastrophic disease in patients younger than 50 years.[11,12] An inherent pathology of the aortic wall leads to faster development of aneurysms and a higher risk of severe

Table 2. Patient age in emergency acute type A aortic dissection repair with (variable = yes) or without (variable = no) the listed characteristics according to anatomical findings.

Variable	No. of patients	Mean age (years)		p value
		Variable = yes	Variable = no	
Overall population (n = 235)				
Extension of dissection flap beyond ascending aorta				
Coronary sinus(es)	50/235 (21%)	57.8 ± 13.2	65.4 ± 13.1	0.0002
Aortic arch	205/235 (87%)	63.6 ± 12.4	65.5 ± 18.7	0.44
Descending thoracic aorta	129/175 (74%)	62.0 ± 12.9	66.6 ± 14.8	0.014
Abdominal aorta	109/171 (64%)	61.9 ± 12.8	66.0 ± 14.5	0.03
Location of primary intimal tear				
Tear identified	196/221 (89%)			
Aortic root	36 (19%)	57.3 ± 13.0	65.2 ± 13.1	0.0007
Ascending aorta	103 (53%)	64.7 ± 13.6	63.1 ± 13.3	0.34
Aortic arch	57 (28%)	66.1 ± 11.0	63.1 ± 14.0	0.13
Excluding connective tissue disorders and bicuspid aortic valve (n = 213)				
Extension of dissection flap beyond ascending aorta				
Coronary sinus(es)	45/213 (21%)	58.4 ± 13.4	65.9 ± 13.1	0.0004
Aortic arch	184/213 (86%)	64.4 ± 12.1	64.5 ± 19.7	0.96
Descending thoracic aorta	118/161 (73%)	63.1 ± 14.0	67.6 ± 14.9	0.044
Abdominal aorta	100/155 (64%)	62.9 ± 12.7	66.8 ± 14.3	0.06
Location of primary intimal tear				
Tear identified	175/200 (88%)			
Aortic root	32 (18%)	57.8 ± 12.4	66.0 ± 13.6	0.0009
Ascending aorta	91 (52%)	65.6 ± 13.4	63.3 ± 12.1	0.24
Aortic arch	52 (30%)	66.6 ± 10.7	63.5 ± 13.6	0.14
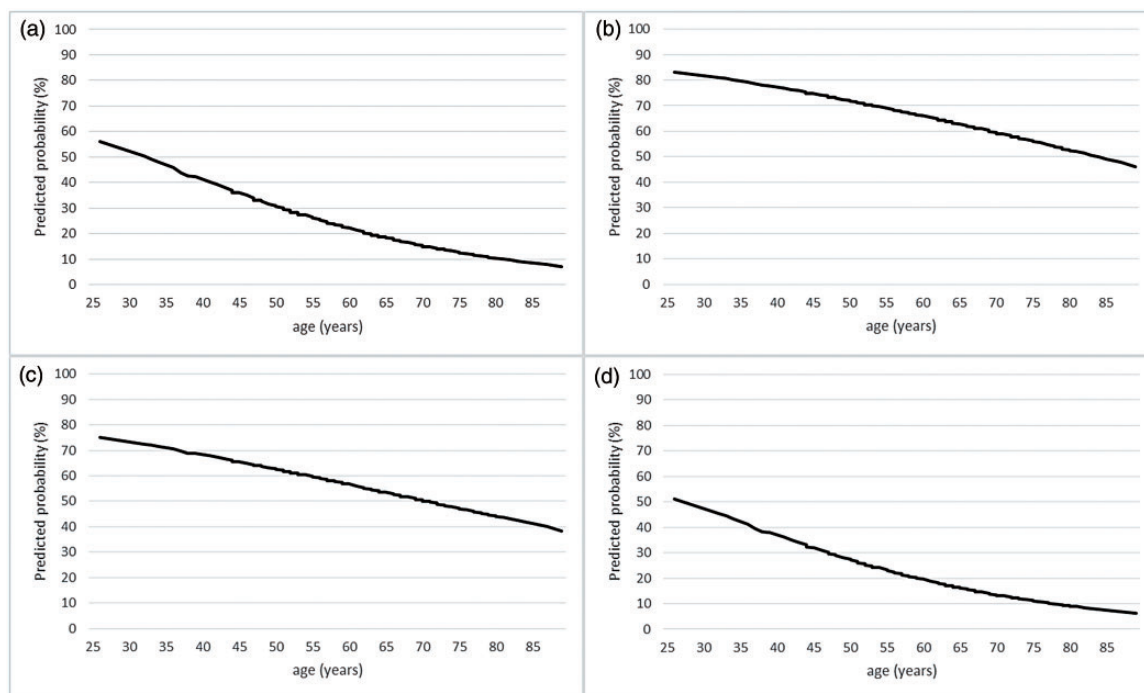
Figure 2. Overall age and probability of (a) coronary sinus dissection (p = 0.0003), (b) descending thoracic aortic dissection (p = 0.016), (c) abdominal aortic dissection (p = 0.029), and (d) an intimal tear in the aortic root (p = 0.0017).
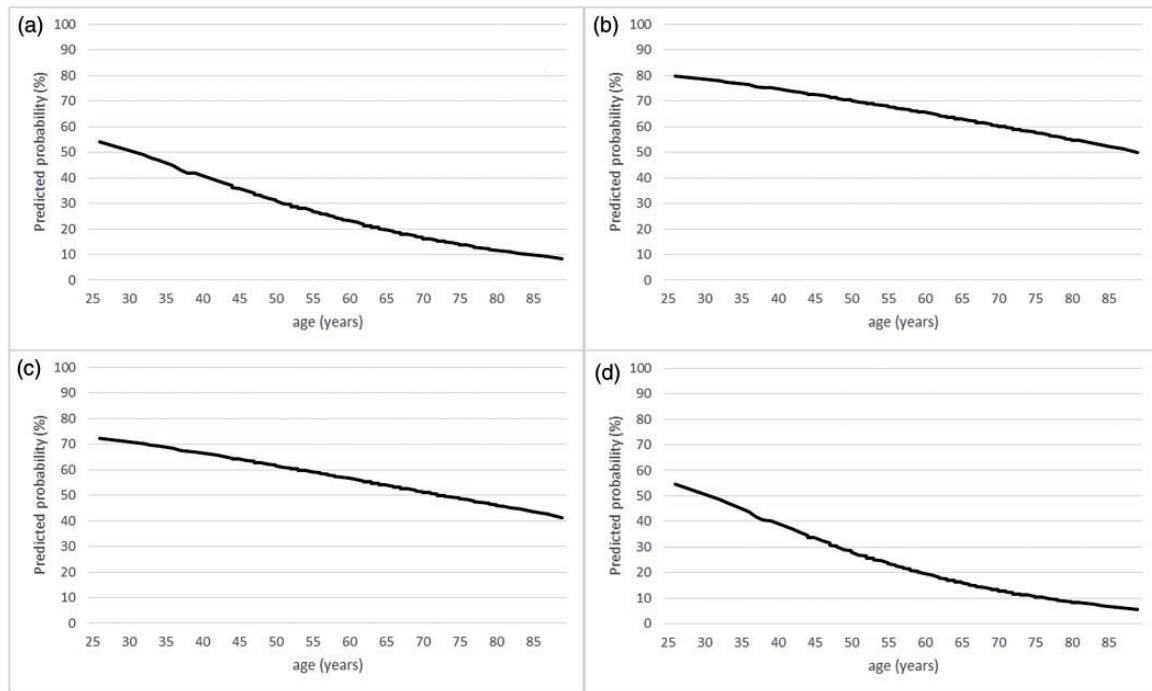
Figure 3. Patients without connective tissue disorders or bicuspid aortic valve. Age and the probability of (a) coronary sinus dissection ($p = 0.0017$), (b) descending thoracic aortic dissection ($p = 0.07$), (c) abdominal aortic dissection ($p = 0.09$), and (d) an intimal tear in the aortic root ($p = 0.0016$).

Table 3. Patient age in emergency procedures for acute type A aortic dissection repair with (variable = yes) or without (variable = no) the listed characteristics according to surgical procedure.

