Spinal cord protection — segmental artery embolization

Christian D. Etz, MD, PhD
Heisenberg Professor for Aortic Surgery
Ischemic Spinal Cord Injury

No definite prevention strategy — essential for safe open and endovascular repair

‘If the theory does not fit the facts — too bad for the facts’

Kurt Biedenkopf (former Ministerpräsident of Saxony) quoting a frustrated UC Berkley student
Die Blutgefäße des menschlichen Rückenmarkes.

I. Theil.

Die Gefäße der Rückenmarkssubstanz.

Von Prof. Dr. Albert Adamkiewicz.

(Mit 6 Tafeln.)

(Institut für experimentelle Pathologie der k. k. Universität Krakau.)

(Vorgelegt in der Sitzung am 3. November 1881.)
‘If the theory does not fit the facts, change the facts’

Albert Einstein
Segmental Artery Occlusion

Yorkshire pigs

\( N = 20 \)
Direct blood pressure measurement
POSTOPERATIVE SCPP

SCPP (mmHg)

1h   5h   24h   48h   3d    4d    5d

Paraparetic Animals
Recovered Animals

~ 95%
> 60%

after ALL clamped
Collateral Network recovers blood flow within 72h!

* $p = .46$ (not significant)

* $p = .0002$ (significant)

* $p = .0007$ (significant)
Lumbar Paraspinous Network

ASA

Spinal canal
cranial

Lumbar Paraspinal Network

Native

5 days after TAASA occlusion
UNDERSTANDING THE IMPLICATIONS
Orientation of the *Paraspinous* Collateral Network
Arterioles *prior to* and *after* complete SA sacrifice

Etz et al., J Thorac Cardiovasc Surg. 2015 Apr;149(4):1074-9
Enlargement of lower thoracic and lumbar collaterals

significant changes!
DEVELOPING A NEW STRATEGY—THE STAGED REPAIR
Experimental solution: the staged repair

Experimental Two-Stage Simulated Repair of Extensive Thoracoabdominal Aneurysms Reduces Paraplegia Risk

Stefano Zoli, MD, Christian D. Etz, MD, PhD, Fabian Roder, MS, Robert M. Brenner, MS, Carol A. Bodian, DrPH, George Kleinman, MD, Gabriele Di Luozzo, MD, and Randall B. Griep, MD

各部门的胸外科手术和心外科疾病

Background. In a pig model, we compared spinal cord injury after extensive segmental artery (SA) sacrifice in a single stage with recovery after a two-stage procedure: lumbar artery followed by thoracic SA sacrifice.

Methods. Twelve pigs were randomly assigned to undergo extensive SA sacrifice at 32°C in a single operation (group 1, n = 10) or thoracic SA ligation 7 days after lumbar artery sacrifice (group 2, n = 10). Spinal cord perfusion pressure (SCPP) was monitored using a catheter placed in the distal stump of L1. Hind limb function was evaluated immunohistochemically using motor-evoked potentials and for 5 days postoperatively using a modified Tarlov score.

Results. Moderate hematomas were found in all pigs within 1 hour after surgery. All pigs in group 2 fully recovered hind limb function, whereas 40% in group 1 experienced paraplegia (median Tarlov scores 9 versus 5; p = 0.004). Group 1 SCPP fell to 28 ± 6 mm Hg after SA sacrifice, compared with 44 ± 8 mm Hg in group 2 (p < 0.0001). After sacrifice of all residual SAs, SCPP in group 2 remained consistently greater than 85% of baseline, significantly higher than group 1 SCPP and until 72 hours after SA sacrifice (p < 0.0001) and lumbar spinal cord (p = 0.0035). Histopathological analysis showed more severe ischemic damage to the lower thoracic (p < 0.001) and lumbar spinal cord (p = 0.035) in group 2.

Conclusions. In contrast with the single-stage approach, a two-stage procedure, starting with ligation of six or fewer lumbar SAs, leads to only a mild drop in SCPP and stimulates vascular remodeling, minimizing the impact of subsequent SA sacrifice on spinal cord function. The greater safety of extensive SA sacrifice when undertaken in two stages has important implications for endovascular and hybrid aneurysm repair.


