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Case Study

Incidence, mechanism and prevention strategies for spinal cord ischaemia in thoracic endovascular aortic repair (TEVAR)

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Key Learning Points
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Spinal cord ischaemia is a known and devastating complication of both open and endovascular thoracic aortic surgery. This case study reports the development of postoperative non-reversible spinal cord ischaemia (SCI) in a patient who underwent an emergency thoracic endovascular aortic repair (TEVAR) for a complicated type B aortic dissection. The patient developed SCI despite prophylactic cerebrospinal fluid drainage peri-operatively, which is recommended by the European Society of Cardiology when performing TEVAR in 'high risk' patients.

This reports aims to highlight the incidence of spinal cord ischaemia following both open thoracic aortic surgery and TEVAR. Evidence from anatomical and animal models will be used to explore the evidence in the literature to identify potential risk factors for the development of spinal cord ischaemia in patients undergoing TEVAR. The report aims to illustrate a number of prophylactic measures that exist, based on these models, to protect spinal cord perfusion during TEVAR. The report will focus primarily in the use of prophylactic cerebrospinal fluid drainage to maintain spinal cord perfusion. Data will be used to explore whether hypotheses and measures extrapolated from these anatomical and animal models predict and reduce spinal cord ischaemia after TEVAR in clinical practice.

Overall, the study concludes that SCI is multi-factorial in origin. Despite the extensive studies, the optimum criteria to identify high risk cases and the optimum measures to reduce incidence of SCI following TEVAR remains unclear. This is due to conflicting data that exists in the medical literature. One of the major challenges with studies on TEVAR, remains the heterogeneity of the patients and the conditions TEVAR is used to treat, which can include acute and chronic aortic dissection, aneurysmal disease and trauma.

Introduction

Thoracic endovascular aortic repair (TEVAR) involves the placing of a stent-graft introduced via a distal artery to treat a variety of problems affecting the aorta. Here we will consider a patient admitted with a complicated type B aortic dissection (TBAD) and who, following this procedure, became paraplegic as a result of spinal cord ischaemia (SCI). We shall discuss the incidence of SCI with TEVAR; the mechanisms by which TEVAR produces SCI; and, how based on this understanding we might best prevent such a devastating complication. In particular, we shall focus on the role of cerebrospinal fluid drainage in protecting against ischaemia, as was used in this patient.

Case history

The 67-year-old male patient was admitted with sudden onset severe left upper back pain and shortness of breath. This had started the day prior to admission but had since worsened. On examination, he was pale and clammy, and the blood pressure (BP) was initially recorded at 73/45 mmHg. The patient was additionally found to have stage 1 acute kidney injury.

His symptoms were found to be a result of a ruptured TBAD that had produced bilateral haemothoraces (Figure 1) and for which he received emergency TEVAR. The dissection was identified on CTA as arising from just beyond the left subclavian artery (LSA) (Figure 2) and extending to the bifurcation of the aorta and into the left common iliac artery. The coeliac, superior mesenteric and renal arteries were supplied by the true lumen.

There was minimal blood loss during the operation and no intraoperative hypotension, with the lower limbs described as well-perfused throughout and no reported obstructions to major vessels. The main body of the stent-graft [36 mm x 161 mm Cook Zenith Alpha™] for the descending aorta was introduced via the right common femoral artery and the 37 mm x 150 mm GORE TAG™ top

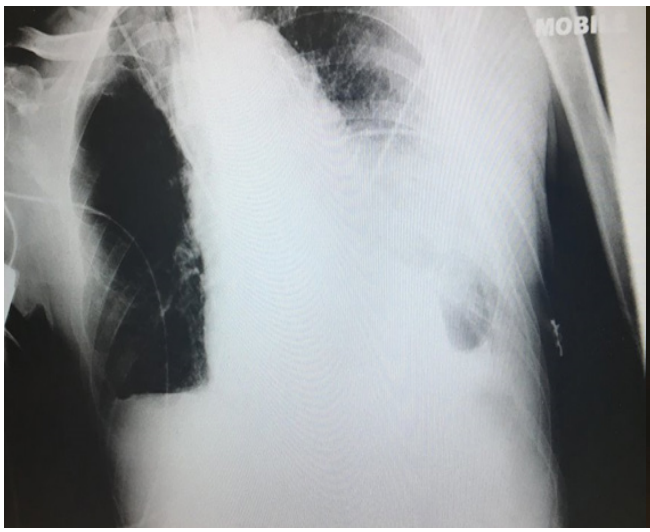

Figure 1: AP chest radiograph taken on admission illustrating bilateral haemothorax (bilateral costophrenic angle loss with menisci), mediastinal bleeding and left lung haematoma.