Variable	No. of patients	Mean age (years)		p value
		Variable = yes	Variable = no	
Ascending aorta replacement	235			
+ Aortic valve replacement	13 (6%)	71.1 ± 10.7	63.7 ± 13.3	0.04
+ Aortic root replacement	61 (26%)	57.2 ± 12.1	66.5 ± 12.9	<0.0001
+ Valve sparing aortic repair	2 (1%)			
+ Proximal arch replacement	65 (28%)	64.2 ± 11.7	64.1 ± 13.8	0.93
+ Total arch replacement	13 (6%)	58.4 ± 12.0	64.4 ± 13.3	0.09
Concomitant coronary artery bypass	22 (9%)	63.5 ± 11.3	64.2 ± 12.7	0.79
30-day mortality	26 (11%)	67.0 ± 11.2	63.7 ± 12.7	0.19

complications. Surprisingly, early pathologic evolution does not characterize only syndromic patients who represent a small subgroup in surgical series. The investigators of the International Registry of Acute Aortic Dissection reported that patients aged less than 40 years had a significantly larger aortic root and ascending aorta compared to the older population.[4] This feature was common in both Marfan and non-Marfan patients. Recent evidence has extended our knowledge of the well-known syndromic disorders in understanding the evolution of aortic diseases in the young. Several nonsyndromic genetic conditions can lead to early development of thoracic aortic aneurysms, which are further characterized by rapid dilatation and a high risk of dissection. These nonsyndromic familial thoracic aortic aneurysms are related to genetically heterogeneous disorders and estimated to represent 20% of diagnosed thoracic aneurysms;[5] mutations in 5 genes (*MYH11*, *TGFßR1*, *TGFßR2*, *MYLK*, and *ACTA2*) have been identified so far, and all have autosomal dominant inheritance.[13] From a molecular point of view, the consequences of these genetic alterations translate into degenerative remodelling of the aortic medial extracellular matrix, leading to progressive

loss of elastic properties.[6,14] This clinical, anatomical, genetic, and molecular evidence suggests that the prevalence of inherited aortic wall disorders in young people, resulting in aortic complications, is probably wider than expected or diagnosed.

The above pathologic background may play an important role in extension of the dissection. In our series, a significantly lower mean age characterized this presentation, featuring involvement of the aortic root and/or distal aorta. These characteristics of our cohort reinforce the conclusions of Nishida and colleagues[15] suggesting a strategy for aortic root repair, and also from the large German Registry for Acute Aortic Dissection Type A analysis that reported decreasing probability of ATAAD extension into the supraaortic vessels and abdominal aorta with increasing patient age.[2] Even after exclusion of syndromic disorders and BAV, we demonstrated that younger age is frequently associated with severe involvement of the aortic root and coronary sinus(es). The association of younger age and dissection of the coronary sinus(es) may also be responsible for preoperative myocardial ischemia. This has already been associated with aortic root complications after dissection repair, and can be seen as a marker of severe proximal aortic tissue disruption.[16]

In our experience, an intimal tear in the aortic root is a feature of the younger subgroup of patients, and this was confirmed after exclusion of patients with known connective tissue disorders or BAV. In a different population, Ma and colleagues[17] described a similar distribution of intimal tear sites and reported age and hypertension as risk factors for an arch entry tear; further research on hemodynamic factors might facilitate the understanding of these findings. In addition to genetic and metabolic contributors, aortic flow properties may play a role in the progression of wall disease,[18,19] and might be an active variable in triggering the onset of dissection. Recent studies have focused on characterization of aortic flow patterns and wall stress, using computational fluid dynamics; wall shear stress seems to have a significant impact on the promotion and progression of medial degeneration, and represents a mechanical force able to separate the aortic layers once the balance between tissue strength and flow-induced wall stress is lost.[20,21] Numata and colleagues[20] studied 6 different anatomical models of aortic disease; in all of their patients, the oscillatory shear index (a parameter describing deviation of wall shear stress from its mean direction) was higher close to the sinotubular junction, near the bifurcation of the head and neck vessels and the lesser curvature of the proximal descending aorta. All of these areas are potential sites of an intimal tear. Clinical evidence is limited but suggests that different patterns of aortic segment dilatation

and blood flow properties across the aortic valve can promote development of an intimal tear in different areas of the proximal aorta: major involvement of the lesser curvature of ascending aorta in patients with a preserved or not extremely dilated sinotubular junction, or the right lateral side of the aorta in the case of a diffusely dilated proximal aorta and sinus(es) of Valsalva or sinotubular junction in the presence of a dilated aortic root.[20,21] Undiagnosed inherited disease of the aortic wall and early dilatation of the aortic root possibly associated with aortic valve dysfunction could well explain why ATAAD presents in younger patients with more severe aortic root involvement, more frequent proximal extension of the dissection flap, and a proximal intimal tear.

Different pathologic and pathogenetic substrates exist between younger and older patients; the latter are affected by longstanding hypertension and a progressive atherosclerotic process, leading to a significantly different approach for proximal repair of ATAAD. We found that full root replacement was performed mainly in young patients, whereas older patients underwent a more conservative proximal repair. The literature reports rates of 23%–25% for full root replacement in the overall population of patients undergoing ATAAD repair, with 40%–60% in people younger than 50 years,[2–4] 10%–20% in septuagenarians, and 5%–10% in octogenarians. Isolated aortic valve and concomitant ascending aorta interposition graft replacement is nowadays reserved for cases of valve leaflet degeneration or calcification, and reported in approximately 5% of cases, mostly in patients aged over 70 years. There is no doubt that younger people require more radical aortic resection, although besides the clinical and prognostic reasons, we should recognize the importance of pathologic background and anatomic features in determining the surgical strategy for proximal repair. Nevertheless, the recommendation for full root replacement in cases of connective tissue disorders, dilated or severely dissected aortic root, or an intimal tear in the aortic root, is now widely accepted, aiming for a safe procedure in acute settings and reduction of the risk of reoperation in the mid- and long-term. Evaluation of anatomical characteristics can also explain the similar prevalence in the literature of arch procedures in younger and older patients;[2] a more extensive distal repair is usually reserved for cases of an intimal tear in the aortic arch or an aneurysmal aortic arch. We were not able to report exact aortic dimensions, but found no difference in patient age regarding the presence of an intimal tear involving the aortic arch.

This was a retrospective study from a single institution over a period of 14 years. No information was available regarding patients who declined the surgical

procedure, were managed conservatively, or died prior to admission. Similarly, we could not include data of patients who were deemed very high-risk or in a terminal clinical condition and were not referred from peripheral hospitals. Availability of preoperative imaging data from district healthcare facilities was limited and, despite a detailed operative description of the aortic valve and root anatomy, we were not able to systematically characterize the size of the different aortic segments. In the absence of pre-dissection studies, interpretation of acute dissection data might be debatable because a significant increase in aortic diameters is expected immediately after the acute dissection event.[22] However, we concluded that the clinical presentation and occurrence of dissection-related malperfusion syndrome were not associated with the age of a patient presenting with ATAAD, apart from the presence of signs of syndromic connective disorders or myocardial ischemia. More extensive progression of the dissection flap into the aortic root and distally to the descending and abdominal aorta characterized younger patients; different pathologic backgrounds promoting the onset of ATAAD in younger and older patients can explain this finding. The higher rate of connective tissue disorders and prevalence of undiagnosed intrinsic underlying proximal aortic wall disease may account for this particular presentation in the young. An intimal tear in the aortic root is more common at a younger age on presentation; this finding associated with the prognostic reasons supports the higher prevalence of full root replacement in younger patients.

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VI

Recent Advances in the Management of Acute Aortic Syndrome

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1. Introduction

Type A acute aortic dissection is one of the most serious cardiovascular conditions and is associated with significant morbidity and mortality. A half century ago, Hirst et al published a milestone article describing the linearized mortality rate of one percent per hour after the onset of an ascending aortic dissection [1]. Hence, the importance of accurate, quick and reliable diagnosis, as the timing of procedure is vital for optimal management of this highly lethal condition. Despite improvements in the diagnostic modalities, surgical techniques and perioperative care, the overall mortality remains high, between 10% and 30% [2].

Due to its major role in systemic perfusion, the aorta and its main branches after dissection are often challenging when trying to prevent surgical morbidity and mortality. The complexity of aortic dissection presents not only a pure cardiovascular surgical task, but also consideration must be given to protection of the myocardium, cerebrum, peripheral tissues and organs. An early fatal result of aortic dissection is due to ischaemic injury to the brain or heart, although longer peripheral ischaemia can cause multiorgan failure resulting in extended hospital stay, increased morbidity and mortality. Alexis Carrel highlighted the risks of surgery in 1910 with the following short summary on aortic interventions: "The main danger of the aortic operation does not come from the heart or from the aorta itself, but from the central nervous system." Even a century later, we are still trying to optimize cerebral protection, despite having significantly wider range of diagnostic and therapeutic modalities.

