A Modern Theory of Spinal Cord Ischemia/Injury in Thoracoabdominal Aortic Surgery and Its Implications for Prevention of Paralysis

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PARAPLEGIA CONTINUES to be a devastating complication of open thoracoabdominal aortic aneurysm (TAAA) repair and endovascular repair of thoracic aortic aneurysm (TEVAR). Various strategies have been used to try to reduce the risk of paraplegia (Table 1). Statistical modeling of paralysis risk (observed/expected [O/E] ratios for paralysis) and animal experiments in an aortic occlusion model demonstrate that neuroprotective interventions reduce paraplegia after TAAA surgery. By applying data from the experimental literature and O/E ratios for paralysis calculated from clinical reports the authors proposed a theory of spinal cord ischemia in TAAA surgery that provides a foundation to explain how neuroprotective interventions reduce paralysis after thoracic (TAA) and thoracoabdominal aortic aneurysm repair.

MATHEMATICAL MODELING OF PARALYSIS RISK: O/E RATIOS OF PARALYSIS

Stanley Crawford, who performed more than 1,500 thoracic and thoracoabdominal aortic aneurysm repairs during his career, classified these aneurysms according to extent of aortic involvement.[1] The most extensive aneurysms, Crawford type I (CI) and type II (CII) thoracoabdominal aneurysms, have the highest paralysis risk because repair interrupts the most segmental arteries.[2] Without protective therapies, paralysis after elective repair of degenerative aneurysms is 10% in CI and more than 20% in CII aneurysms[1] (Era 1 in Figure 1). Published series confirm that the primary factors determining paralysis risk in TAAA surgery are extent of aneurysm, presence of dissection, and acuity of presentation.[1–4,5]

Considering percent paralysis alone in retrospective analyses can be very misleading because populations have different inherent risk based on the number of extensive aneurysms, the number of dissections, and acuity. To solve this problem, Acher developed a model of paralysis risk to calculate the number of expected deficits in a patient population based on extent of aneurysm, presence of dissection, and acuity of presentation. In the model, expected deficits (E) equals extent of aortic replacement by Crawford's classification times a risk coefficient for each Crawford-type aneurysm plus a factor for acute presentation and dissection.[6]

$$E = [0.1 \times CI + 0.2 \times CII + 0.05 \times CIII + 0.02 \times CIV + 0.01 \times TAA] + [0.3(\text{acute} + \text{dissection})]$$

The equation for the estimated number of deficits in any patient series is based on the number of patients with each Crawford TAAA-type aneurysm, the number of thoracic aneurysms, the number of acute presentations, and the number of dissections. Risk coefficients were inferred from Crawford's published results and represent treatment without neuroprotective adjuncts (but with intercostal artery reattachment).[6] The model was validated initially by testing it in 16 series that did not use neuroprotective measures, and the correlation coefficient was 0.997 ($r^2 = 0.994$) with Crawford's data and 0.927 ($r^2 = 0.859$) without.[6] When the model was tested with 1,881 patients from 32 additional reports, which also did not use neuroprotective adjuncts, the correlation coefficient was 0.9746 ($r^2 = 0.9499$) without Crawford's data.[7] The model predicted the expected number of paralyzed patients from clinical series that used Crawford's cross-clamp technique (XCL) or assisted circulation (AC) without any spinal cord–protective adjuncts and accounted for 95% of the variability among reports from different centers. The evaluation of the predictive ability of this formula in the second series of patients (1,881 in 32 reports) confirmed the strength and validity of the model.

The number of expected deficits calculated from the formula can be compared with the number of observed deficits in a population to calculate an Observed deficits/Expected deficits (O/E) ratio for paralysis.

Calculating the ratio of observed-to-expected deficits for paralysis (O/E ratio) is a much more informative way to evaluate paralysis risk in a population than percent paralysis because O/E ratio accounts for the inherent risk in the population (Fig 2).

Every published TAAA surgical series reports the number of each Crawford-type aneurysm (CI, CII, CIII, CIV TAAAs, and TAA), the number of dissections, and the number of patients operated acutely. The model can be used to calculate the expected deficits (E) that would occur in the population reported if no protective strategies were used, based on the numbers of each Crawford-type aneurysm, number of dissections, and number of acute patients. Every series also reports the number of patients with paresis or paralysis after repair (observed deficits). The observed (reported) number of deficits (O) is then used to calculate the ratio of observed paralysis (O) to expected paralysis (E). O/E ratios for all cited series and surgical techniques referenced here were calculated in exactly this way. The O/E ratio tells whether a surgical series has fewer or more deficits than expected. An O/E of 1 means a series has

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Table 1. Strategies to Protect the Spinal Cord in TAAA Surgery

Hypothermia
Spinal fluid drainage
High mean arterial pressure
Intercostal artery reimplantation
Pharmacologic adjuncts (papaverine, steroids, mannitol, free radical scavengers, excitatory neurotransmitter inhibitors, naloxone)

Abbreviation: TAAA, thoracoabdominal aortic aneurysm.

the expected number of deficits; an O/E of 0.5 means observed deficits are half the expected deficits.