During the past few decades, considerable effort has been expended in searching for strategies to prevent spinal cord ischemic damage after surgical and endovascular repair of extensive thoracoabdominal (TAAA) aneurysms. A core body temperature of 32°C has been found [1] in experimental settings to be effective in increasing spinal cord ischemic tolerance by reducing metabolic requirements, and almost all aortic surgeons now perform TAAA resection under at least moderate hypothermia. A catheter for cerebral spinal fluid drainage is usually placed during aortic surgery to enhance spinal cord perfusion [2, 3] and, with increasing frequency, even when extensive aortic coverage is carried out with stent grafts [4, 5]. Several perfusion strategies have been reported to be effective in reducing the risk of intraoperative ischemia and hence paraplegia [6], including use of profound hypothermia [7]. However, the belief that re...
conventional repair

paraplegia rate: 20-30%
staged repair

100% recovery!
After total SA Occlusion: regeneration of arterial perfusion in 5 days —

**Graph Details**

- **Postoperative Collateral Network Pressure (CNP)**
  - in % of MAP
- **Postoperative Follow-Up**
  - Time points: baseline, 1h, 5h, 24h, 48h, 72h, 96h, 120h

**Graph Description**

- The graph depicts the postoperative collateral network pressure (CNP) expressed as a percentage of mean arterial pressure (MAP) over the postoperative follow-up period.
- The data points show a significant decrease in CNP immediately after occlusion, followed by a gradual increase over the subsequent 120 hours, indicating recovery.

**Legend**

- The graph includes error bars indicating variability in the data.

**Additional Information**

- **Two-staged thoracic first** graph
- Neurological recovery using modified Tarlov score
- Time points: 5h, 24h, 48h, 72h, 96h, 120h

**Reference**

ONSET TIME OF POSTOPERATIVE PARAPLEGIA

Concept: Delayed Paraplegia, timing of delayed paraplegia, and clinical support of the “Griepp/Etz Observation”

Mean: 36.8 ± 38.9 hrs (1st Episode)
Median: 21.6 hrs (1st Episode)
7.3 Days or 176 hrs (2nd episode)

COURTESY OF JOE BAVARIA
Retrospective clinical data: significant lower incidence of SCI with ‘staged repair’ (= staged occlusion of SAs)

*PARAPLEGIA PARAPARESIS 8/55

SA sacrificed
SA sacrificed during PREVIOUS procedures
Procedure with Hypothermic Circulatory Arrest

Editor's Choice — The Impact of Early Pelvic and Lower Limb Reperfusion and Attentive Peri-operative Management on the Incidence of Spinal Cord Ischemia During Thoracoabdominal Aortic Aneurysm Endovascular Repair

Staged and adjunctive procedures to preserve spinal cord flow in group 2

Following the demonstration of the potentially beneficial effects of a staged repair to encourage spinal cord preconditioning during extensive TAAA repair, the thoracic endovascular component was implanted during the first procedure in all cases in which the anatomy was suitable (i.e., when a distal sealing zone with a maximum diameter <42 mm was present). Every effort was made to maintain the perfusion of at least one internal iliac artery (IIA); if required, iliac branched devices were employed. When left subclavian artery (LSA) coverage was deemed necessary for proximal seal, carotid subclavian transposition or bypass was performed as an initial procedure. These “first stage” procedures were performed 6–10 weeks before definitive TAAA repair.

management significantly reduces SCI following type I–III TAAA endovascular repair. With the use of these modified protocols, extensive TAAA endovascular repairs are associated with low rates of SCI.

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Keywords: Endovascular repair, Peri-operative management, Spinal cord ischemia, Thoracoabdominal aortic aneurysm
EXPERIMENTAL 'PRIMING' OF THE COLLATERAL NETWORK
Hypothesis: Preemptive Conditioning with Minimally Invasive Segmental Artery Coilembolisation (MISACE) may help to prevent SCI
no histologic damage in coiled areas

Figure 3. Histological outcome
This figure shows the average Kleinman score per group for each individual level of the spinal cord: higher scores indicate greater histopathological damage, as detailed in the text. Spinal cord damage was most prominent in the T9–T13 region. Almost no necrosis is seen in the coiled region (T11-L3) for Group 2.