Advances in our understanding of varying pathologies of aortic dissections have improved as have the technological developments in the modes of detection. These advances together with improved therapeutic options have raised expectations for better outcomes.

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2. Acute aortic syndrome

The term "acute aortic syndrome" (AAS) became widely accepted in the last decade. It involves not only aortic dissections, but intramural haematomas and penetrating atherosclerotic ulcers in the same anatomical location. This constellation of presentations have similar emergency status, diagnostic and therapeutic requirements. As a definition, AAS is an acute pathophysiological process involving the tunica media of aortic wall, which results in rupture or any further life-threatening complications.

2.1 Epidemiology

Population-based epidemiological studies suggest an incidence of AAS of about thirty cases per one million people per year. Eighty percent is represented by acute aortic dissections, 15% by intramural haematomas and 5% as penetrating ulcers. Seventy percent of the affected population is male with an average of 60 years [3]. A Swedish epidemiological study found the same incidence in an observational period between 1987 and 2002 among 4425 cases. In this study, the incidence of AAS has increased by 50% in men and 30% in women over study period. This may be related to enhanced diagnostics, although a further component could also be the increasing age of the population. Overall, 20% of affected patients died before reaching a medical facility, 30% during the hospital stay and further 20% over the following 10 years [4]. Both circadian and seasonal variations have been observed in the occurrence of AAS, with the peak frequency found between 0800hr and 0900hr, with an increased likelihood during the winter period. The most likely explanation is a link to the circadian variation in blood pressure [5, 6].

2.2 Pathophysiology

The mechanisms leading to AAS arise from many sources, although preexisting medial degeneration is proven to be an important risk factor for acute aortic dissection. Cystic medial necrosis is a hallmark of the histology, especially in aortic aneurysm patients. Microscopic features include decreased amount of vascular smooth-muscle cells, mucoid deposits and elastin deficiency [7]. However, over 80% of acute dissections occur in absence of a pre-existing aneurysm. The International Registry of Acute Aortic Dissection (IRAD) has collected an impressive amount of data for the demography of patients who present with AAS. The most commonly associated factors are:

- Hypertension
- Atherosclerosis
- Elderly
- Previous cardiovascular surgery, especially previous aortic aneurysm or dissection repair
- Connective tissue disorders (Marfan`s syndrome, Ehlers-Danlos` syndrome, Erdheim-Gsell`s syndrome)
- Infective involvement of the aortic tissue (Lues, Takayashu aortitis)
- Congenital causes (PDA ampulla, Sinus of Valsava aneurysm, bicuspid aortic valve)
- External factors (Trauma, cocaine abuse)

Improvements in the resolution of aortic imaging has led to the identification of pathological submodalities, i.e. intramural haematoma or penetrating atherosclerotic ulcer. Histological

findings of these lesions generally demonstrate significant intimal atherosclerosis, which is not a constant finding in aortic dissection biopsies. Studies suggest that aortic dissection is an end process with a wide pathological spectrum, many of which facilitate weakening and/or increased stress of the aortic wall. The chain of pathological events might begin with a small superficial intimal rupture; atherosclerotic ulcers may provide a good millieu for development of such a tear. Alternatively, disruption of vasa vasorum might result in an intramural haematoma, which later ruptures into the aortic lumen or leads to dissection. However, it is likely that many aortic dissections develop without having a pre-stage of intramural haematoma or penetrating ulcer [8].

2.3 Presentation and diagnosis

Although the typical symptom is described as sharp, tearing, ripping chest pain, the presentation is diverse and about 10% do not complain of pain; sometimes the aortic pathology is an accidental clinical finding. In some patients shoulder or back pain occurs or just a husky voice, with or without shortness of breath and/or haemophthysis. Hypotension or shock is seen in 25% of patients, whereas hypertension can also be a presenting symptom, although more often found in type B dissections. Further findings, such as migrating pain, neurological deficits, acute abdomen, cardiac failure, myocardial ischaemia, aortic valve regurgitation are less common. Connective tissue diseases are characterized by additional specific symptoms, i.e. skeletal, pharyngeal or lens abnormalities and extreme laxity [3].

Early acute diagnosis can be vital, as an emergency surgery may be indicated. Blood pressure control is essential, and a goal of systolic ≤110 mmHg is recommended. The administration of β-blockers, sodium-nitroprusside, calcium-channel-blockers with analgesia is helpful, if indicated. In some advanced dissections resustitative measurements such as intubation and pericardiocentesis may be required.

	Transthoracic echocardiography	Transoesophageal echocardiography	Computed tomography	Magnetic resonance imaging
Aortic dissection	+	+++	+++	+++
Intramural haematoma	-	++	++	+++
Penetrating ulcer	-	+	+++	+++
Dissection entry	+	+++	++	++
Aortic regurgitation	+++	+++	-	+++
Pericardial effusion	+++	+++	++	++
Periaortic bleeding	-	+	+++	+++

Table 1. Efficacy of different imaging modalities in AAS.

In patients with suspected acute aortic dissection various investigations are performed on admission including blood tests, electrocardiography, chest radiography, echocardiography, computed tomography and magnetic resonance imaging. Some investigations, such as ECG, chest radiography and routine blood tests do not carry sufficient sensitivity and specificity to exclude or confirm the diagnosis of an acute aortic dissection. Biomarker assays are increasingly utilized in the diagnosis of AAS, i.e. elastin fragments, smooth-muscle myosin heavy-chain protein, D-dimers, but are not widely available and provide only supporting evidence. The definite diagnosis can only be established using an imaging modality [9]. Table 1. summarizes efficacy of different imaging modalities in AAS. Table 2. shows the diagnostic features of the imaging modalities currently available in a hospital setting.

	Transthoracic echocardiography	Transoesophageal echocardiography	Computed tomography	Magnetic resonance imaging
Availability	+++	++	+++	+
Speed	+++	+++	++	+
Portability	+++	+++	-	-
Tolerance	+++	+	++	++
Monitoring	+++	++	++	++

Table 2. Diagnostic features of imaging modalities in AAS.

2.4 Management of AAS

Currently, there are no randomized trials available to guide the management of AAS. The European Society of Cardiology has developed guidelines for diagnosis and management of aortic dissection based on a task force of international societies [10], although in most of decision making clinical pathways are usually based on case series or registries, systematic reviews, local experience, consensus based guidelines. Following initial stabilization of the patient, after diagnostic measurements and imaging, a treatment should be tailored to the pathological entity:

- *Type A dissection*

Over 50% mortality in the first 48 hours without surgical intervention, only 1-10% survives the first 5 weeks on conservative treatment. The perioperative mortality is 10-30%. Contraindications are quite limited as type A dissection is a highly lethal condition without surgical treatment, although age >80 years, ongoing coma with definitive extensive cerebral lesions (but not localized ischaemia or paraplegia!) or extensive abdominal necrosis may be contraindications for surgery. A subacute type A dissection, is a rare finding that requires an elective/semi-urgent operation as the patient has already successfully survived the high mortality period may now benefit from a well planned elective procedure [10].

- *Intramural haematoma*

Classical therapeutic indication as for type A dissection, although in an uncomplicated and non-progressing situation, without ongoing pain and periaortic bleeding, patients can undergo surgery on an urgent basis (within 24 hours) rather than as an emergency. Over the age of 80 years, accompanied by significant comorbidities, conservative therapy in an intensive care

facility with the support of repeat imaging should be considered. If sudden progression occurs, a surgical intervention may be life saving. In this patient group 40% of intramural haematomas resolve after 4 years of follow up without mortality according to a small patient cohort study [11]. Another study demonstrated 34% regression of the disease, while 36% progressed into a dissection (12% acute type A dissection, 24% localized dissection) and 30% resulted in aneurysm formation over long term. They have also demonstrated, that a rupture or dissection is a very rare phenomenon with an aortic diameter of <60 mm at any location with an intramural haematoma [9]. These observations guide the clinical management of intramural haematomas, despite the lack of large multicentric studies, each patient requires a tailored individual management plan. As penetrating atherosclerotic ulcers are usually incidental operative or postmortem findings and are seldom discovered at imaging, there are no widely discussed clinical therapeutic strategies available.

- *Typ B dissection*

As this diagnosis generally requires conservative medical treatment in an intensive care setting, we only briefly discuss the indications for surgery. Medical treatment is associated with a mortality of 20%, compared to surgery, which has much higher mortality of 30%; medical therapy is therefore considered first. Classical operative indications are progressive organ malperfusion, ongoing pain with uncontrollable hypertension. In the last decade stent grafting of the affected region has become an alternative option as it can treat these problems at a low risk profile in most of the cases and without need for further cardiovascular surgery [12].