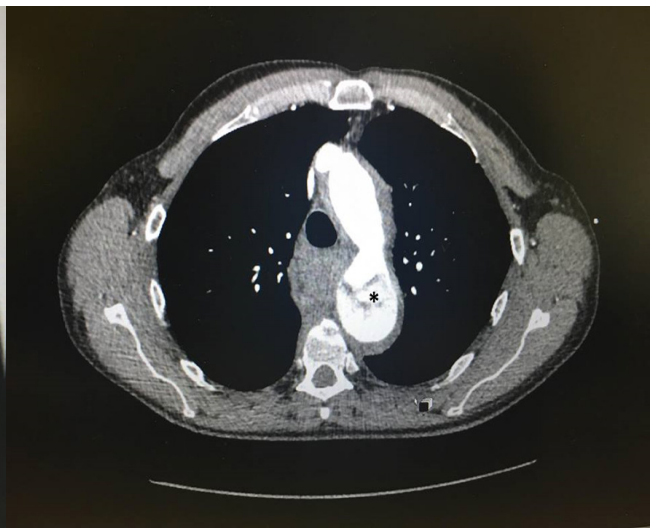

Figure 2: CT illustrating the entry tear (marked with asterisk) in the aortic arch.

piece was placed at the origin of the LSA (Figure 3). The procedure was performed with good final angiographic results, digital subtraction angiography (DSA) showing the stent extending from the LSA origin to just above the coeliac origin.

Perioperative prophylactic measures were taken to reduce the incidence of SCI. This included the use of prophylactic cerebrospinal fluid (CSF) drainage via a spinal drain. The drain was inserted pre-operatively, and the following 24-hour protocol was followed with a regimen of 20 mL/hour CSF drainage for the first 4 hours, followed by 10 mL/hour thereafter. Noradrenaline was used to maintain a high target mean arterial blood pressure (MABP) during the procedure. Despite these measures, the patient developed bilateral lower leg weakness post-operatively (power 0/5 bilaterally) on waking from anaesthesia. Neurological examination identified a loss of reflexes at the right knee and ankle but both were preserved on the left; the patient also reported some sparing of sensation. A subsequent magnetic resonance imaging (MRI) of the spine identified an ischaemic spinal cord, showing T2-hypersensitivity of the central grey matter, from T5 to the conus. Incidentally, the patient was also separately noted to exhibit Grey Turner's sign, indicative of retroperitoneal haemorrhage.

The patient was, understandably, extremely upset but was thankful, being a guitar-player and artist, that his hands had been spared. Unfortunately, the SCI also meant that he would be doubly incontinent as well as impotent. As a young man, the patient had had several spontaneous pneumothoraces to which he compared the pain of the dissection. Patient was known to have a diagnosis of mild chronic obstructive pulmonary disease (COPD) and was a current smoker. He underwent a radical prostatectomy in 2017, but otherwise had no other outstanding medical history.

As well as pain management, the patient was placed on the following antihypertensive regime post-operatively to maintain a systolic BP ⩽ 130 mmHg: labetalol (200mg; twice daily); ramipril (2.5mg; twice daily); and, amlodipine (10mg; once daily). Aspirin (75mg; once daily) was also added as part of medical management to reduce cardiovascular disease risk. The patient was subsequently transferred to the specialist spinal rehabilitation unit at Stoke Mandeville Hospital, Aylesbury, for extensive specialist spinal rehabilitation.

