#### TAAA: open, hybrid or endovascular repair?

#### **Michael Jacobs**

European Vascular Center, Aachen-Maastricht, Germany-the Netherlands

Treatment modalities for Thoracic Aortic Aneurysms (TAA) and Thoraco Abdominal Aortic Aneurysms (TAAA) have changed significantly during the last decade. Following the evolution of open repair without adjunctive measures, the era of protective strategies was introduced, including extracorporeal circulation, spinal fluid drainage and techniques to assess spinal cord integrity. However, despite these supportive techniques, overall mortality and morbidity following open repair remained considerably high, especially in low volume hospitals. There is enough evidence now that these open procedures should take place in highly experienced centres who perform these procedures with the required infrastructure and multidisciplinary teams.

The rapidly developing endovascular techniques have made TAA and TAAA treatment less invasive and short term outcome seems to be promising. Hybrid procedures consist of debranching techniques, combined with endovascular exclusion of the aneurysm. These procedures can be performed simultaneously or with interval planning. However, morbidity and mortality of hybrid procedures are significant.

Total endovascular repair is not only a matter of deploying stent grafts. Pre-operative aortic measurements and case planning is a specialty on its own. Three-dimensional reconstruction of CT-images and subsequent designing an endograft with fenestrations and sidebranches is a complex part of total endovascular repair. Also here it is obvious that experience and infrastructure is necessary in order to produce acceptable results.

Is there still a role for open TAA and TAAA repair?

There are several indications for which endovascular repair is now the first choice of treatment: traumatic aortic rupture, localised penetrating aortic ulcer, post operative false aneurysms, localised descending thoracic aneurysms and probably aorto-brochial fistula.

There is debate on the indication for endovascular treatment in extensive TAAA, especially in young(er) patients who are fit for open surgery. Even more debatable is endo treatment in patients with connective tissue disease. Also, patients with aorto-esophageal fistula seem not to be good candidates for the endovascular approach.

In our centre the indications for endovascular repair are as mentioned above.

In patients suffering from TAAA who are not good candidates for open repair will have total endovascular treatment with fenestration or side branch technology. This also accounts for redo surgery patients.

Open repair is offered to young patients and patients who suffer from connective tissue disease. Adequate short and long term outcome is warranted. In addition, failed endovascular repair, for example type I endoleak in chronic dissection, is also a reason for open repair if additional endovascular solutions are not possible anymore. This is the situation in 2011, however, in less than 10 years this approach will have changed completely.

# Using TEVAR for Aortic Disease: Aneurysm, Dissection, and Trauma

#### William D. Jordan

Section of Vascular Surgery and Endovascular Therapy, University of Alabama, Birmingham, USA

**BACKGROUND:** With the introduction of thoracic endovascular aortic repair (TEVAR), endografts have been widely used for aneurysm disease of the thoracic aorta but also other pathologic conditions. After initial experience in carefully selected aneurysm population, we have also used thoracic endografts to treat aortic dissection and traumatic transection. We then reviewed our prospectively maintained clinical database to evaluate a 10 year experience of clinical application for TEVAR.

**METHODS:** Health system charts, medical communication and national death indices were periodically reviewed while also tracking each clinical encounters with patients. We then evaluated outcomes of TEVAR with particular attention towards early and late mortality of different aortic pathologies. We further analyzed our prospective protocol of expectant spinal drainage to prevent spinal cord ischemia after TEVAR.

**RESULTS:** Between January 2000 and December 2010, 263 patients underwent 307 separate TEVAR procedures to treat aneurysms (71%), dissections (18%), and transections (9%) with most of the experience (95%) since 2005. Early mortality (including ruptures) was 9% while 3 year mortality was 43%. Secondary interventions were required for 17 patients with endoleak and 3 patients who had endograft collapse. Spinal cord ischemia (SCI) was identified post-operatively in 6% of patients and was associated with longer length of aortic coverage, presence of infrarenal aortic pathology, or a history of stroke. SCI was note associated with left subclavian artery coverage which was required in 29% of patients. When patients were drained after the onset of SCI symptoms, 70% regained some neurologic function, but only 30% had a full recovery.

**CONCLUSIONS:** TEVAR offers a less invasive method of treating a wide range of aortic pathologies with acceptable early survival. Spinal cord drainage can be used post-operatively to selectively drain patients who experience symptoms of SCI. Late mortality remains high suggesting the advanced degenerative condition of the aneurysm and dissection patients.