3. Surgical considerations and recent techniques for repair of type A dissections

3.1 Perfusion approaches in type A dissections

Cannulation of an extended type A dissection often represents a challenge for surgeons when either the subclavian or lower limb arteries are involved in the process. There are some alternative cannulation sites published in current literature i.e. brachiocephalic trunk, right common carotid artery, transapical cannulation, although we prefer an innovative method through non dissected aortic wall on lesser curvature at level of Botallo`s ligament using a Seldinger technique.

Our first experience was a 50 year-old man with sudden onset of ripping chest pain, admitted unconscious accompanied by anisochoria. Computed tomography scan revealed an extensive type A aortic dissection. The dissection began exactly over the aortic valve; maximal diameter of ascending aorta measured 60 x 55 mm. On the lesser curvature of arch, particularly at Botallo`s ligament, preservation of the true lumen with an intact wall was observed, although the dissection involved all supraaortic vessels. Visceral arteries originated from the true lumen except the left renal artery. Dissection in both iliac arteries was also present. Rapid deterioration of the patient with cardiovascular instability led us to cannulate at Botallo`s ligament applying a minimal invasive cannulation method with a Seldinger technique [Figure 1, 2]. At Botallo`s ligament the aorta is firmly bound to pulmonary trunk with a mass of connective tissue, which usually protects it from a complete dissection in this area. Position of cannula has to be guided by either transoesophageal or epiaortic ultrasonography. With this rapid and safe cannulation method extracorporeal circulation can be easily established, thus reducing the risk of perioperative shock and increased mortality [13].
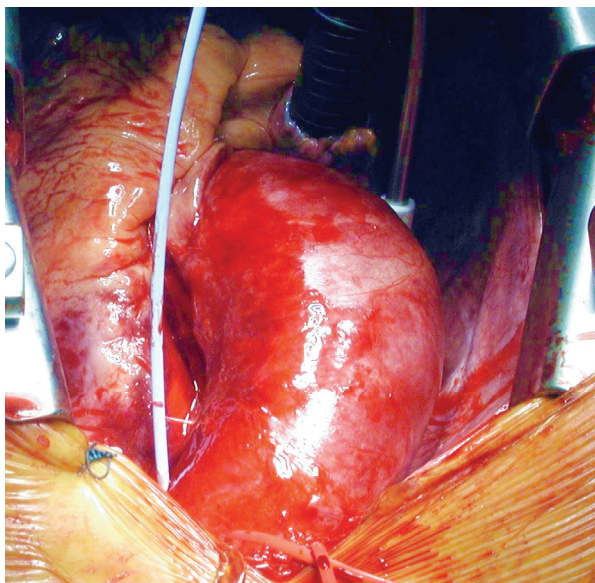
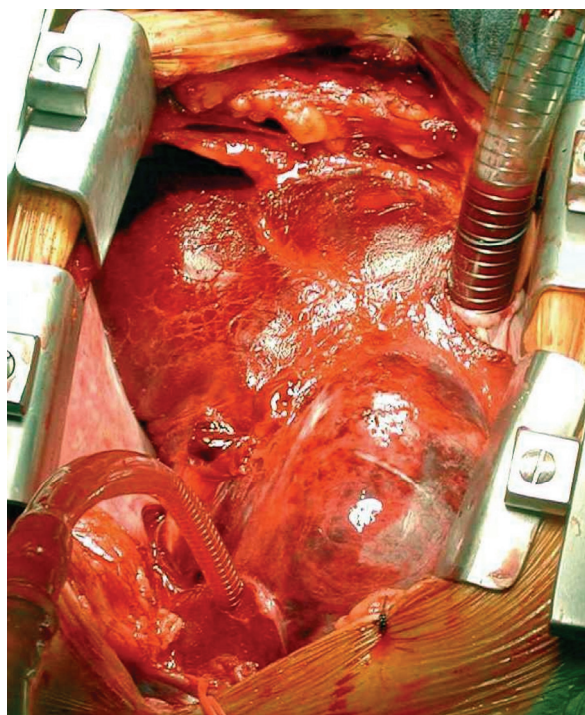Fig. 1. Seldinger cannulation of a type A aortic dissection (first dialation step)

Fig. 2. Arterial cannula in situ at Botallo´s ligament

Cardiopulmonary bypass via axillary/subclavian artery has become an alternative perfusion site in the past decade, predominantly in acute aortic dissections but also for patients with severe aortic atherosclerosis [14-20]. Despite several advantages of axillary/subclavian artery cannulation such as dominantly antegrade perfusion of the aorta, this technique is not without its complications. Establishment of axillary/subclavian artery inflow may not be ideal for providing rapid antegrade perfusion in cases with hemodynamic instability, as dissection and cannulation can take too long. In small patients, a limitation of CPB pump flow due to a narrow axillary artery may be a concern [21, 22]. Applying the standard technique, however, only the right hemisphere is continuously perfused, which can result in malperfusion of the contralateral hemisphere, as Merkkola et al demonstrated, up to 17% of the patients having incomplete circle of Willis [23]. Even with a complete circle of Willis, concern has been raised, if this type of perfusion alone can sufficiently supply the left hemisphere.

Transapical cannulation is another technique for establishing reliable antegrade arterial access, as described by Wada et al [24]. In large cohort of 138 patients, cannula was placed through a 1 cm apical incision into true lumen via aortic valve under transoesophageal echocardiography guidance. Impact of causing an acute aortic insufficiency in this context is not discussed in detail. This technique carries disadvantage of resulting in prolonged cardiopulmonary bypass times, since no additional manipulations can be performed during cooling phase, i.e. inspection and preparation of aortic root.

Right carotid artery cannulation, performed by Urbanski in 100 patients, including 27 with type A dissections, provides another possible alternative, but also carries the risk of left hemisphere malperfusion and potential complications when the vessel is de-cannulated [25]. Experience with innominate artery cannulation by Di Eusanio et al includes 55 patients with only two in acute aortic dissections [26], so it is difficult to evaluate the efficacy of this method due to the small experience.

Fusco at al presented their results in femoral artery cannulation in 2004 [27]. With a conversion rate of 2.5% to ascending aortic cannulation, they conclude that femoral cannulation is appropriate and yields excellent clinical results. They are not aware of having encountered retrograde embolism from the descending aorta, probably since atherosclerosis is less common in dissection patients.

3.2 Cerebral protection in dissection surgery

Avoiding neurological damage is one of the main aims of dissection surgery, as Carrel emphasised a century ago. Deep hypothermia with circulatory arrest (HCA) is the most common technique for cerebral protection in aortic surgery with a well defined safe period for circulatory arrest, of 45-50 minutes at a core temperature of 20°C. Systemic hypothermia to extend the period of safe cerebral ischaemia has been the mainstay of neuroprotection for many decades [28, 29]. Safety of this approach relies on adequate systemic cooling and if this is incomplete, it risks the patient for neurological injury. Introduction of selective antegrade carotid perfusion (ACP) has prolonged this safe period. A combination of cold selective antegrade cerebral perfusion and deep/moderate hypothermic circulatory arrest allows adequate protection for the body and is not associated with higher risk of cerebral microemboli [30, 31]. The efficacy of selective antegrade cerebral perfusion as an adjunctive to hypothermic arrest has been proven by numerous publications [32, 33].

Unilateral brain perfusion, i.e. right subclavian/axillary artery, right carotid artery, brachiocephalic trunk is safe under monitoring with near infrared spectroscopy (NIRS), as nearly 1/5 of the population has an incomplete circle of Willis. Therefore a significant number of patients require bilateral ACP, on the other hand, in the rest population it is still debatable, if in left haemisphere the same temperature can be achieved as the contralateral hemisphere, with unilateral perfusion, after blood has perfused the right side. Further concern is raised with unilateral perfusion, that by aiming for bilateral equal brain saturations, the right haemisphere is may be slightly overperfused, leading to right hemishperal oedema. Near infrared spectroscopy does not provide this type of information, so unilateral perfusion enhances but cannot guarantee cerebral protection. These latter considerations require further research, although applying bilateral ACP may resolve these issues.

