Staged Approach Prevents Spinal Cord Injury in Hybrid Surgical-Endovascular Thoracoabdominal Aortic Aneurysm Repair: An Experimental Model

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Background. **In a porcine model, we investigated the impact of sudden stent graft occlusion of thoracic intercostal arteries after open lumbar segmental artery (SA) ligation.**

Methods. **After randomization into two groups, 20 juvenile Yorkshire pigs (27.1 ± 0.6 kg) underwent open lumbar SA sacrifice (T_{13}-L_5) followed by endovascular coverage of all thoracic SAs (T_4-T_{12}) at 32°C, either in a single operation (group 1) or in two stages separated by seven days (group 2). Collateral network pressure (CNP) was monitored by catheterization of the SA L_1, and postoperative hind limb function was assessed using a modified Tarlov score.**

Results. **The CNP in group 1 decreased to 34% of baseline, whereas CNP after lumbar SA ligation in group 2 fell to 55% of baseline (74 ± 2.4 to 25 ± 3.6 mm Hg vs 74 ± 4.5 to 41 ± 5.5 mm Hg; $p < 0.0001$). Subsequent thoracic stenting (group 2) led to another significant but milder drop ($p = 0.002$ versus stage 1) from the restored CNP (71 ± 4.2 to 54 ± 4.9 mm Hg). Five of ten pigs in group 1 suffered paraplegia, in contrast to none in group 2 (median Tarlov score 6, vs 9; $p = 0.0031$). Histopathologic analysis showed more severe ischemic damage to the lower thoracic ($p = 0.05$) and lumbar spinal cord ($p = 0.002$) in group 1.**

Conclusions. **These results underline the potential of the staged approach in hybrid procedures. Furthermore they highlight the need for established adjuncts for preventing paraplegia in hybrid and pure stent-graft protocols in which sudden occlusion of multiple SAs occurs.**

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Repair of thoracoabdominal aortic aneurysms (TAAA) represents a formidable challenge. The open surgical approach, although considered the gold standard because of its solid long-term outcome, is being questioned increasingly as new, technically very appealing endovascular treatment options become available. Total endovascular repair and hybrid repair involving debranching procedures may improve outcome in selected patients, particularly in those not suitable for conventional surgery because of their general condition or significant comorbidities [1, 2]. Although cardiopulmonary bypass, aortic cross-clamping, and dual-cavity exposure can be avoided in endovascular settings, reducing the insult to the cardiac and respiratory systems, the risk of spinal cord injury (SCI) still persists [3].

With endovascular techniques as with open surgery for TAAA, interruption of spinal cord blood supply from sacrifice or occlusion of segmental arteries (SAs) cannot be avoided. Thus, despite recent technical advances, paraplegia and paraparesis remain devastating complications after extensive aortic repair, jeopardizing postoperative quality of life and long-term survival [4].

Contemporarily, the risk of SCI in extensive open thoracoabdominal resections can be less than 5% if adequate adjuncts are used and optimal conditions for spinal cord perfusion are ensured [5–7]. The prerequisite for achievement of these results is a fundamental understanding of the spinal cord circulation. Recent anatomic studies have provided insight into the extensive collateral vasculature surrounding the spinal cord, and underline the notion that SCI in TAAA repair can be prevented by exploiting the physiologic capacity of this vascular network [8, 9]. Moreover, recently published clinical data suggest that a staged approach to extensive TAAA repair, based on utilizing the reserve capacity of the collateral network, can further reduce the incidence of SCI in humans [10].

In a chronic porcine model, the staged repair strategy has led to impressive results: open surgical sacrifice of all thoracic and lumbar SAs, if undertaken seven days apart, can be performed with no occurrence of paraplegia [11]. These findings confirm the hypothesis that the vascular

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Abbreviations and Acronyms

CNP	= collateral network pressure
KS	= Kleinman score
MAP	= mean arterial pressure
SA	= segmental artery
SCI	= spinal cord injury
TS	= Tarlov score
TAAA	= thoracoabdominal aortic aneurysm

remodeling necessary to restore an adequate spinal cord blood flow after extensive sacrifice of SAs may be a time-dependent process, requiring an interval of three to five days to develop.

