

## Thesis summary

There are three main directions which can be distinguished in our scientific and research activity:

- 1) Aorta pathology
- 2) Chest wall reconstruction
- 3) Intra-thoracic transplantation

### 1. Aortic pathology

#### a. Anatomy of the aortic root and consequences of an external subvalvular prosthetic ring

##### Introduction:

In order to understand the complexity of aortic disease we performed an anatomical study of the entire ascending aorta.

The aortic root is often the site where various life-threatening conditions as dissections or aneurysms occur. The aim of our study was to perform a detailed anatomical study of the aortic root and its components and to assess the morphologic consequences on the aortic valve of a subvalvular prosthetic ring.

Methods: We examined 11 adult cadavers (6 women and 5 men) with ages between 56 and 89 years. Different measures of the aortic root at each level were made. We measured the distances between each commissure and calculated the surface of the aortic valve opening ( $\sigma$ ) and the surface of the aortic opening at this level (S). A PTFE ring of 10 mm width was then placed in subvalvular position and tightened around the aortic root; we stopped the procedure as soon as aortic root morphology was lost. Results: The normal aortic root has a 29,09 mm (SD  $\pm$  3,08 mm) aortic trunk mean diameter, a 25,90mm ( $\pm$  2,59mm) Sino-Tubular-Junction one, a 30,45 mm ( $\pm$  2,42 mm) sinus of Valsalva one and 25,80 mm ( $\pm$  4,26 mm) aortic annulus one. The angle between the two coronary arteries opening is 128, 8° ( $\pm$  9, 59°). Before the correction S was 548, 1 mm<sup>2</sup> ( $\pm$ 117, 3) and after it, the new surface of the aortic opening (S1) was lowered to 443, 9 mm<sup>2</sup> ( $\pm$  73, 3) (p-value=0.0025). Ring correction produces though a loss of surface of 17, 8% ( $\pm$  8, 7).

Conclusion: this anatomic study offers aid to minimize or avoid clinical complications in patients who undergo an aortic valve sparing procedure or any other type of surgery of the aortic root.

**b. Preoperative predictive factors for mortality in acute type A aortic dissection: an institutional report on 217 consecutives cases**

Surgical treatment of type A acute aortic dissection remains a challenge, especially in elderly patients or in patients with a critical preoperative status. We have retrospectively assessed our series over a 15-year period starting in 1990, including patients operated under cardiac massage for preoperative cardiac arrest occurring in the operating room. There were 217 patients (mean age,  $61.5 \pm 13.5$  years; 16 patients  $>80$  years). Preoperative shock was noted in 21.7%, including 14 patients operated under cardiac massage. Operating procedures were: modified Bentall (31%), aortic tube (67.1%), other (1.9%), aortic arch procedure in 26.4%. Overall mortality rate was 19.8% with an exponential increase with age (50% over 80 years). Of 14 patients operated under cardiac massage, three have been discharged: one ventricular fibrillation due to an acute myocardial infarction and two among the 13 with acute aortic ruptures in cardiac arrest (one being a redo, the adhesions limiting the tamponade). Our results confirmed age and preoperative shock prior to surgery as risk factors, and the fact that operating on a patient under cardiac massage for cardiac arrest due to an aortic rupture is probably not a reasonable therapeutic choice.

**c. Minimal Invasive - Aortic arch embolization of an Amplatzer occluder after an atrial septal defect closure: hybrid operative approach without circulatory arrest**

Percutaneous closure of the secundum type atrial septal defects is becoming increasingly popular. We report the case of a 49-year-old man who presented for an unusual embolization of an Amplatzer occluder (AO) 6 weeks after a percutaneous closure of his secundum type atrial septal defect. Emergency cardiac surgery was performed and the device was safely removed by a combined surgical and endovascular approach with no need of circulatory arrest or of profound hypothermia.

**d. One-Year Outcomes Following Repair of Thoraco-abdominal Aneurysms with the Multilayer Flow Modulator: Report from the STRATO Trial I**

Purpose: To evaluate endovascular repair of type II and III thoraco-abdominal aortic aneurysms (TAAA) using the Multilayer Flow Modulator (MFM) in patients with contraindications for open surgery and fenestrated stent-grafts.