In our practice, during HCA, selective antegrade cerebral perfusion is applied through both carotid arteries (DLP Retrograde Coronary Sinus Perfusion Cannula with manual Inflating Cuff®, Medtronic Inc., Minneapolis, USA) at a flow rate adapted to keep a constant cerebral O_2 saturation each side with a perfusion pressure of 35-40 mmHg [Figure 3]. Cerebral monitoring is performed using NIRS, with the aim of maintaining brain tissue oxygen saturation measures at 65-70% continuously during perfusion, which should correspond to the induction values.
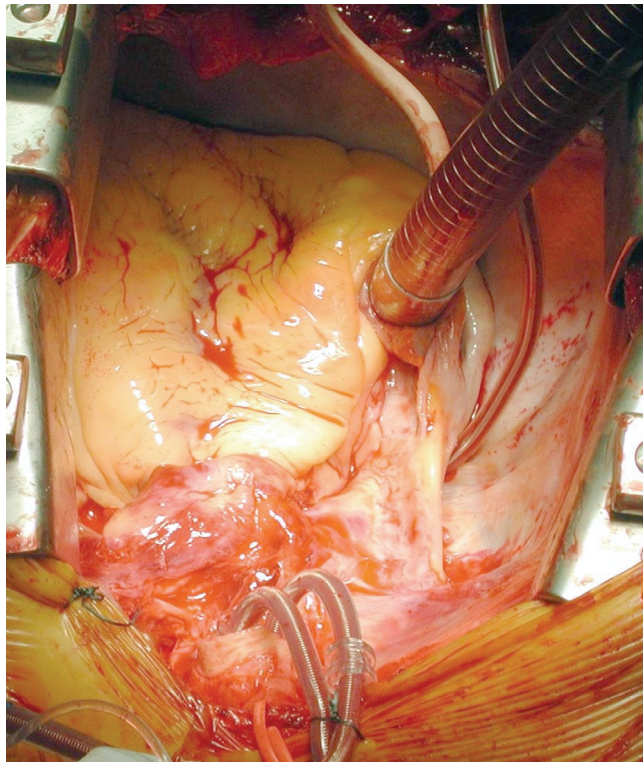

Fig. 3. Selective antegrade carotid perfusion

Retrograde cerebral perfusion via superior vena cava may also be undertaken, although in arch surgery carotids are available for ACP. If the carotids are severely destroyed by dissection, retrograde cerebral perfusion may be considered as an option, so long carotids are replaced by tube grafts. However, retrograde cerebral perfusion is associated with a significantly higher incidence of temporary neurological complications, later extubation, longer ICU-stay, hospitalization, than ACP [34].

In a study of 4670 patients who underwent extensive aortic surgery between 1985 and 2002 at the Heart Centre Leipzig, Germany, superiority of ACP over retrograde cerebral perfusion or stand-alone deep hypothermia was confirmed. ACP was associated with 5-14% mortality and 4-10% permanent neurological deficit, retrograde cerebral perfusion showed 12-22%; 10-20%, stand- alone deep hypothermia 15-30%; 8-24%, respectively.

Rigorous patient temperature monitoring is crucial to a balanced cerebral protection during CPB. As a standard body temperature measurement, rectal monitoring has been widely used for decades in many departments. In the past decade tympanic and urinary bladder temperature monitoring has been studied and suggested as an alternative to gold standard. Tympanic measurements provide a very good estimation of the brain temperature with minimal delay in the changes due to its close proximity to the central nervous system [35, 36]. Tympanic measurements are well established even in everyday body temperature measurement with portable thermometers in general health care. However, to obtain reliable values from the tympanic membrane, debris free status of the ear channel has to be proven by otoscopy prior to placement of probe, followed by a good heat insulation of ears by i.e. using swabs to prevent accidental heat loss due to theatre ventilation system.

Urinary probes are available built into urinary catheters, so their placement is very convenient, although measurement reliability depends slightly on urine flow [37]. Rectal measurements are less reliable, since faecal matter prevents sudden heat exchange [38]. Nasopharyngeal/oesophageal temperature monitoring in HCA as standard measurement site, has limitations as it may significantly over- and underestimate brain temperatures during the cooling and rewarming phases [39-41]. Akata et al have furthermore demonstrated, that pulmonary artery temperatures closely reflect changes in brain temperatures, but nasopharyngeal/oesophageal measurements could not be considered as a reliable index of brain temperature during the rapid induction of moderate/deep hypothermia [42].

4. Follow-up

As aortic dissections often develop on a background of preexisting aortic aneurysms, this mandates regular follow-up in these patients to facilitate elective intervention when required. These elective operations carry less risks as the patient can be thoroughly prepared using the ideal imaging modalities and optimizing the patient's medical condition for major surgery. At the Department of Cardiothoracic Surgery, University Hospital Regensburg, Germany there is a regular aortic day-clinic available on weekly basis for pre- and postoperative follow-ups, that has been running for over a decade, which allows this endangered patient population to be monitored on a 6-monthly basis. Regular postoperative monitoring is essential to provide good long term results with the early discovery of endo-leaks, progression of aortopathy, control of hypertension, etc. As the AAS population is

young, average age of involved is sixty years [3], regular follow up contributes to the restoration of health in this still relatively active age group.

Patients with AAS have a long-term outcome which is less favorable when associated with a past medical history of previous cardiac surgery or generalized atherosclerosis [43]. Surgical repair has been recommended when maximal ascending aortic diameter reaches 50 mm (45 mm at Marfan´s syndrome) or 60 mm when involving the descending aorta, although decision making has to be individualized to patient and other comorbidities [10]. Blood pressure control is essential for these patients, with the aim of maintaining the blood pressure no more than 130/80 mmHg [44]. If there is a well know hereditary component present, the patient´s complete family should be offered the opportunity to be genetically tested and councilled.

Some recent publications have already highlighted the role of angiotensin II in progression of aortic aneurysms, although the relative contribution of its type 1 (AT1) and type 2 (AT2) receptors remain unknown. Habashi et al demonstrated that loss of AT2 expression accelerates the aberrant growth and rupture of aorta in a mouse model of Marfan`s syndrome. Losartan, a selective AT1 blocker reduces aneurysm progression in mice; a full protection required intact AT2 signaling. The angiotensin-converting enzyme inhibitor enalapril, which limits signaling through both receptors, is less effective. Both drugs attenuated transforming growth factor-ß (TGF ß) signaling in the aorta, but losartan uniquely inhibited TGF ß-mediated activation of extracellular signal regulated kinase, by allowing continued signaling through AT2, which shows the protective nature of AT2 signaling and the choice of therapy in aortic aneurysms [45].

International multicentric studies are currently evaluating the possible pharmacological prevention and postoperative medical supportive therapy options in Marfan´s syndrome provided by AT1 blockers, especially losartan in a combination with a ß-blocker, such as nebivolol. The key molecule in aortic aneurysms, TGF ß, normally attached to extracellular matrix, is free and activated. Under experimental circumstances, TGF ß blockade prevents aortic wall damage and dilatation. AT1 blockers exert an anti-TGF ß effect; trials are now ongoing for evaluating the effect of losartan compared with atenolol or nebivolol. The third generation ß-blocker nebivolol retains the ß-adrenergic blocker effects on heart rate and further exerts antistiffness effects, typically increased in aortic aneurysms [46, 47].

After evaluation these ongoing human studies we have more insight to the pharmacological support of AAS and aortic aneurysms, which completes the surgical management possibilities of this severe disease group.

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VII

Double-locus lymphoplasmacytic aortitis

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Abstract

Thoracic aortic aneurysm is an indication for major cardiovascular operative procedures. The etiology is usually hypertension and/or atherosclerotic disease; reaching a certain diameter often results in acute aortic syndrome. Immunoglobulin G4-related aortitis, characterized by lymphoplasmacytic vascular tunica media induration without well-defined underlying infectious or autoimmune systemic causes, is uncommon. Histological similarity to immunoglobulin G4 disease in other organs suggests that this aortitis might be a manifestation of systemic pathology. We describe a case of double-locus lymphoplasmacytic aortitis in a 72-year-old man who had the incidental finding of intramural hematoma on elective thoracic computed tomography as part of a respiratory work-up.