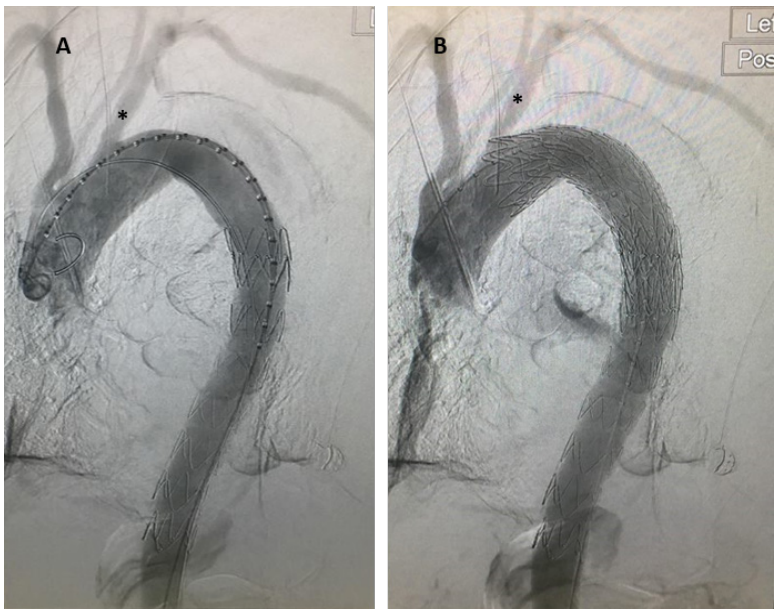

Figure 3: Digital subtraction angiography of stent placement; [A] after insertion of body, and [B] top piece. The left subclavian artery is marked by an asterisk.

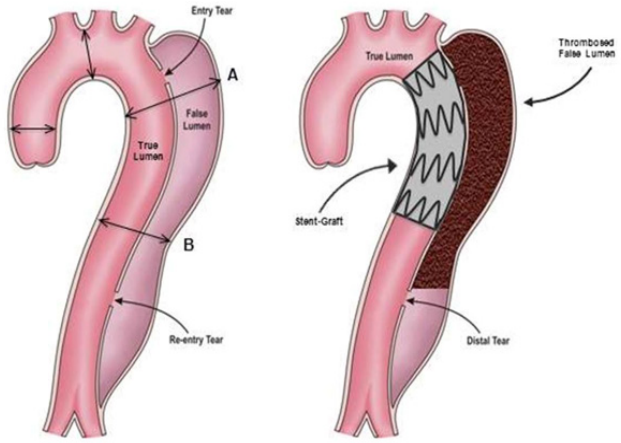

Figure 4: Illustration of TEVAR. TBAD does not implicate the aortic valve (left). An endoprosthesis or 'stent-graft' is used to seal the entry tear into the false lumen; the result is that the true lumen is reconstructed with thrombosis occurring in the false lumen (right).[2]

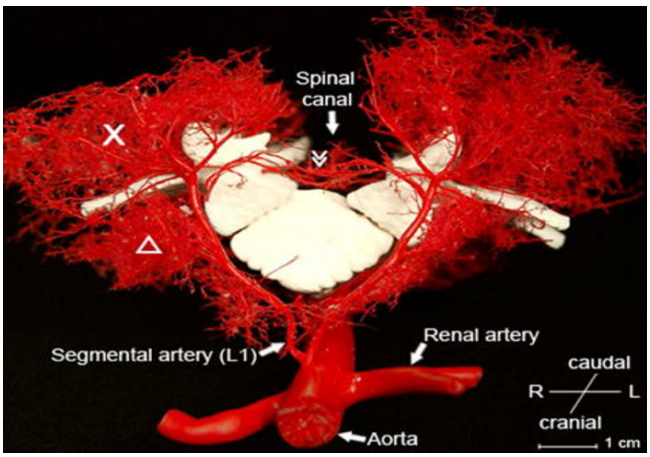

Figure 5: Anatomical study of the collateral network supplying the spinal cord in a porcine model. '>>' indicates the anterior spinal artery. Etz et al. 2011

An introduction to TEVAR

An aortic dissection is a potentially life-threatening condition that occurs when a tear forms in the wall of the aorta. A Stanford type B or DeBakey III dissection originates in the descending thoracic aorta (distal to the LSA) without retrograde expansion into the ascending aorta.[1] Acute TBADs are classified as either uncomplicated or complicated. Complicated refers to signs of rupture, organ malperfusion, continuous pain (despite adequate analgesia), or haemodynamic instability.[1] There are major differences in treatment between the two types. The management of uncomplicated TBAD has traditionally been non-invasive, aggressive medical therapy focusing on tight blood pressure control. The management of complicated TBAD involves surgical intervention, via either open or TEVAR procedure, in order to cover the proximal entry tear, improve perfusion, and obtain false lumen thrombosis to allow for aortic remodelling (Figure 4).

A meta-analysis by Moulakakis et al.[1] looking at 2,531 patients with acute complicated TBAD treated with TEVAR obtained pooled estimates for the incidence of cerebrovascular events, SCI and total neurologic events, which were 3.9%, 3.1% and 7.3% respectively. The authors also produced pooled estimates for these same categories for 1,276 patients who had undergone open surgical repair for acute complicated TBAD; these stood at 6.8%, 3.3% and 9.8% respectively. This study suggests that the incidence of post-operative SCI is low in both endovascular and open intervention, but that the risk is likely lower with TEVAR.