Geisbüsch et al.
zero paraplegia after coil embolization
‘FIRST-IN-MAN‘ EXPERIENCE
MISACE

Minimally invasive coil deployment - schematically

Coil-occluded (right) / patent SA (left)
MISACE – pt #1

Conventional open repair as 2\textsuperscript{nd}-stage

- 1-month interval
- conventional repair
- Intra op course uneventful
- no significant back bleeding
- short cross clamp time

discharged home w/o neurological impairment
MISACE – pt #2

Endovascular repair

2nd-stage

- 8 week interval

- Endo repair with a four-branched stent-graft (T-branch, CE-marked, Cook Medical, Bjaeverskov, Denmark) in general anesthesia with adjunctive CSF-drainage

- all remaining open SAs between the T7 and the infrarenal aorta occluded w/o endoleakage

Discharged home w/o neurologic deficit on POD #8
There are several important breakthroughs relating to managing and preventing spinal cord injury that have been simultaneously brought together with the MISACE technique.

The first is that optimal perioperative management [...] is not enough to prevent cord ischemia.

The second breakthrough represented by the MISACE technique is the capacity to selectively coil-embolize segmental arteries.
CREATING EVIDENCE
RCT ‘PAPAArtis’ starting in 2017
Paraplegia Prevention in Aortic Aneurysm Repair by Thoracoabdominal Staging with ‘Minimally-Invasive Segmental Artery Coil-Embolization (MISACE)’: A Randomized Controlled Multicentre Trial (PAPA_ARTiS)

**Sample size**
- To be assessed for eligibility: n = 450
- To be assigned to the trial: n = 306
- To be analysed: n = 160 (interim 1), 220 (interim 2), 275 (final)

**Efficacy:** In the control arm success is expected in 75% of patients compared to 90% in the experimental (MISACE staging) arm.

Description of the primary efficacy analysis and population: Mixed logistic regression

**Secondary endpoints:** Analysis of binary outcomes will be analogous to the primary analysis. ICU time will be analysed with a linear mixed model. Re-operation and endoleak will be considered for the subgroups of surgery/TEVAR respectively.
PAPA_ARTiS EUROPE – Horizon 2020 funded with 6.3M €

1. CH: Bern
2. DE: Freiburg
3. DE: Hamburg
4. DE: Leipzig
5. FR: Bordeaux
6. FR: Lille
7. IT: Bologna
8. IT: Milan
9. NL: Maastricht
10. PL: Zabrze
11. SE: Malmö
12. SE: Örebro
13. UK: Liverpool
14. US: Houston
15. US: Philadelphia

Figure 10 - Participating centres PAPA-ARTiS (EU, Switzerland and the US). Red stars represent recruitment centres and the yellow stars represent the radiology core lab (Copenhagen, WP6) and the health economics group (Grenada, WP3).

starting in 2017
Side project #1 – Near-Infrared real-time Monitoring of the Collateral Network (real-time cnNIRS)
Side project #3 ICCAS: Patient-based individual modeling of Paraspinal Collateral Network Perfusion after Segmental Artery Occlusion (Pim-PaP)

spin labeled 4D MRI
DISCUSSION
INCIDENCE
**Inzidenz der Paraplegie Endo / Stentgraft**

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**“The severity of the SCI (paraplegia versus paraparesis) and the potential for recovery did not differ between treatment modalities … SCI was more commonly noted immediately after OPEN REPAIR (29% versus 13%) and in a delayed presentation (up to 6 days) after ER”**
## Inzidenz der Paraplegie offene Chirurgie

<table>
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<th>year</th>
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*Paraplegie 5.3%, paraparesis 3%*
**Aortic X-clamping** vs. **Segmental Artery Occlusion**

### Table for Open Repair

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### Table for Endovascular Repair

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MISACE – side effects and Cx
CONCLUSIONS

