Brain protection in thoracic aortic surgery – An interdisciplinary challenge

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In thoracic aortic disease, diagnostic imaging, prognostic information, surgical outcomes and follow-up have improved substantially within recent years [1, 2]. As a consequence, cardiovascular anesthesia and surgery are faced with an increasing caseload of thoracic aortic procedures [3].
With decreasing overall and perioperative mortality, permanent or transient neurological deficits (ND) become the major cause of morbidity, low quality of life and cost in this group [4-6].

Etiologies and risks for perioperative ND include
a) the natural course of disease (e.g., cerebrovascular involvement [7], embolization, malperfusion [8,9], dissection, rupture);
b) emergency and complexity of repair [2,10]
c) use of hypothermic circulatory arrest (HCA) [2,11-13].
d) CPB-related damage (e.g., embolization of debris, gas, fat; malperfusion, dissection, hypoperfusion, reperfusion injury)

Clinical strategies of all specialties involved in thoracic aortic surgery must focus on CNS protection:

A) diagnosis and preparation
a) early diagnosis, close control, elective repair, close follow-up
b) surgical indication must balance individual disease risks against institutional perioperative risks.
c) elective cases (ascending/arch/thoracoabdominal aneurysms/chronic dissections) require
  - comprehensive diagnostic workup (angioCT, MRI; coronaries, carotids; echo, neurological assessment etc.) and
  - interdisciplinary planning with a focus on CNS protection
d) emergencies (Type A aortic dissection, rupture) require swift, comprehensive, standardized management.

B) surgical strategies
e) usually aim for definitive repair; however, staged or hybrid procedures may be indicated to reduce ischemic risks [14,15]
f) include careful selection of cannulation/crossclamp sites; axillary/subclavian cannulation is nowadays preferred over femoral artery cannulation for fear of retrograde embolization, false lumen perfusion or dissection [5, 16,17]
g) cannulation injury/embolization can be reduced by TEE and epiaortic scanning [18-20]
h) periods of hypothermic circulatory arrest (HCA) without any perfusion support for the brain should be limited to < 30 min at < 20°C nasopharyngeal temperature [21,22].
i) de-airing must be meticulous, using positioning, CO_2-insufflation, flushing, venting or even retrograde perfusion.

C) perfusion management
j) must ensure homogeneous cerebral cooling with temperature gradients of < 10°C, should last for a sufficient amount of time; EEG silence should always precede HCA.
k) must minimize periods of cerebral no-flow/low flow by
  - antegrade cerebral perfusion (ACP) [23,24] and variants [9, 25-29] using right axillary artery cannulation [5] and/or only moderate body hypothermia during arrest [30-33]
  - HCA may be avoided altogether by appropriately combining ACP with distal body perfusion [28,34-36]

- retrograde CP [6, 10, 37,38] is still used by some groups despite unproven neuroprotective advantage [39], with the main goals of maintaining brain hypothermia and removing embolic load

l) optimizing venous drainage [40]

m) rewarming must be controlled to levels strictly below 37°C [41]

D) anesthesia management

n) *Opioid-based regimes* are supplemented with volatile agents or i.v. sedatives. Both for propofol and current volatiles, neuroprotective and/or neuronal ischemic preconditioning effects have been demonstrated experimentally. However, evidence of clinical superiority of any such regime in terms of neurological outcome is lacking in this patient population [42,43). Relaxants are empirically indicated to reduce oxygen demand from subclinical shivering during cooling/rewarming.

o) Neuromonitoring:
- Cerebral perfusion pressure must be reliably monitored by appropriate arterial line placement, exactly adapted to surgical plan and individual anatomy. This should be combined with continuous proximal internal jugular pressure monitoring [40]
- Processed EEG helps to monitor for adequate depth of anesthesia, for episodes of EEG silence due to hypothermia, hypnotics or ischemia, and EEG recovery thereafter.
- Multi-site temperature monitoring (nasopharyngeal, bilateral tympanic, bladder, CPB inflow etc [44]) is required to control cooling and rewarming of brain, core and shell.
- TEE and epiaortic ultrasound have evidence-based indications in this field [18,45], e.g., assessment of aortic pathology, atheromatosis, valvular and myocardial function; guidance of cannulation and de-airing procedures etc.
- Cerebral oximetry by near-infrared spectroscopy (NIRS) or invasive jugular bulb oximetry is used to detect critical cerebrovascular Hb desaturation due to malperfusion, hypotension, hypocapnia, insufficient cooling or ACP flow, brisk rewarming or other causes of regional or global ischemia. Evidence towards reduction of postoperative ND in cardiothoracic patients is accruing slowly for non-invasive continuous NIRS (40,46), but less so for invasive jugular bulb oximetry [47-49].
- Transcranial Doppler has been found useful for monitoring adequacy of antegrade or retrograde cerebral perfusion setups [50,51] and for assessing supraaortic malperfusion or embolic load.