## The Albany Vascular Experience of EVAR/ TEVAR for Ruptured Aortic Aneurysms

Manish Mehta The Vascular Group PLLC, USA

The metamorphosis of abdominal aortic aneurysm (AAA) repair and thoracic aortic aneurysm repair (TAA) from open surgical to endovascular means has evolved substantially over the past 2 decades. Today, endovascular abdominal aneurysm repair (EVAR) and Thoracic endovascular aortic aneurysm repair (TEVAR) are considered as the first choice of therapy for treatment of infrarenal AAA and descending TAA in patients with favorable morphology. Furthermore, in "real world" clinical scenarios, with increasing physician experience and ability, the indications of EVAR and TEVAR have expanded from treatment of elective to emergent aneurysms and from favorable morphology to sometimes complex and unfavorable anatomy, particularly in high-risk patients. This discussion will focus on a and standardized technical approach for treating patients presenting with ruptured abdominal and thoracic aortic aneurysms, and traumatic thoracic aortic transections by endovascular means that can maximize our ability to offer this treatment of most patients and optimize outcomes. (1)

Today, the question is not weather patients with ruptured aortic aneurysms should undergo EVAR/ TEVAR, rather how to develop systems that allow for broader utilization of these complex procedures that have shown great benefit in high risk patients with aneurysm rupture. There remain several fundamental concerns regarding EVAR/ TEVAR for ruptured aortic aneurysms that include the availability of preoperative imaging (CTA) in all patients to identify anatomical suitability, the availability of dedicated staff and equipment to perform emergent procedures at all hours, feasibility of treating hemodynamically stable and unstable patients, and the surgeon/ interventionists ability to manage unexpected scenarios under emergent circumstances. Although one or more of the above mentioned 'limitations' might have some impact on ones ability to incorporate endovascular techniques in managing patients with ruptured aortic aneurysms, the fundamentals for success begin from establishing an infrastructure of a standardized approach that is multidisciplinary and inclusive of the emergency room (ER) physicians, the anesthesiologists, the operating room (OR) nurses, technologists, and the vascular surgeons. To get started, the surgeon/ interventionist should 1) become comfortable performing EVAR/ TEVAR under elective circumstances, 2) obtain an inventory of standard equipment (wires, catheters, sheaths, balloons, particularly the compliant aortic occlusion balloons, and fluoroscopic equipment) that is needed to perform elective EVAR/ TEVAR safely, 3) pick and chose the stentgrafts that one is most comfortable using, 4) become comfortable with adjunctive procedures such as iliac interventions that might be needed to facilitate access, use of compliant aortic occlusion balloon, placement of Palmaz stents at the aortic neck, and 5) only treat hemodynamically stable patients with preoperative CT scans. With increasing experience one can easily modify their inclusion and exclusion criteria for EVAR of ruptured AAA that can accommodate even hemodynamically unstable patients. Figure 1.

#### **EVAR for Ruptured Abdominal Aortic Aneurysms**

1. The Fundamental Techniques: Adequate resuscitation of patients with ruptured AAA is vital to a successful

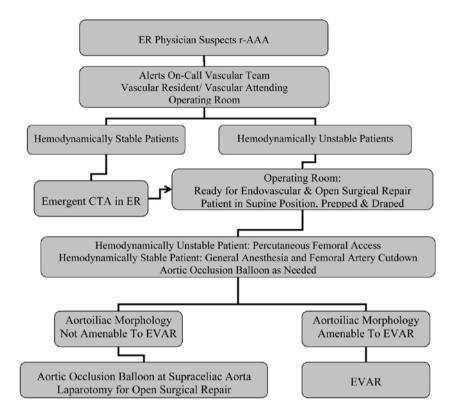


Figure 1 Albany Vascular Group standardized protocol for endovascular aneurysm repair (EVAR) of ruptured abdominal aortic aneurysm (r-AAA). BP, blood pressure; CTA, computed tomographic angiography; ER, emergency room.

outcome. As long as the patients maintain a measurable blood pressure, the techniques of 'hypotensive hemostasis' by limiting the resuscitation to maintain a detectable blood pressure can help minimize ongoing hemorrhage. The patient is prepped and draped in supine position and via a femoral artery cut-down ipsilateral access is obtained using a needle, floppy guidewire, and a guiding catheter. The floppy guidewire is exchanged for a superstiff wire that can be used to place a large sheath (12Fr – 14Fr x 45 cm length) in the ipsilateral femoral artery and the sheath advanced up to the juxtarenal abdominal aorta so it is ready to be used to deliver and support the aortic occlusion balloon if needed. A compliant occlusion balloon should always be available in these procedures, and in hemodynamically unstable patients, the occlusion balloon is advanced through the ipsilateral sheath over the super-stiff wire into the supraceliac abdominal aorta under fluoroscopic guidance, and the balloon is inflated as needed. In our experience of over a hundred ruptured EVARs, the aortic occlusion balloon is needed in <25% of cases. Access is subsequently obtained from contralateral femoral artery cut-down in similar fashion, and a 'marker flush-catheter' advanced to the juxtarenal aorta for an arteriogram.