The model can be used to calculate O/E ratios for individual series, and by combining the data from different series the model can be used to calculate O/E ratios for surgical technique (cross-clamp, assisted circulation, hypothermic circulatory arrest) and neuroprotective adjuncts (spinal fluid drainage and hypothermia). Using the model to evaluate results is much more informative than relying on percent incidence because the model describes the population risk mathematically and with better precision.

Average O/E paralysis ratios from all reports improved from Era 1, before 1998, before neuroprotective therapies were widely used, to Era 2, from 1998 until the present, as groups began to apply protective therapies routinely. In 2012 the best centers achieved the paralysis percentages seen in Figure 1 in the elective treatment of degenerative aneurysms.[8–13] This is in large part the result of applying interventions shown to be effective in animal experiments to clinical treatment and evaluating their effects.

Randomized controlled clinical trials are very difficult to accomplish in TAAA surgery because small patient numbers limit single-center studies, different institutional protocols and techniques limit multicenter studies, and ethical considerations limit randomized controlled trials in patients having high-risk surgery in which good results are being achieved with established protocols. Comparing O/E ratios for paralysis after thoracic and thoracoabdominal aortic surgery provides a useful tool to evaluate whether interventions are effective in more limited populations or pooled analyses.

PATHOPHYSIOLOGY OF SPINAL CORD ISCHEMIA AND INFARCTION

The results of experimental studies of spinal cord ischemia in animal models suggest that spinal cord injury after thoracic aortic occlusion can be explained by an ischemia-reperfusion injury that progresses to infarction. In the last 20 years experimental findings have been adopted clinically by centers performing TAAA surgery in an effort to reduce the ischemia produced during aortic clamping, unclamping, and replacement that leads to infarction and paralysis in TAAA surgery. Examination of the O/E ratios from these same clinical reports for paralysis indicates that interventions that prolong ischemic tolerance and improve spinal cord perfusion during clamping reduce paralysis risk in all series. Observing the reduction in paralysis that occurred after interventions shown to be effective

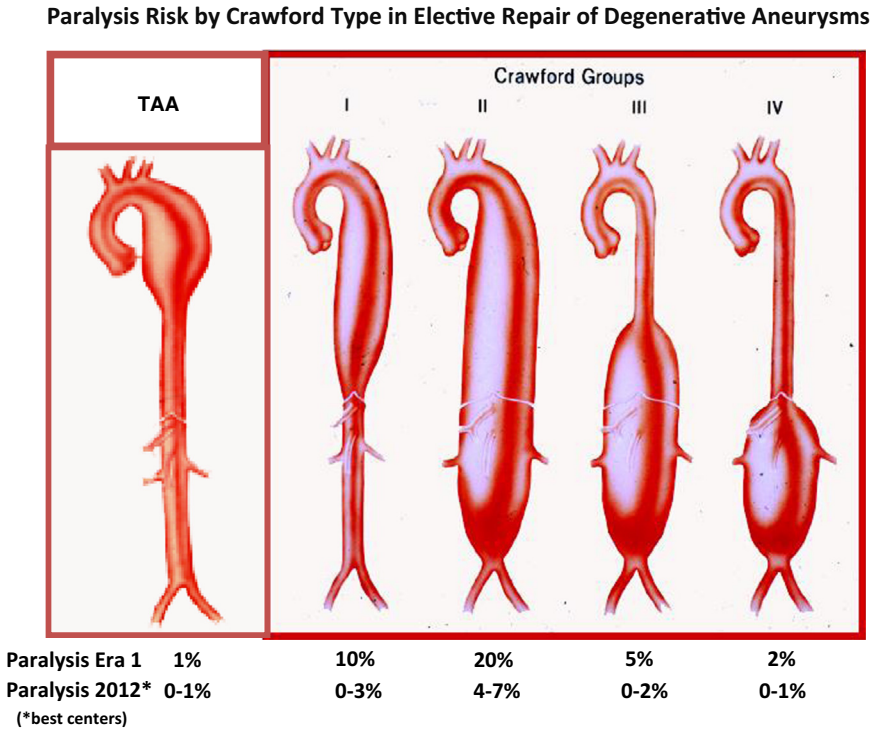

Fig 1. Crawford's classification of thoracoabdominal aortic aneurysms showing paralysis risk in the elective repair of degenerative aneurysms by Crawford type during Era 1[1] and in the best centers in Era 2.[8–10,12,13,98] (TAA involves the proximal third of the descending thoracic aorta. Crawford type-I TAAA involves the descending thoracic aorta from the subclavian artery to just above the celiac artery. Crawford type-II TAAA involves all of the descending thoracic aorta and all of the abdominal aorta from the subclavian artery to below the renal arteries, including the visceral arteries. Crawford type-III TAAA involves the distal third of the descending thoracic aorta and all of the abdominal aorta to below the renal arteries, including the visceral arteries. Crawford type-IV TAAA involves the visceral arteries and all of the abdominal aorta.) (Color version of figure is available online.)