Mechanisms of spinal cord ischaemia: potential risk factors

To understand SCI, we need to understand the blood flow to the spinal cord and how this might be disturbed during surgery. We might reasonably expect that such high percentage coverage of the aorta by stent as in our patient's case [~310 mm] predisposes to a high individual risk of SCI.

Historically, it was believed that the artery of Adamkiewicz, typically arising from a left intercostal artery, played a key role in supplying blood to the anterior spinal artery. This view has been superseded by a collateral network theory of spinal circulation set out by Griepp and Griepp in 2007[3] who put forward the following key principles:

1. That there exists a network of small arteries in the spinal canal and in the peri- and para-vertebral tissues that anastomose with each other;
2. Inputs into this network include the left subclavian and the hypogastric [internal iliac] arteries as well as the segmental [lumbar and intercostal] arteries, giving four 'independent vascular territories'[4] supplying the spine; and,
3. This network can increase cord nutrient flow from one of these territories when another is reduced. Conversely, cord nutrient flow can be 'stolen' by demand if a low resistance pathway is opened up in this collateral network, starving the cord.

This is supported by anatomical studies by Etz and Griepp[5] in a porcine model, which detail this network (Figures 5 and 6).

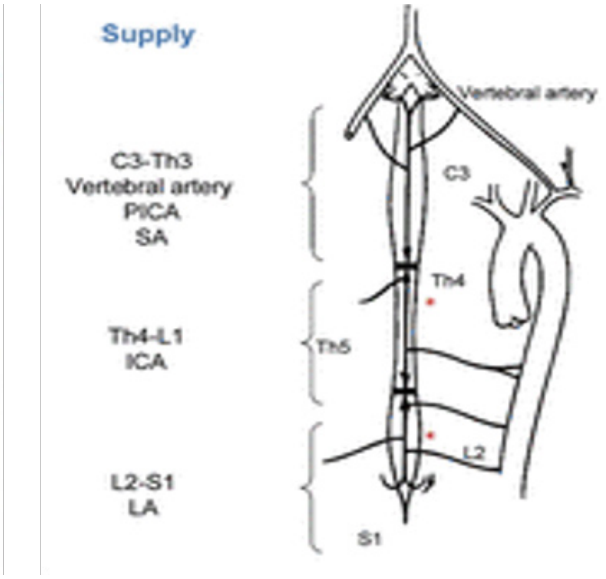

Figure 6: Illustration depicting some of the different vascular territories: LA = lumbar arteries; ICA = intercostal arteries; LSA supplies the vertebral artery. Etz et al 2015[6].

Importantly, this hypothesis explains why extensive coverage of intercostal arteries by a thoracic stent-graft is rarely associated with symptomatic SCI, hence, the low incidence seen in the literature. Therefore, the length of the stent is potentially irrelevant provided we are only sacrificing a single vascular territory. In support

of this Eagleton et al.[7] found that 17/1251 (1.4%) patients who underwent endovascular repair of aortic aneurysms between 1998 and 2010 developed immediate symptomatic SCI. For these patients, the only factor associated with early onset of symptoms was the presence of at least one collateral bed occlusion (p = 0.021*). The authors found no link between percentage aortic coverage by the stent and incidence of SCI. They classified 'one occlusion' as an occlusion of either a single hypogastric (internal iliac) or subclavian artery. Segmental patency was not assessed in this study.

Although there are a large number of patients considered in Eagleton's study, the sample size of affected patients is very small at only 17. This is a major limitation. The finding of no association between aortic coverage and SCI is in contrast to the link reported by Feezor et al.[8] This study showed that patients with permanent SCI (n = 33) had a greater absolute (260.5 ± 40.9 mm versus 195.8 ± 81.6 mm, p = 0.002***) and proportionate (88.8% ± 12.1% versus 67.6% ± 24.0%, p = 0.001***) length of aortic coverage compared to patients without permanent SCI (n = 208).

In the case reported in this study, the intercostal arteries [single territory] will have been extensively covered but as the stents extend from the LSA to the coeliac trunk. The lumbar arteries will have been spared as the acute stenting did not extend beyond the coeliac axis. However, the aortic dissection may have disrupted the flow through the internal iliac and lumbar territories. This in conjunction with the loss of patency of intercostal arteries from stenting could result in the procedure tipping the spinal cord into a state of ischaemia. This raises the potential questions of how much of the spinal cord circulation is expendable and how residual are the territories supplying the spinal cord?