1. Staged preconditioning to significantly reduce iatrogenic SCI after TAAA-repair — now clinically available.

2. Much safer treatment with only 1-2 sessions in the cath lab.

3. Reduction of backbleeding through SAs during open repair reducing steal and shortening OR times.

4. Reduction of type II endoleakage after endo repair.
X-clamping
ischemic Spinal Cord Injury

Aortic X-clamping  

Segmental Artery Occlusion
Aortic X-clamping

→ open TAA/A repair
SPINAL CORD BLOOD FLOW
prior to, *during* and after SCP @ 28°C

baseline flow

desc X-clamp: NO flow below T₈
UNKNOWN
open questions to be clarified
2 Bestimmung des optimalen Okklusionsmusters

_Hypothese: alternierend schnellere Arteriogenese (besser als regional)_

Okklusion

alternierend vs. regional

(N=10)                                (N=10)

Perfusionsdruck – Blutfluß – Ultrastruktur im Verlauf
3 Optimales Timing / Intervall?

2. Stufe nach 5, 10 oder 20 Tagen

(je N=10)

Etz et al., J Thorac Cardiovasc Surg. 2015 Apr;149(4):1074-9
4 Optimales Monitoringverfahren / Validierung Tiermodell

Hypothese: Regionale Nahinfrarot Spektroskopie (NIRS) korreliert mit Kollateral Perfusion / spinaler Oxigenierung in Echtzeit

Etz et al., Eur J Vasc Endovasc Surg. 2013 Dec;46(6):651-6
Direct Spinal Cord Perfusion Pressure Monitoring in Extensive Distal Aortic Aneurysm Repair

Christian D. Etz, MD, PhD, Gabriele Di Lucco, MD, Stefano Zoli, MD, Riccardo Lazala, MD, Konstadinos A. Plessis, MD, Carol A. Bodian, DrPH, and Randall B. Griesp, MD

Departments of Cardiothoracic Surgery and Anesthesiology, Mount Sinai School of Medicine, New York, New York

Background. Although maintenance of adequate spinal cord perfusion pressure (SCPP) by the paraspinal collateral network is critical to the success of surgical and endovascular repair of descending thoracic and thoracoabdominal aortic aneurysms, direct monitoring of SCPP has not previously been described.

Methods. A catheter was inserted into the distal end of a ligated thoracic segmental artery (SA) (T6 to L1) in 13 patients, 7 of whom underwent descending thoracic and thoracoabdominal aortic aneurysm repair using deep hypothermic circulatory arrest. Spinal cord perfusion pressure was recorded from this catheter before, during, and after arterial SA sacrifice, in pairs, from T3 through L4, at 32°C. Somatosensory and motor evoked potentials were also monitored during SA sacrifice and until 1 hour after cardiopulmonary bypass. Target mean arterial pressure was 50 mm Hg during SA sacrifice and after nonpulsatile cardiopulmonary bypass, and 60 mm Hg during cardiopulmonary bypass.

Results. A mean of 9.3 ± 2.4 SAs were sacrificed without somatosensory and motor evoked potential loss. Spinal cord perfusion pressure fell from 62 ± 12 mm Hg (76% ± 11% of mean arterial pressure) before SA sacrifice to 53 ± 13 mm Hg (58% ± 15% of mean arterial pressure) after SA clamping. The most significant drop occurred with initiation of nonpulsatile cardiopulmonary bypass, reaching 29 ± 11 mm Hg (46% ± 18% of mean arterial pressure) before deep hypothermic circulatory arrest. Spinal cord perfusion pressure recovered during re-warming to 40 ± 14 mm Hg (61% ± 30% of mean arterial pressure), and further within the first hour of reestablished pulsatile flow. Somatosensory and motor evoked potentials returned in all patients intraoperatively. Recovery of SCPP began intraoperatively, and in 5 patients with prolonged monitoring, continued during the first 24 hours postoperatively. All but 1 patient, who had remarkably low postoperative SCPPs and experienced paraplegia, regained normal spinal cord function.

Conclusions. This study supports experimental data showing that SCPP drops markedly but then recovers gradually during the first several hours after extensive SA sacrifice. Direct monitoring may help prevent a fall of SCPP below levels critical for spinal cord recovery after surgery and endovascular repair of descending thoracic and thoracoabdominal aortic aneurysms.