Keywords

Aortic aneurysm, Thoracic, Aortitis, Intramural hematoma, Immunoglobulin G4, Plasma cells

Introduction

Immunoglobulin G subclass 4 (IgG4)-related aortitis is part of a systemic disease with high variability in diverse organ manifestations, including autoimmune pancreatitis, retroperitoneal fibrosis, IgG nephropathy, sclerosing cholangitis, mediastinal pseudotumors, and inflammatory pericarditis. It is commonly observed in elderly men with abdominal aortic aneurysm (AAA) and concomitant retroperitoneal fibrosis; 3/4 have increased serum IgG4 levels.[1] Studies have identified significant differences between the abdominal and thoracic presentations; the latter appears more frequently in females and correlates less with serum IgG4, although the histopathological picture is similar in both.[2] Inflammatory aortic aneurysms represent 4% of all thoracic aneurysms according to Kasashima and colleagues,[3,4] but IgG4 aortitis accounts for 57% of all inflammatory aortic diseases. Although the pathological process is mainly localized in the adventitia, some observers have described variable extensions of intramural lymphoplasmacytic infiltrations, suggesting an autoimmune response directed against the different aortic wall layers.[2]

Case report

A 72-year-old man attended Respiratory Outpatient Care with coughing over 5 years and recent shortness of breath; he denied any form of angina. Past medical history consisted of hypertension, previous smoking, and inflammatory infrarenal abdominal aortic aneurysm (AAA) repair with an interposition tube graft 4 years earlier. Previous abdominal computed tomography (CT) findings were not available at this admission. Histology had confirmed lymphoplasmacytic changes in the intraoperative abdominal specimens. Vascular surgical follow-up did not discover any further progression of aortic disease. Recent spirometry suggested mild chronic obstructive pulmonary disease, but the transfer factors were not reduced. Elective chest CT was initiated by the respiratory team. As an incidental finding, CT demonstrated an intramural hematoma (Figure 1a) throughout the ascending aorta, appearing to terminate in the transverse arch, but no evidence of morphological pulmonary disease.

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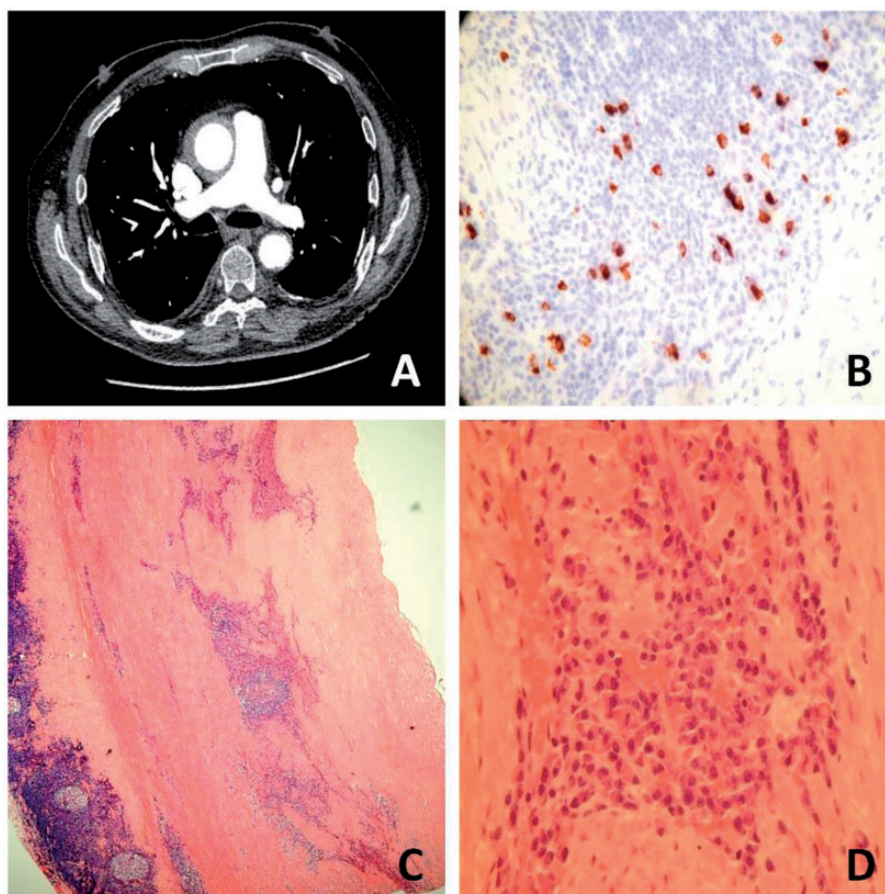Email: isartor@hotmail.com

Figure 1. (a) Computed tomography showing the unfolded ascending aorta with a rim of intramural hematoma to a depth of up to 14 mm at the level of the pulmonary artery bifurcation. (b) Immunostaining of plasma cells with IG4 antibody. Immunoperoxidase staining, original magnification × 600. (c) Low-powered view of the aorta with lymphoplasmacytic inflammation in the media. Hematoxylin and eosin stain, original magnification × 200. (d) High-powered view of the aortic media, showing plasma cells and lymphocytes. Hematoxylin and eosin stain, original magnification × 700.

The maximal aortic diameter was 5 cm, and the coronary calcium score was positive at 2769 (equal to the 96 percentile matched for ethnicity, sex, and age). CT-angiography revealed extensive coronary artery calcification in the proximal left anterior descending, proximal and mid right coronary arteries. Echocardiography showed left ventricular pump function in the lower normal range, without regional wall motion abnormalities or valvular pathologies. The patient underwent supracoronary interposition graft replacement of the ascending aorta (28-mm Vascutek Gelweave; Vascutek Ltd., Inchinnan, Scotland, UK), as per our institutional protocol for intramural hematoma, within one week of admission, using the "closed distal" technique, and additional double-coronary artery bypass with saphenous venous grafts to the left anterior descending and right coronary artery. The aortic crossclamp time was 76 min, cardiopulmonary bypass time was 104 min. Histopathology demonstrated lymphoplasmacytic aortitis (Figure 1c, 1d) associated with the intramural hematoma; a similar microscopic picture to the previous AAA repair. The ascending aortic specimen stained for IgG4 within the plasma cells (Figure 1b). Serum investigations revealed normal IgG4 levels ($<1.3 \, \text{g} \cdot \text{L}^{-1}$), autoimmune and inflammatory markers were within the normal ranges, and the eosinophil count was twice the upper limit of normal ($<0.5 \times 10^9$/L). After an uneventful postoperative course, the patient was discharged home on steroids on postoperative day 10. Follow-up CT after six months confirmed a settled intrathoracic status and excluded any further abdominal organic manifestations and retroperitoneal fibrosis. Therefore, an interdisciplinary decision by us and the hematology-immunology team recommended no long-term steroid treatment.

Discussion

IgG4-related disease, first defined as an independent disease less than 15 years ago, has been reported in several organs. Inflammatory aortic aneurysms are uncommon and differ in etiology, but the

lymphoplasmacytic subtype is probably associated with IgG4-related systemic disease. IgG4-related disease is usually characterized by fibrous tissue proliferation with numerous infiltrations of IgG4-positive plasma cells, raised IgG4 plasma levels, and steroid sensitivity. The efficacy of long-term steroid therapy is still debated because it might reduce adventitial thickening and peri-organ fibrosis, although it could also increase the risk of aortic rupture by thinning the aortic wall.[4] There are several triggers anticipated in the background of IgG4-related aortitis, leading to aneurysmal dilatation or acute aortic syndrome, including autoimmune reactions against aortic wall elements,[5] and chronic aortic wall infections caused by *Cytomegalovirus* or *Chlamydia*.[6,7] Some studies have found that [18]fluorordeoxyglucose positron-emission tomography might be helpful for initial diagnosis and follow-up of IgG4-related disease if this pathology is suspected from the initial presentation.[8] These aspects require further investigation, although the relatively low patient numbers do not facilitate large-scale multicenter studies. Our report highlights a fairly unusual double-locus thoracic and abdominal lymphoplasmacytic aortitis, which initially presented as AAA and later as thoracic intramural hematoma as an incidental outpatient finding. However, this patient did not have raised serum IgG4 levels, which feature in 25% of lymphoplasmacytic aortitis cases.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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VIII

Transapical perfusion for peri-arrest salvage during transcutaneous aortic valve implantation

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Abstract

An 80-year-old man developed severe haemodynamic instability during a transapical aortic valve implantation. He was not suitable for a conventional surgical approach due to comorbidities and patent aortocoronary bypass grafts also limited further stabilizing actions. As a bail-out procedure, we demonstrate the feasibility of transapical arterial cannulation by crossing a newly implanted TAVI valve in order to establish an emergency bypass circuit

Keywords

TAVI; haemodynamic instability; transapical perfusion; ECMO; bridge-to-recovery

Introduction

Transcutaneous aortic valve implantation (TAVI) is increasingly the treatment of choice for high-risk patients with aortic stenosis who are not suitable for conventional aortic valve replacement. Implantation can be performed either through a vascular route, e.g., femoral artery, or transapically via a mini-thoracotomy if the transvascular route is contraindicated. However, if sustained haemodynamic instability occurs, this limited access poses a technical challenge to the institution of heart-lung bypass. As a bail-out procedure and to avoid the conventional median sternotomy, which could be extremely challenging in a significant proportion of this patient population, we report a case in which transapical arterial cannulation was used to establish a bypass circuit through the already implanted prosthetic valve.