The placement of the stentgraft mainbody is planned based on the aortoiliac morphology that is best suited for EVAR. Unless prohibitive, <u>in hemodynamically stable patients</u>, following the initial arteriogram, the aortic occlusion balloon is removed from the initial ipsilateral side and the stentgraft mainbody advanced under fluoroscopic guidance; this limits the number of catheter exchanges. <u>In hemodynamically unstable patients</u> that require infla-

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tion of the aortic occlusion balloon, the 'marker flush-catheter' is exchanged for the stentgraft mainbody which is delivered up to the renal arteries. An arteriogram is done via the sheath that is used to support the aortic occlusion balloon, the tip of the stentgraft mainbody is aligned with the lowermost renal artery, the occlusion balloon is subsequently deflated and withdrawn back with the delivery sheath into the AAA, and the stentgraft mainbody deployed. The remainder of the EVAR procedure is performed similar to as in elective circumstances; 1) the tip of the stentgraft mainbody aligned with the lowermost renal artery, 2) the contralateral gate aligned to facilitate expeditious 'gate-cannulation', 3) the ipsilateral and contralateral iliac extensions planned and deployed as needed.

2. <u>Availability of Preoperative CT Scan</u>: The question is whether one has the time to get an emergent CT scan prior to EVAR, and if not are there other tools available that might help us manage these hemodynamically unstable patients by endovascular means? Currently available data suggests that majority of patients with ruptured AAA have the time to undergo an emergent CT scan, particularly if there is an established protocol that facilitates early diagnosis and transfer of patient from the ER to the OR. The obvious questions that remains is, how often are ruptured AAAs suitable for endovascular repair? Recently we have tried to answer just that by evaluating CT scans of 50 consecutive patients that presented with ruptured AAA and had an available CT scan. The endovascular anatomical inclusion criteria was slightly modified from the standard 'Indications for Use' defined by each of the FDA approved devices and focused on feasibility of EVAR for ruptured AAA; this included aortic neck length  $\geq$ 10 mm, aortic neck diameter  $\leq$ 32 mm, aortic neck angulation  $\leq$ 75°, and bilateral iliac artery diameter  $\leq$ 5 mm. Using the above-mentioned criteria, our findings indicated that 80% of ruptured AAA patients could be considered anatomically suitable for EVAR, and this is comparable to our clinical findings of treating over 120 ruptured AAA patients by endovascular means.

3. <u>Choice of Anesthesia and Approach</u>: Depending on ones comfort level and the logistics, EVAR for rupture can be performed under local anesthesia via percutaneous approach to general anesthesia and femoral artery cutdown. The percutaneous techniques have several limitations since currently available stentgrafts are delivered through large sheath sizes ranging from 18Fr-24Fr, and one has to be comfortable with obtaining percutaneous access and using closure devices in patients that might be hemodynamic unstable with difficult to palpate femoral pulses. In hemodynamic stable patients, particularly in the hands of experienced operators, these percutaneous procedures are quite feasible. We have reserved the percutaneous approach for endovascular aneurysm repair of ruptured abdominal aortic aneurysm in select patients that are considered to be hemodynamically unstable, are conscious, and can cooperate with the anesthesiologist and the vascular surgeon/interventionalists. In these patients we prefer to access the femoral artery percutaneously <u>without</u> a closure device, advance an appropriately sized sheath 18-22fr as needed and carry out the endovascular aneurysm repair procedure. At the completion of the endovascular procedure, the femoral sheathes are removed via femoral artery cut down and direct femoral artery repair.