Paraplegia remains the most devastating complication after repair of extensive descending thoracic (DTA) and thoracoabdominal aortic aneurysms (TAAAs). The maintenance of adequate spinal cord perfusion pressure (SCPP) is critical to the success of open and endovascular repair of DTAAs and TAAAs to prevent spinal cord ischemia when blood flow to the segmental arteries (SAs) is interrupted.

Monitoring of spinal cord function using motor (MEP) or somatosensory evoked potentials (SSEP) is widely accepted in the assessment of intraoperative spinal cord viability during aortic procedures, but is an indirect measurement of the adequacy of spinal cord perfusion [1-6]. If MEPs or SSEPs diminish, the response usually involves anesthetic and hemodynamic maneuvers to improve spinal cord perfusion—chiefly by increasing mean arterial pressure (MAP) and improving cerebrospinal fluid (CSF) drainage—but the assessment of the efficacy of these measures is likewise indirect. It is possible that inadequate spinal cord perfusion may occur even when MEPs and SSEP monitoring indicates no cause for alarm, and that a more direct, sensitive way of monitoring spinal cord perfusion could be helpful intraoperatively, although the presence of intact MEP and SSEP already provides considerable reassurance of adequate intraoperative spinal cord perfusion.

A recent prospective study of our clinical cases has suggested, however, that spinal cord vulnerability to inadequate perfusion is likely to be highest not during operation, but in the early postoperative period, and that inadequate perfusion resulting in spinal cord injury may occur with systemic pressures below the individual patient’s usual blood pressure even though those systemic pressures fall within limits usually regarded as normal.
SCPP-CATH PLACEMENT
SCPP = CN pressure – CSF pressure
SCPP = CN pressure – CSF pressure

Five patients 9 ± 3 SA sacrificed

$p = .016$
CN NIRS
Detection of ischemic spinal cord injury during and after extensive open or endovascular TAA/A repair utilizing SSEP and/or MEP monitoring: invasive and expensive
## Spinal cord monitoring

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<th>MEP</th>
<th>Direct SCPP</th>
<th>Laser Doppler</th>
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**Definitions:**
- SSEP = Somatosensory evoked potentials
- MEP = Motor evoked potentials
- SCPP = Spinal cord perfusion pressure
- cnNIRS = near-infrared spectroscopy of the collateral network
= LIGHT (!)
Collateral Network

Near-infrared Spectroscopy Monitoring of the Collateral Network Prior to, During, and After Thoracoabdominal Aortic Repair: A Pilot Study


① Lumbar cnNIRS sensitive to X-clamping & distal perfusion

① Diminished lumbar cnNIRS = postoperative SCI*
HYPOTHESIS

Perfusion & oxygenation of the collateral network directly reflects spinal cord microcirculation?

Can cnNIRS depict spinal cord oxygenation?
Experimental setup

- Seven juvenile male pigs
- Subcutaneous 
- T5/6
- Direct muscle and spinal cord oxygenation + flow by Laser Doppler (LDF)
Experimental Sequence

✧ Baseline
✧ **X-clamping** (ischemia: 8 min.)
✧ **Clamp release** (recovery)

 consecutively 4 times

LDF - OXYGENATION

LDF - FLOW
Direct Invasive Laser Doppler (LDF)

Collateral Network

Spinal Cord

X-clamp

Clamp release

Oxygenation

Flo
HYPOTHESIS: oxygenation of the CN = spinal cord?
Paraspinous CN oxygenation directly reflects spinal cord tissue oxygenation.
Question: lumbar cnNIRS = Spinal cord oxygenation? √
cnNIRS vs. Spinal Cord Oxygenation

Lumbar cnNIRS directly reflects spinal cord tissue oxygenation
Conclusions

① CN oxygenation reflects spinal cord oxygenation

① Lumbar cnNIRS reflects spinal cord oxygenation

Lumbar cnNIRS is an effective tool to non-invasively monitor spinal cord oxygenation
BP MANAGEMENT
PAPA-ARTIS dissemination, flow of information and communities

- Project data & communication
  - Project Team
- Clinical benefits
  - Practitioner Community
- Research & regulatory
  - Scientific/Policy-makers
- Results & education
  - Wider Society & General Public
Ultimate goal: Translation of the 'staged repair' concept into clinical practice for ZERO PARAPLEGIA