## Treatment related differences in the incidence of spinal cord ischemia should be discussed during shared decision-making with fit patients planned for complex abdominal aortic aneurysm repair

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Endovascular aortic repair (EVAR) has been increasingly used for the treatment of complex abdominal aortic aneurysms (cAAA). Mortality is among the most commonly reported primary outcomes in studies comparing open surgical repair (OSR) with EVAR1. It is often used as the main proxy when it comes to shared decision-making between the clinician and the patient and sometimes drives the decision towards the endovascular repair. However, other important outcomes, such as the rate of spinal cord ischemia (SCI) are rarely highlighted and are usually overlooked. A recent review study<sup>2</sup> has found that EVAR was associated with lower 30-day mortality, but increased SCI during juxtarenal aortic aneurysm repair. In another recent review<sup>1</sup>, the authors did not detect significant association of surgical modality with the incidence of SCI, while a lower, but not statistically significant, peri-operative mortality after EVAR was found after fenestrated or branched repair for cAAAs. However, the first study<sup>2</sup> was not designed to specially focus on SCI, while studies with zero events in both treatment arms did not participate in the meta-analysis. Moreover, the second meta-analysis<sup>1</sup> reported outcomes on all types of Crawford classification thoracoabdominal aneurysms, while finally only two studies investigating SCI were deemed suitable for the SCI meta-analysis, based on the strict inclusion criteria of propensity score matched populations or adjusted regression models.

In light of these conflicting results concerning SCI rates after EVAR and OSR, we conducted a hypothesis-driven meta-analysis to specifically test for SCI rate difference between EVAR and OSR after treatment for cAAAs, namely suprarenal, juxtarenal, pararenal and Crawford type IV thoracoabdominal aneurysms. A systematic review of all published comparative studies on SCI was performed, including single and both-armed zero-event studies, and Crude rates and pooled

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Odds Ratios (ORs) with 95% Confidence Intervals (CIs) were appropriately calculated. A total of 8 studies <sup>1, 3-9</sup> (Figure 1), with 2,819 patients, including 2,156 patients treated with OSR and 663 patients treated with EVAR, were finally included. The endovascular cohort presented with higher rates of hypertension (75% vs 58.3%, p<0.001), hyperlipidemia (48.0% vs 37.2%, p<0.001), coronary artery disease (34.1% vs 14.6%, p<0.001), chronic obstructive pulmonary disease (COPD) (29.1% vs 17.6%, p<0.001) and chronic kidney disease (17.9% vs 10.2, p<0.001%), compared to patients treated with OSR (Figure 1). In addition, only 4.2% of patients who underwent endovascular repair were American Society of Anaesthesiologist (ASA) score I, compared to 24.1% of the patients treated with OSR (p<0.001).

Crude SCI rate was more than four times more frequent after endovascular repair (11/621; 1.77%), compared to OSR (8/2,085; 0.38%). The meta-analysis on SCI rates also supported this finding and showed that EVAR patients were at higher risk for SCI, compared to OSR (EVAR vs. OSR: pooled OR =3.42, 95%CI: 1.41-8.30), p=0.001; Figure 1). On the contrary, pooling of the eligible studies showed that there was no difference in mortality between the two populations (OR:1.00, 95%CI: 0.64-1.56, p=0.99) with crude rates of 4.9% (106/2,156) for open vs. 4.1% (27/663) for the endovascular approach.

Our meta-analysis demonstrated that the endovascular cohort had a significantly higher burden of comorbidities, compared to OSR. We found that SCI rate was more prominent in patients with cAAAs who underwent endovascular, compared to open repair, while mortality remained the same. The higher rate of SCI in the endovascular cohort is likely related to the more extensive aortic coverage and higher number of fenestrations necessary, when compared to the length of the replaced aorta in the open repair group, for similar aortic aneurysm anatomy. Given that the endovascular cohort included sicker patients, it may be fair to consult prospective relatively young and fit patients with cAAAs, who are going to be submitted to complex aortic intervention, that the lower incidence of the catastrophic outcome of SCI should be a factor to be considered when they provide a preference between an open or endovascular intervention. Another topic of discussion is the higher potential for future re-interventions in the EVAR group<sup>1</sup>, which may carry significant morbidity, and that should also be weighted in a discussion with a patient regarding treatment selection. Interestingly, a recent study

Spinal Cord Ischemia Rates for Endovascular versus Open Repair of Complex Abdominal Aortic Aneurysms A hypothesis-driven meta-analysis 2,819 patients Hypertension Spinal cord ischemia Hyperlipidemia (SCI) rate **OPEN EVAR** CAD Odds Ratio 3.42 COPD (95% CI: 1.41 - 8.30, p=0.001) CKD **Favours OPEN repair ENDO** OPEN 663 2.156 Shahverdyan, 2015 Michel, 2015 % 94 0.97 [ 0.02, 4.81 [ 1.35, 50.36] 17.17] 88.5 89.9 0.86 0.66 1.14 0.3 Sala-Almonacii. 2017 3.29 [ 0.13, 82.61] 3.47 [ 0.14, 86.49] 1.04 [ 0.05, 22.63] 75.0 58.3 2.14 1.76 2.60 < 0.001 Deery, 2017 48.0 37.2 1.56 1.30 1.88 Manunga, 2018 2.50 [ 0.10, 62.27] 10.37 Fiorusci, 2018 8.49 [ 0.43, 166.47] 8.53 12.7 0.54 13.6 1.08 0.84 1.40 8 studies 34.1 14.6 3.03 2.48 3.71 < 0.001 3.42 [ 1.41, 8.30] Overall Test of 0, = 0; Q(7) = 1.69, p = 0.97 1.92 2.35 < 0.001 Test of  $\theta = 0$ : z = 2.72, p = 0.0110.2 < 0.001 17.9 1.93 1.52 2.47 Suprarenal EVAR patients were sicker, with >3 times higher risk for SCI, compared to OSR Juxtarenal **Pararenal** Crawford type IV SCI should be discussed during shared-decision making with fit and (cAAAs) young patients with cAAAs

**Figure 1.** Graphical abstract of methodology and results of hypothesis-driven meta-analysis for spinal cord ischemia (SCI) after EVAR and OSR for complex abdominal aortic aneurysms

Abbreviations: cAAA (complex abdominal aortic aneurysm), CAD (coronary artery disease), CI (confidence interval), COPD (chronic obstructive pulmonary disease), CKD (chronic kidney disease), EVAR (endovascular aortic aneurysm repair), OSR (open surgical repair), OR (odds ratio)

has failed to demonstrate cost effectiveness of endovascular repair over OSR in para/juxtarenal and infradiaphragmatic thoracoabdominal aneurysms and highlights the fact that open repair should be preferred in eligible patients. Moreover, the meta-analysis of propensity-score matched studies did not show a significant difference in acute kidney injury between endovascular and open repair for cAAA, which may further support the preference for open repair against endovascular treatment, especially in fit patients. Despite the retrospective nature of the included studies, as well as the small number of events in each treatment arm, it seems that patients' selection might help in identifying a cohort of those with cAAAs, who will mostly benefit from the open repair.

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