It has been hypothesised that simultaneously closing at least 2 of these independent vascular territories and / or prolonged hypotension, which will reduce perfusion from all vascular territories, may be associated with SCI after TEVAR.

To assess this, a risk model was applied to the EuREC (European Registry of Endovascular Aortic Repair Complications) database, focusing on 38 patients with post-TEVAR symptomatic SCI.[4] Direct correlations were seen between the occurrence of symptomatic SCI and both prolonged intraoperative hypotension (Positive Predictive Value = 1.00, p=0.04*) and simultaneous closure of at least 2 independent spinal cord vascular territories (PPV = 0.67, p=0.005***). The combination of prolonged hypotension and simultaneous closure exhibited the strongest association (PPV = 0.75, p<0.0001***) of all the risk factors assessed. In contrast, previous closure of a single vascular territory (for example, from a previous endovascular repair) was not associated with an increased risk of SCI. This stands in contrast to previous findings[9] which associated SCI with a history of previous aortic repair. The patient in this report had no relevant history of previous aortic repair and, therefore, these findings may not apply to this particular case but may be relevant identifying patients at higher risk of developing SCI. Furthermore, Feezor et al.[8] found that neither the patency of the hypogastric (internal iliac) arteries nor of the LSA were associated with SCI.

With regards to the status of the LSA in our patient, the proximal landing zone of the stent must securely cover the primary entry tear site, meaning that the covered portion of the stent must commence proximal to the entry tear. As a result of the proximity between LSA origin and tear, the stent had to be positioned at the origin of the LSA. Angiographic images (Figure 3) during the procedure and at the end of the procedure indicated that LSA perfusion was preserved throughout the procedure. If the LSA is shuttered or covered during the stenting procedure, the artery can be revascularised by creating a carotid-subclavian bypass, using the left common carotid artery, or endovascularly by placing a chimney stent from the arch of the aorta into the LSA. Prophylactic pre-operative LSA revascularisation in such cases to prevent SCI is not routinely performed in emergency cases.

Overall, the exact mechanism of SCI after TEVAR remains unclear but is probably multi-factorial. The evidence would suggest that TEVAR covering of multiple vascular territories (such as the LSA, intercostal and lumbar arteries) or compromise to the internal iliac arteries from existing peripheral vascular disease or previous aortic or iliac surgery may contribute to the development of SCI. The association between stent length and SCI risk remains controversial. Importantly, peri-operative fall in MABP, for example from the rupture in this report or due to anaesthesia, will lead to global or systemic hypoperfusion of all the spinal cord territories. Therefore, hypotension is likely to be another potential factor in the development of SCI in patients undergoing TEVAR for TBAD. This may be a major contributing factor in the case reported here, given that the patient's MABP on admission was low and it is difficult to assess how prolonged that period of hypotension had been prior to admission.

Lastly, a number of studies have identified COPD as an important predictor of SCI after TEVAR;[18] and this association has been postulated to be due to compromised oxygen kinetics. However, it is beyond the scope of this case report and will not be considered further.

Prophylaxis for SCI

Discovering the mechanisms and risk factors behind SCI, allows for the introduction of prophylactic measures to protect the spinal cord during surgery and mitigate from patients developing SCI.

Many methods to prevent SCI developing have been suggested in the literature, but we can broadly group these into three categories:

1. Minimising anatomical disruption to blood supply (e.g. carotid-subclavian bypass for revascularisation);
2. Maintaining perfusion pressure gradient in the collateral network (includes increasing MABP and prophylactic CSF drainage (CSFD)); and,
3. Reducing metabolic needs of the tissues [systemic hypothermia].

This report will focus on the use of CSFD, which was performed in this case. The basis for CSFD is that spinal perfusion pressure is the difference between the MABP and the CSF pressure. It has been shown in animal models10 that reducing CSF pressure leads to an increase in spinal cord perfusion pressure, suggesting that SCI may be ameliorated through use of CSFD.

Furthermore, the efficacy of perioperative CSFD in open thoracic aortic repair in humans has been investigated in three randomized trials [Crawford et al. 1991;[11] Svensson, 1998;[12] Coselli, 2002[13]]. The results from these are conflicting, however two showed a significant protective effect, with a reduction in SCI incidence of up to 80%.