p) Guidance of surgical cannulation
- During arterial and venous cannulation, TEE, multisite arterial lines, and CVP readings from the lumen most proximal to the jugular bulb help to avoid cannulation disasters (atheroma dislodgement, malposition, dissection, venous obstruction etc.)

q) Guidance of brain cooling and rewarming
- multi-site temperature monitoring assesses homogeneity and bilateral synchrony of head temperature changes.
- Head cooling should be accompanied by appropriate EEG suppression and recovery, as well as by reversible mydriasis. Mydriasis should rather be induced by hypothermia than by arrest.
- Topical head cooling prevents external rewarming; despite wide empirical use, optimal technique and neuro-outcome benefits remain unclear [52-54]

r) Monitoring and guidance of ante- or retrograde cerebral perfusion
- flow meter, tympanic T, data from NIRS [46] and TCD [50,51,55] all give some indication about adequacy of selective cerebral perfusion.
- The Circle of Willis is incomplete in about 15% of patients [56]: unilateral (RA-) ACP may not suffice, and may need to be supported by selective L carotid ACP.
- Run-off of ACP flow (into IMA or L subclavian), malperfusion or embolism do occur and may be detected by appropriate monitoring.

s) Guidance of de-airing
- By TEE, head-down positioning, intermittent carotid compression etc. anesthesia contributes to – largely empirical – efforts to de-air the left heart and arterial tree (like field flooding with CO2 [57], short RCP, slow reperfusion, agitation, needle venting etc).

t) “Pharmacologic neuroprotection” [42,43]
- A variety of agents is in wide use, but still without – even empirical – evidence of benefit [58]
- Steroids: there is no evidence for neuroprotective efficacy in HCA [59], but hyperglycemic risk is promoted.
- Thiopental, Propofol: since decades, clinical evidence for benefit prior to HCA remains insufficient [21]; bolus doses interfere with EEG monitoring and are cerebral vasoconstrictors. Both may

be useful to normalize cerebral O2 balance at rewarming [40].
- Volatiles: evidence for clinically useful neuronal protection and preconditioning is insufficient [42]; agents may reduce CPP but promote cooling and improve post-CPB myocardial function.
- Aprotinin: despite some neuroprotective evidence [60], the substance has been withdrawn in 2007.

u) Blood gas management
- There is wide agreement to use a-stat monitoring of blood gases
- Inadvertent hypocapnia may impair CBF and cerebral oxygenation and is to be avoided.
- Many institutions employ mild hypercapnia during cooling for HCA, and α-stat normocapnia during rewarming.

v) Monitoring/guidance of glycemia
- Hyperglycemia is known to worsen ischemic CNS damage. Postoperatively, "tight" normoglycemic control (4.4 – 6.1 mmol/L) has been shown to improve survival after high-risk cardiac surgery [61], but at a substantial risk of hypoglycemia. Intraoperatively, a RCT in cardiac surgery failed to show any benefits of intraoperative "tight" glycemic control but undesirable trends in death and stroke rate [62]. Therefore, intraoperative glycemic control (e.g., to 4.5 - 9 mmol/L) appears preferable to "tight" schedules with hypoglycemic risks.

w) Management of coagulation
- Large transfusion requirement is an independent predictor of perioperative stroke risk in cardiac surgery [63]. Tranexamic acid has been shown to reduce transfusion requirement in thoracic aortic surgery [64]. Reduction of homologous transfusion (and in particular, platelets) by appropriate point-of-care testing and transfusion algorithms may open new approaches to reduce ND in thoracic aortic surgery.

x) Temperature management
- Postischemic hyperthermia worsens neurologic outcome [41]. After thoracic aortic surgery, T > 37° in perfusate, core, nasopharynx or tympanon of patients must be avoided at all times, by early start of rewarming, by keeping patient-perfusate gradients < 10 °C, by stopping rewarming at nasopharyngeal T ≤ 36.5°Core (even at the cost of some afterdrop), and slow correction by external warming devices [65].

Summary

In thoracic aortic surgery and anesthesia, caseload and complexity is increasing. The variety of mechanisms contributing to adverse neurological outcomes is large and difficult to control in this type of surgery. Nevertheless, in most published series, rates of major neurodeficits are clearly decreasing over time.
Major progress in neuroprotection has been made by modifying surgical and perfusion strategies, but mostly experimentally and empirically with relatively few human RCT. Cardiac anesthesiology has contributed substantially by echocardiographic and neuromonitoring input, and improved management of cerebral hemodynamics, coagulation, metabolism and temperature. Disappointingly, after decades of well-conducted preclinical research, pharmacologic neuroprotectants have yet to produce clinical evidence of efficacy and safety.
Further progress is expected to come both from new hybrid technology, from increasing institutional caseload and intensified team experience. At the moment, the observational character of most studies in the field makes development of evidence-based recommendations difficult.

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