Case Report

An 80-year-old man presented with severe aortic valve stenosis. He had undergone coronary bypass grafting in 1999. Recent angiography had shown patent grafts without new native disease. He was relatively immobile as a result of a previous laminectomy and had severely impaired lung function due to chronic obstructive pulmonary disease. For these reasons, the multidisciplinary TAVI meeting concluded that he was a candidate for this procedure. However, as the peripheral vascular access was inadequate on both sides due to significant

flow-limiting lesions with extensive calcification, a transapical implantation route was planned through an anterolateral mini-thoracotomy.

During deployment of the transcatheter aortic valve (23 mm Edwards Sapien XT Transcatheter Heart Valve°, Edwards Lifesciences, Irvine, CA, USA), the patient developed profound hypotension. This condition did not respond to inotropic support. A decision was, therefore, made to establish heart-lung bypass, although the arterial access was significantly limited by both the heavily calcified peripheral vascular bed and the mediastinal adhesions due to the previous bypass surgery with patent grafts. As an emergency salvation, a transapical Seldinger type arterial cannula (18 Fr Medtronic EOPA° elongated one-piece arterial cannula,

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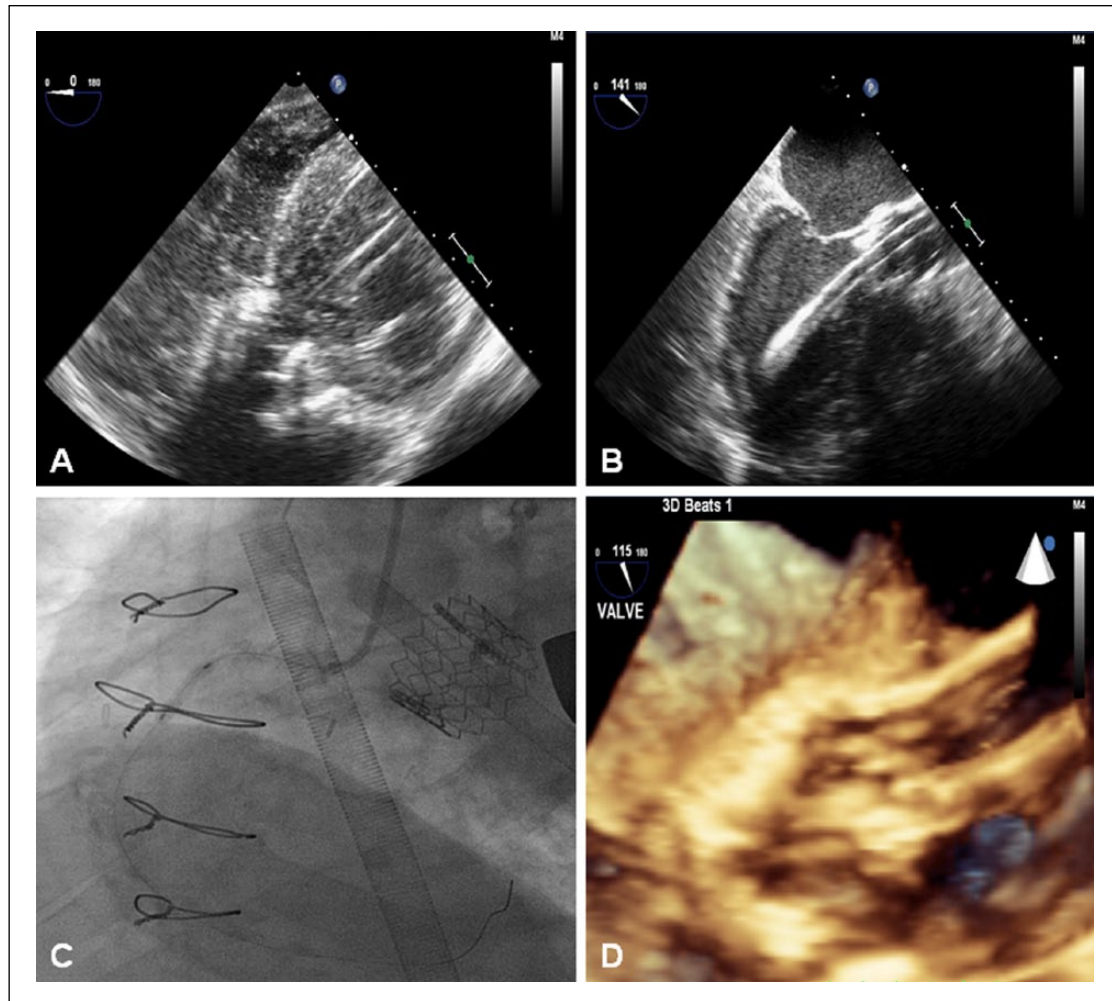UK.
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Figure 1. Panel A – Apical view of left ventricle with the arterial cannula in situ on the transoesophageal echocardiogram.
Panel B – Transvalvar position of the arterial cannula on the transoesophageal echocardiogram.
Panel C – Fluoroscopic image of both arterial and venous cannulae; arterial in the transvalvar position.
Panel D – 3D echocardiographic reconstruction of the transvalvar cannula.

Medtronic Inc., Minneapolis, MN, USA) was inserted, following the removal of the TAVI applicator sheath, with the aid of a guide-wire under simultaneous transoesophageal echocardiography and fluoroscopic guidance through the already implanted TAVI valve (Figure 1) and bypass was established between this site and the right femoral vein. During resuscitation, echocardiography demonstrated profound new right ventricular systolic dysfunction and inferoposterior left ventricular regional wall motion abnormality. Flow down the native right coronary was occluded and a balloon angioplasty was performed to re-establish flow. The left ventricular function improved with reperfusion, although the right ventricular dysfunction persisted. The patient was kept on an extracorporeal membrane oxygenation (ECMO) circuit (Maquet Rotaflow®, Maquet Cardiopulmonary AG, Hirrlingen,

Germany) as a bridge-to-recovery for 24 hours, at which time, a haemodynamic stable stage was achieved and the patient could be weaned from the cardiorespiratory support. Although the immediate postoperative course was uneventful, the patient developed an irreversible severe lower respiratory tract infection several days later and died on the 10th postoperative day.

Discussion

Aortic valve stenosis is the most widely prevalent valvular disease in the ageing population. Surgical valve replacement is the standard of care for both symptomatic and prognostic aspects; however, the conventional surgical approach is associated with an increased peroperative risk for those patients who present with pre-existing comorbidities.[1–3] For the high peroperative

risk population, an alternative was first provided by Cribier at al. in 2002; a transcatheter aortic valve was implanted following balloon valvuloplasty.[4] Hence, this approach is using a minimal access, either through the femoral artery or the apex of the heart; in case of an emergency, further salvation steps are also limited. Furthermore, previous heart surgery results in significant mediastinal adhesions; therefore, an urgent sternotomy during profound haemodynamic instability is not feasible. A femoral artery cannulation is - even without pre-existing severe peripheral vascular disease - a time-consuming technical challenge during resuscitation in a frail patient; the already exposed heart apex offers an excellent arterial inflow target in this extreme situation. The safety of transapical aortic cannulation has already been proven by Wada et al.[5] in a large number of type A aortic dissections although, in these patients, the set-up and the surgical control is not as much limited. We describe a case that illustrates the feasibility of transapical arterial cannulation by crossing a newly implanted TAVI valve in order to establish an emergency bypass circuit. This approach can provide nearly immediate circulatory support in a hybrid theatre and show an alternative for these high-risk patients as a bridge-to-recovery.

Declaration of Conflicting Interest

The authors declare that there is no conflict of interest.

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IX

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BENTHAM SCIENCE

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CASE REPORT

An Aortic "Supravalvular Shelf" is Not Always Innocuous

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Abstract:

Supravalvular aortic stenosis is a rare cause of secondary aortic root distension and/or aortic valve regurgitation. Non-syndromic aortic aneurysms may also occur in young adults and can develop silently, representing an asymptomatic, life-threatening condition. Clinicians should, therefore, be alert to the possibility of this uncommon, but potentially serious disease, often first revealed by an imaging modality requested for other indications, even in case of an established, more benign diagnosis.

Keywords: Aortic valve, Supravalvular membrane, Chronic, Aortic dissection, Aortic root.