The extent to which this evidence can be extrapolated to the endovascular management of aortic disease is unclear. However, a systematic review by Wong et al.[14] has looked at whether preoperative CSFD reduces

SCI after TEVAR procedures. However, of importance is that the use of TEVAR in this large systematic review was not limited to TEVAR in TBAD. The authors identified 46 eligible studies, involving 4,936 patients. The incidence of SCI was 3.89%, in keeping with the findings of Moulakakis. Series reporting routine prophylactic drain placement or no prophylactic drain placement reported pooled SCI rates of 3.20% and 3.47%, respectively. Therefore, this would suggest that there is minimal benefit in prophylactic CSFD. However, it is difficult to draw conclusions from this review as considerable heterogeneity exists among the included studies. The studies used mixed emergency and elective patients undergoing a range of thoracic aortic procedures, with stents covering a range of aortic lengths, and were used to treat a variety of different aortic pathologies, including aneurysmal disease, acute and chronic aortic dissection, and traumatic disruption of the aorta. Attempting to refine the sample to only include patients with TBAD, would have been difficult without individual patient level data which was not available to the authors at the time of the systematic review. A more recent review comes from Dijkstra et al. [2018][15], which analyses 43 studies. The pooled post-TEVAR permanent SCI estimate was 1.0% [4/310] for prophylactic CSFD usage versus 2.1% [3/118] for no CSFD. However, if one looks at the studies using selective drainage for high risk patients only, the pooled SCI incidence appears bizarrely to be higher compared to when no drainage is used. The authors concluded that 'no definitive recommendations' can be made regarding the use of prophylactic CSFD in TEVAR to mitigate SCI.

In this case report, CSFD was used in conjunction with a vasopressor, noradrenaline, to improve spinal cord perfusion pressure by increasing MABP and decreasing CSF pressure to maximise spinal cord perfusion. Of note most adjuncts are rarely used in isolation, and the majority are used in different combinations. This further adds to the heterogeneity of the sample and creates difficulty when attempting to assess the effect of prophylactic CSFD in TEVAR for complicated or acute TBAD.

Importantly, it is recognised that the use of CSFD can itself lead to complications. Commonly reported complications include infection and spinal bleeding. CSFD can also cause intracranial hypotension which can lead to acute intracranial bleeding, subdural haemorrhage (SDH). This is due to the enlargement and rupture of venous sinuses or veins.[16] Thus, even before assessing the role of CSFD in reducing SCI, the risks of CSFD must be taken into account. Song et al.[17] consider such complications, none of which were reported in our patient's case. In their series of 81 patients, 23 (28.4%) developed CSFD-related complications. The majority of patients recovered quickly with the exception of one patient who required surgery for SDH. Although the complication rates seem high, the study included minor complications such as mild headaches and pain from the spinal drain. In this small cohort of patients, two patients (2.5%) developed SCI despite the prophylactic use of CSFD. In contrast, among the patients who did not receive pre-operative prophylactic CSFD, only one developed SCI (1.2%). The study suggests that CSFD may have little benefit in reducing the incidence of SCI, but worryingly that it may expose patients complications arising from its use.

However, it should be noted that prophylactic CSFDs were only used in patients classified at 'high risk' of perioperative SCI. Therefore, the analysis had an inherent bias as patients who received CSFD were more likely to be predicted to develop SCI in the first place.

The current guidelines on SCI prevention with TEVAR set out by the European Society of Cardiology recommends the selective drainage in 'high-risk' patients. Criteria for classifying patients to be 'high-risk' remain unclear given the variety of conclusions drawn from numerous heterogenous studies as discussed in this report. For most of the hypothesised risk factors, based on animal or anatomic models, there are conflicting results. However, it is postulated that these risk factors include long segment aortic coverage (>200mm) and emergency admission.[15] This would include the patient discussed in this report. Dijkstra[15] notes that there is 'no generally accepted uniform algorithm to determine when a patient is 'high risk'. Overall, the level of evidence for these recommendations, as considered above, is low.

Conclusions

SCI is a rare but potentially devastating complication of endovascular repair. It is of likely to be multi-factorial in origin and it is estimated to occur in approximately 1-3 % of patients who undergo TEVAR for acute complicated TBAD. The literature does not entirely clarify what the potential risk factors for the development of SCI following TEVAR are, given the conflicting evidence from the studies. The data also remain unclear as to whether prophylactic measures are useful in preventing SCI following TEVAR. Considerable debate persists around the use of CSFD not only because of a lack of robust evidence for its supposed protective effects but because it can produce severe complications in its own right.

Conflicts of interest

None.

Funding

None.

Consent

The patient has consented to the publication of this case study.

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