In order to investigate the impact of extensive sudden SA coverage by endovascular stent-graft deployment on spinal cord perfusion, we used a setting designed in analogy to hybrid clinical repair of TAAA in our porcine experimental model: open lumbar SA sacrifice followed by endovascular stenting of the descending thoracic aorta. Based on the favorable experience with the staged approach in open surgical repair, one group of pigs underwent complete SA sacrifice with an interval of seven days between stages, while the control group had all SAs sacrificed in a single stage. The restoration of perfusion was documented by direct collateral network pressure (CNP) monitoring [12, 13]. The CNP monitoring, clinical outcome, and histopathology were compared between the groups.

Material and Methods

All animals received humane care in accordance with the guidelines from Principles of Laboratory Animal Care formulated by the National Society for Medical Research, and the Guide for the Care and Use of Laboratory Animals published by the National Institutes of Health. The Mount Sinai Institutional Animal Care and Use Committee reviewed and approved the protocol for this research.

Study Design

Twenty female juvenile Yorkshire pigs (about 3 months old; Animal Biotech Industries Inc, Danboro, PA), weighing 27.1 ± 0.6 kg, were randomized into two groups. Group 1 (n = 10) underwent complete thoracic and lumbar SA sacrifice under mild hypothermia (32°C) in a single operation. Group 2 (n = 10) underwent the same extent of SA sacrifice in two stages, both at 32°C, one week apart. Both groups had lumbar SAs sacrificed by open sequential clamping, whereas the thoracic SAs were simultaneously covered by endovascular stent graft deployment. Mean arterial pressure (MAP) and CNP were monitored by catheterization of the proximal and distal stumps of the transected L_1 segmental artery. Catheters were tunneled to the intrascapular area and postoperative patency was maintained with periodic heparin flushes. Blood pressures and arterial blood gas data were collected intraoperatively before clamping (baseline), immediately postoperatively (end), at one and five hours post-sacrifice, and then once daily for five days (Table 1). Hind limb function was evaluated daily for five days, using a modified Tarlov score [14]. Five days after complete SA sacrifice, all animals were euthanized. The spinal cord was harvested and analyzed by a neuropathologist blinded to the experimental group.

Stent Grafts

All stent devices were donated for research purposes by W. L. Gore & Associates, Inc (Medical Division, Flagstaff, AZ). To fit the thoracic aorta of the juvenile Yorkshire pigs used, the GORE EXCLUDER AAA Endoprosthesis was chosen. Two stents were placed in each animal (catalogue number: PXC141400 and PXC121200). Oversizing of 15% to 25% was used to prevent migration at deployment, and to achieve coverage of all thoracic SAs (n = 9, over an aortic length of about 20 cm). Anatomically, the covered area extended from 2 to 3 cm distal to the left subclavian artery to 1 cm proximal to the celiac axis, including all SAs from T_4 to T_{13}.

Perioperative Management and Anesthesia

The anesthesia techniques and medications during open lumbar SA sacrifice did not differ from the previous study [11]. The perioperative protocol differed during thoracic stenting, however: propofol alone was used, since the operation was considered less invasive and adequate pain medication had been given. Anesthesia was switched to 2% isoflurane to permit lowering of MAP to 70 mm Hg during stent deployment in order to avoid stent migration induced by the aortic pressure wave. Immediately after deployment, anesthesia was discontinued, allowing the pressure to rise to 90 mm Hg or higher.

Operative Details

The surgical technique of open lumbar SA sacrifice has previously been described in detail [11]. Briefly, the abdominal aorta was accessed through a left-sided retroperitoneal approach, and the SAs T_{13}-L_5 were dissected to reveal their origins. A cooling blanket was utilized to achieve mild hypothermia (32°C). Once the target temperature had been reached, baseline aortic and CNP measurements were obtained. Starting with T_{13}, all SAs were sacrificed in craniocaudal direction, one every three minutes. As the SA at the level of T_{13} , the most cranial artery clamped, is usually located 1 to 2 cm above the celiac axis, the origin of the celiac trunk was carefully exposed by surgical dissection.

After completion of abdominal SA sacrifice, group 1 animals underwent thoracic stenting immediately, whereas group 2 animals had an interval of seven days between clamping and stenting. Intraoperative and postoperative CNP and MAP were monitored by antegrade and retrograde catheterization of the transected first lumbar artery (L_1) [11].

Thoracic Stenting

Thoracic aortic stent-graft deployment was performed at 32°C in an adjacent catheterization laboratory. The CNP