1. INTRODUCTION

Supravalvular aortic stenosis is a rare congenital cardiac anomaly characterised by a variable degree of left ventricular outflow tract obstruction, originating from just above the aortic valve. Although the proximal aortic root is not primarily involved, it may show secondary pathological changes leading to the development of aortic valve regurgitation and/or coronary ischaemia. Thickening of the tunica media in the aortic wall secondary to excessive collagen deposition and hypertrophied smooth muscle cells leads to the build-up of the obstructive membrane in cases of supravalvular stenosis [1, 2].

Non-syndromic aortic aneurysms are also deemed uncommon in comparison to other cardiovascular conditions in young adults, and may represent an asymptomatic, life-threatening condition. Therefore, clinicians should be vigilant in the evaluation of patients, as aneurysms are often first detected incidentally on imaging requested for other indications. Any evidence of an enlarged aorta should trigger further investigations; awareness of aortic aneurysms facilitates the reduction of morbidity and mortality associated with this pathology [3 - 5].

2. CASE DESCRIPTION

We report the case of a 26-year-old woman who collapsed during her university exam. Her medical history was significant only for morbid obesity (body-mass index of 62

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kg/m^2). Echocardiography on admission diagnosed severe aortic valve regurgitation with a dilated aortic root and a supravalvular membrane above both the right- and left coronary cusps of the aortic valve (Fig. 1; Panels A, B). Surgical correction was recommended, however the patient refused to undergo surgery.

One month later, she was re-admitted with acute pulmonary oedema secondary to cardiac decompensation to our hospital. On physical examination, a faint, soft, decrescendo murmur was detected in the second intercostal space, on Erb's point, in addition to the bilateral crackles up to the mid-pulmonary zones. Routine blood sampling did not reveal any major pathological changes except mild hypokalaemia and mild iron deficiency anaemia. Chest X-ray showed a bovine heart without any further concomitant pathologies. In addition to the known severe aortic regurgitation, a DVT was diagnosed by ultrasound of the left calf, and a chest CT performed to assess for possible PE. Further to a segmental pulmonary embolus within the right upper lobe artery, CT measured a 55 mm aortic root diameter, and a structure consistent with either the supraaortic membrane considered previously from the echo, or the differential diagnostic possibility of a dissection flap was seen (Figure 1; Panel C). No further flaps or false lumen were visible, and the mid-ascending aorta demonstrated a diameter within the normal range. The peak gradient through the aortic valve measured 11 mmHg with a peak velocity of 163 cm/s on Doppler investigation. The aortic regurgitant radius was 1.1 cm, EROA 0.48 cm^2, regurgitant jet pressure half time measured 102 ms. The right ventricle was mildly dilated with

normal systolic function and a moderated pulmonary hypertension was registered.

Intravenous heparin was commenced as a treatment for the PE, and the patient underwent a biological aortic root replacement as part of a Bentall-procedure with a preformed 29 mm xenograft (Medtronic Freesytle®, Minneapolis, USA) one week later. The flap containing ascending aorta was resected, which appeared to be rather a localised chronic TAAD (Figure 1; Panel D) than a supravalvular shelf lesion on a visual inspection and was replaced by an interposition tube graft.

Histopathology revealed nodular myxoid degenerative changes in the aortic valve, focal myxoid degeneration and fibrosis of intima and media, with focal cystic medial degeneration in the resected aortic wall segment. There was no evidence of hemorrhage in the vessel wall.

After a short recovery period, the patient was discharged on anticoagulation for the PE and with advice to undergo genetic testing for consideration of hereditary connective tissue disease; the latter was refused by the patient.

3. DISCUSSION

Aortic aneurysms are exceptionally uncommon in young adults and are often asymptomatic, and first discovered incidentally. Surgical solution for younger patients should be more radical than for the elderly TAAD population, to achieve reliable long-term outcomes. More extensive involvement of proximal and distal aorta, myocardial ischaemia and syndromic connective disorders characterise younger patients. Intimal tears localised in the aortic root are also more common at the lower age of presentation. Besides the well known syndromic connective tissue disorders and bicuspid aortic valve, non-syndromic familial thoracic aortic aneurysms are discovered in 20% of cases in diagnosed thoracic aneurysms and represent genetically heterogeneous disorders. Mutations in five genes (MYH11, TGFßR1, TGFßR2, MYLK, and ACTA2) have been identified so far with all autosomal dominant inheritance in these cases. From a molecular point of view, consequences of genetic alterations translate into a degenerative remodelling of the aortic medial extracellular matrix resulting in progressive loss of elastic properties. Clinical, anatomical, genetic and molecular evidence suggests that the prevalence of inherited aortic wall disorders in young people presenting with aortic complications is probably higher than expected and diagnosed [6]. Therefore, genetic testing for hereditary aortopathies is essential in young patients having aortic aneurysms.
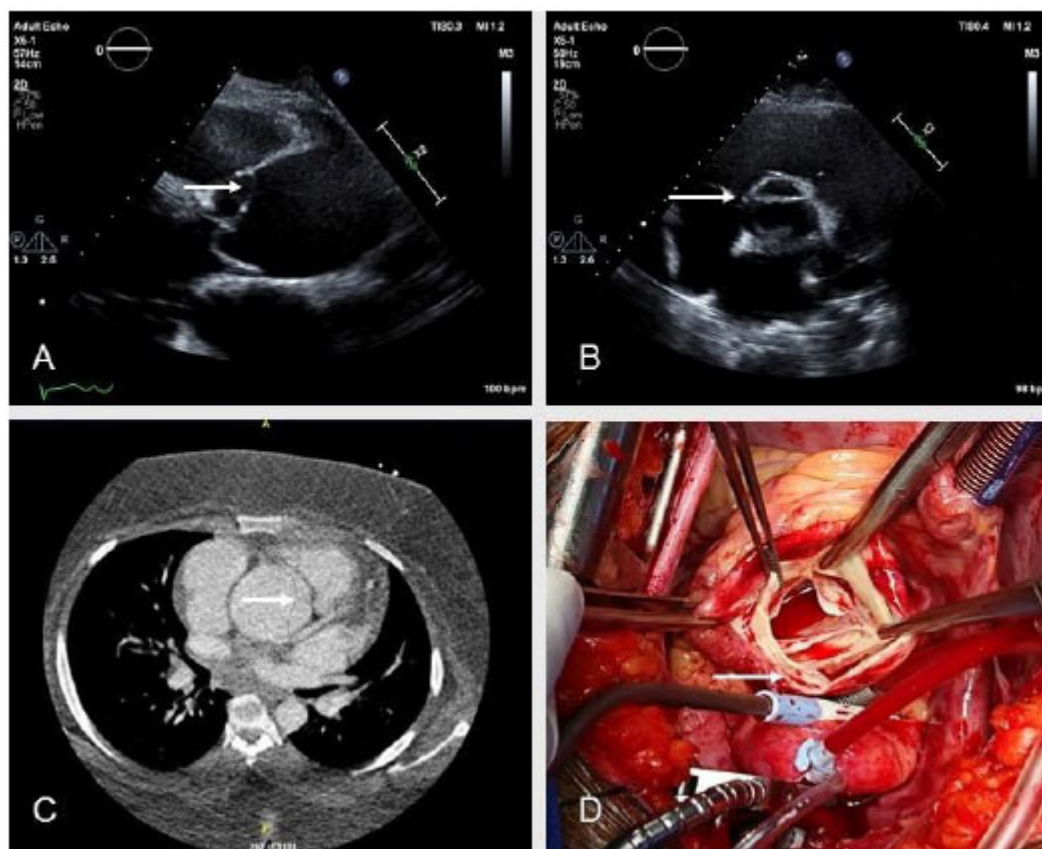

Fig. (1). Chronic aortic dissection; pre- and intraoperative views.
Panel A – Parasternal long axis echocardiographic view; arrow points on supravalvular flap
Panel B – Parasternal short axis echocardiographic view; arrow marks supravalvular flap
Panel C – Chest computed tomography at level of left main stem; arrow highlights the flap
Panel D – Intraoperative view of chronic aortic dissection; arrow shows the flap

Our patient had been treated with an intravenous heparin infusion for a DVT discovered incidentally on admission. In cases of a chronic TAAD, heparin does not pose any significant risks as strong connective tissue stabilises the aortic wall lesions. Nevertheless, in acute TAAD heparinisation may lead to fatal complications, including exsanguination from a covered aortic rupture or rapidly developing pericardial tamponade. Therefore, it is essential to distinguish between the symptoms and signs of the acute coronary syndrome and TAAD whenever possible.

LIST OF ABBREVIATION

DVT	=	Deep venous thrombosis
CT	=	Computed tomography
PE	=	Pulmonary embolism
TAAD	=	Type A aortic dissection

AUTHOR CONTRIBUTIONS

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CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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