Methods: In this prospective, multicentre, nonrandomized trial (EudraCT registration: 2009-013678-42; Clinical Trials. Gov. Identifier NCT01756911), 23 patients (19 men; mean age 75.8years) with Crawford type II (43.5%) and III (56.5%) TAAA (mean diameter 6.5 cm) were treated with the MFM between April 2010 and February 2011. The primary efficacy outcome measure was stable aneurysm thrombosis with associated branch vessel patency at 12months; the primary safety endpoint was 30-day and 12-month all-cause mortality.

Results: The rate of technical success was 100%. In 20 patients with computed tomography scans at 12 months, the primary efficacy outcome was met in 15 patients. The rate of primary patency of covered branch vessels was 96% (53/55); 1 patient with 2 occluded visceral branches underwent successful surgical re-intervention. Endoleaks were identified in 5 patients (3 attachment site and 2 at device overlap), 4 of whom underwent re-intervention (3 additional MFMs and 1 stent-graft implanted). At 12 months, aneurysm diameter was stable in 18 of 20 patients; the mean ratio of residual aneurysm flow volume to total volume had decreased by 28.9%, and the mean ratio of thrombus volume to total lumen volume had increased by 21.3% (n=17). There were no cases of device migration, loss of device integrity, spinal cord ischemia, or aneurysm rupture.

Conclusion: At 1 year, endovascular repair with the MFM appears to be safe and effective while successfully maintaining branch vessel patency. Continued follow-up is on-going.

**e. Three-Year Outcomes with the Multilayer Flow Modulator for Repair of Thoraco-Abdominal Aneurysms: A Follow-up Report from the STRATO Trial**

Purpose: To evaluate long-term outcomes of endovascular repair of type II and III thoracoabdominal aortic aneurysms (TAAA) using the Multilayer Flow Modulator (MFM) in patients contraindicated for open surgery and fenestrated stent grafts.

Methods: In this prospective, multicentre, nonrandomized trial, 23 patients (mean age 75.8 years, 19 male) with Crawford type II (43.5%) and III (56.5%) TAAA (mean diameter 6.5

cm) were implanted between April 2010 and February 2011. Endpoints included stable aneurysm thrombosis with associated branch vessel patency and all-cause mortality.

Results: Through 36 months, there were 7 deaths, none aneurysm related, no cases of spinal cord injury, aneurysm rupture, or device migration or fracture, and no respiratory, renal, or peripheral complications. Aortic and device patency remained 100%. Aneurysm exclusion was achieved for 75% at 12 months, 92.3% at 24 months, and 90.9% at 36 months. The rate of branch patency was 96.5% at 12 months (primary patency), 100% at 24 months, and 96.6% at 36. Overall, 9 patients suffered from endo leaks, with 5 of 6 successfully corrected; 9 patients underwent 11 re-interventions (3 surgical). Maximum aneurysm diameter was stable for 90% at 12 months, 84.6% at 24 months, and 81.8% at 36. For 10 patients with CT imaging at 36 months, the mean ratio of aneurysm flow volume to total volume had decreased by 83.0%; the mean ratio of thrombus volume to total volume increased by 158.9%.

Conclusion: Through 3 years, endovascular repair with the MFM appears to be safe and effective while successfully maintaining branch vessel patency.

*EudraCT registration: 2009-013678-42. ClinicalTrials.gov identifier NCT01756911.*

#### **f. The use of multilayer flow modulators in the endovascular treatment of complex aortic aneurysms and aortic dissections**

For a very long time, complex thoracoabdominal aneurysms involving spinal and visceral branches have been a challenge to both surgical and endovascular treatment. Both, open surgical repair and endovascular repair with fenestrated endografts, are accompanied with high complications and mortality. Hybrid techniques that have been recently adopted by some authors also present unconvincing results, accumulating the complications of both open and endovascular approaches.

The concept of multilayer flow modulator is a solution in the treatment of both complicated and standard aneurysms, being safe and effective, with low morbidity and mortality and a relative low cost compared with other therapeutically options.

The MFM is a promising technology that may be the solution in the treatment of simple or complex aortic aneurysmal pathology and type B chronic aortic dissection—not only in elderly patients with heavy comorbidities, but also for the younger ones. The MFM offers a physiological modulation of the aneurysm with off the shelf availability, decrease of mean diameter and length, and thrombus constitution in the aneurysm, signifying a totally different mechanism in modelling the laminar flow. At this stage, the technology has shown low mortality, low morbidity, and low costs compared to other known techniques.

**g. Streamliner Multilayer Flow Modulator stents as a therapeutic option in the management of complex thoracoabdominal aortic pathology report from Global SMFM Registry**

Complex thoraco-abdominal aortic aneurysm (TAAA) patients remain a challenge irrespective of treatment choice. These patients are at high risk of death, renal failure and paraplegia. This high incidence of morbidity and mortality has driven the incentive for discovery of a less invasive, more efficacious and universally reproducible solution for TAAA repair. The Streamliner Multilayer Flow Modulator (SMFM) is an alternative modality of treatment and it is conceptually at variance with conventional treatment modes.

Preliminary results show that treatment of infra-renal AAA, juxta-renal AAA, Stanford Type B dissection and Crawford Type V by the SMFM device were most successful. Large volumes of more than 450 cm<sup>3</sup> in pathologies such as Crawford Type II and Type IV, should be labelled as a contraindication for use of the SMFM. C-reactive protein, haemoglobin, aneurysm volume and maximum diameter all play major roles in successful treatment. The greater the length of the aorta to be covered and the greater the number of stents utilized, the greater the risk of adverse events and mortality. Patient requiring a reintervention with an additional SMFM(s) within 200 days of primary treatment increases mortality. Both length of the pathology and rate of reintervention indicate a severe aortic pathology burden and its aggressive nature. The SMFM harnesses the body's innate physiological processes to modulate the aneurysm, with no risk of critical shuttering or loss of native side branches. The SMFM offers less operative trauma, shorter procedure times and reduced hospital stays. It offers simplicity, consistency and reproducibility in one treatment. However, the SMFM is not a solution for patients living on borrowed time. It is a promising disruptive technology, only in safe hands, and must be utilized under strict instructions for use.

**2. Chest wall reconstruction**

**a. Recurrent sternal infection following treatment with negative pressure wound therapy and titanium transverse plate fixation**

Objective: To provide a definition for recurrent sternal infection (RSI), analyse the risk factors and describe the management of this complication following treatment of deep sternal

wound infection (DSWI) with horizontal titanium sternal osteosynthesis and coverage with pectoralis major myocutaneous flaps.

Methods: Between 2002 and 2007, 10 665 patients were submitted to open-heart surgery (OHS) in our institution, of whom 149 (1.4%) developed a DSWI. Negative pressure wound therapy (NPWT) followed by sternal osteosynthesis with muscular-cutaneous coverage was used in 92 (61.7%) patients. A retrospective review was done using a prospectively maintained database to identify risk factors for recurrent infection in this group of patients.

Results: Of the 92 patients who underwent sternal osteosynthesis, nine (9.8%) developed recurrent sternal infection requiring hardware removal. Univariate analysis showed that preoperative methicillin-resistant *Staphylococcus aureus* (MRSA) status (33.3% vs 6.1%  $p=0.03$ ) and prolonged intubation time in ICU (44.4% vs. 14.6%;  $p<0.05$ ) were significant risk factors. Two-thirds of these patients were also found to be infected with the same germ as the one responsible for their initial DSWI. No death was reported and sternal integrity was preserved in all patients despite plate removal.

Conclusions: To lower the rate of RSI in patients treated with transverse sternal osteosynthesis along with myocutaneous coverage for DSWI, surgeons must consider the MRSA preoperative status as a significant predictor of RSI and/or persistent infection. Chest-wall integrity in patients with RSI can be maintained after hardware removal, even after only a few weeks following initial plating.

### **3. Intra-thoracic transplantation**

**LUNG TRANSPLANTATION (LT)** has become a well-established treatment for selected patients suffering chronic respiratory failure due to end-stage vascular and/or parenchymal diseases without possible alternative medical treatments.

This increase in demand for LT was related in part to significant improvements in LT survival over time, as noted in various registries.

The operative technique for LT has been standardized with all organs being harvested after flush perfusion of anterograde pneumoplegia.

The systematic use of extracellular solution for lung preservation may account for the good results, even if it is difficult to be sure this plays a major role, since ischemia-reperfusion is a complex condition involving many factors.