4. <u>Aortic Occlusion Balloon</u>: The appropriate use of aortic occlusion balloons is hemodynamically unstable patients is vital to the success of EVAR in these emergent circumstances. Our preferred method for placing aortic occlusion balloons is to use the femoral approach, and we have found this to have several advantages: (1) it allows the anesthesia team to have access to both upper extremities for arterial and venous access; (2) the patients who require the aortic occlusion balloon are often hypotensive and, in these patients, percutaneous brachial access can be difficult and more time consuming than femoral cut-down; and (3) the currently available aortic occlusion balloons require at least a 12-F sheath, which requires a brachial artery cut-down and repair, and stiff wires and catheters across the aortic arch without prior imaging under emergent circumstances might lead to other arterial injuries and/ or embolization causing stroke. There are several important points to consider during procedures that require inflation of the aortic occlusion balloons to maintain hemodynamic stability. To facilitate stabilization of the balloon catheter during inflation and maintain aortic occlusion at the suprarenal/ supraceliac level, the sheath supporting the balloon should be advanced and supported fully into the aortic neck prior to inflation of the occlusion balloon as this will prevent downward displacement and prolapse of the occlusion balloon into the AAA. Inability to fully engage the sheath into the aortic neck due to the presence of significant aortoiliac stenosis, calcifications, or tortuosity might result in downward displacement of the inflated occlusion balloon; this often required forward traction on the inflated balloon catheter to maintain adequate position at the suprarenal/ supraceliac aorta. During the procedure, just prior to deployment of the stentgraft mainbody, the aortic occlusion balloon should be deflated from the suprarenal level and withdrawn. The stentgraft mainbody is subsequently deployed; this will avoid trapping the compliant aortic occlusion balloon between the aortic neck and the stentgraft. This temporary deflation of the aortic occlusion balloon rarely results in hemodynamic collapse and usually is of little consequence. In hemodynamically unstable patients, the occlusion balloon can be redirected into the aortic neck from the side ipsilateral to the stentgraft mainbody and re-inflated at the infrarenal aortic neck within the stentgraft mainbody; this allows for aortic occlusion and does not interfere with the remainder of the endovascular procedure.

5. <u>Abdominal Compartment Syndrome</u>: The pathophysiology of ACS after EVAR for ruptured AAA is multifactorial; 1) the retroperitoneal hematoma is a space-occupying lesion and a significant factor contributing to intraabdominal hypertension, 2) ongoing bleeding from lumbar and inferior mesenteric arteries into the disrupted aneurysm sac in the setting of severe coagulopathy might be a contributing factor, and 3) the shock state associated with ruptured AAA is associated with alterations in microvascular permeability that can lead to visceral and soft tissue edema. In our own series of EVAR for ruptured AAA in hemodynamically stable and unstable patients, the incidence of ACS was noted to be 18%, and several variables were identified as significant contributing factors. These include, 1) Use of aortic occlusion balloon, 2) need for massive blood transfusions (mean 8 units PRBC), and 3) coagulopathy with elevated aPTT at completion of case. In our experience, patients that developed ACS had a significantly increased mortality (67%) when compared to those without ACS (10%).

#### **TEVAR for Ruptured Thoracic Aortic Aneurysms**

TEVAR also has evolved from treatment of elective thoracic aortic aneurysms (TAA) to emergent acute thoracic aortic emergencies including ruptured TAA and traumatic thoracic aortic transections. Similar to ruptured AAA, Ruptured TAA are a life threatening emergency that have traditionally been associated with a significant mortality ranging from 35%-90%. Similar to ruptured EVAR, the potential benefit of ruptured TEVAR in decreasing the morbidity and mortality is all too obvious; however, there are several limitations that surgeons/ interventionists have to better understand to optimize outcomes of TEVAR for acute thoracic aortic emergencies, including advances and limitations of stent graft technology and imaging. A meta-analysis of contemporary published reports on ruptured TEVAR evaluated 29 studies that included 224 patients (mean age 70  $\pm$  5.6 years) with ruptured TAA; 143 (64%) treated with TEVAR, and 81 (36%) treated with open surgical repair. The results indicated that when compared to open surgical repair, the 30-day mortality for of ruptured TAA was significantly lower for TE-VAR (19% vs. 33%, P<0.05), and at 3 years the estimated aneurysm related survival was 71% in the TEVAR group. (2) Although the TEVAR patients had a trend towards lower morbidity, the differences in the immediate postoperative complications of myocardial infarction, stroke, or paraplegia among the 2 groups were not statistically significant. The complexities of ruptured TEVAR evolve around imaging, access, and dealing with the arch great vessels at the proximal stent graft landing zones and the visceral vessels at the distal stent graft landing zones. Furthermore, complications of stroke and spinal cord ischemia are additional risks that one has to consider

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when treating ruptured TAA patients via endovascular techniques. Although there are no set guidelines for cerebrospinal fluid (CSG) drainage during ruptured TEVAR, we generally follow CSF drainage recommendations similar to those during elective TEVAR; CSF drainage is reserved for patients with prior abdominal aortic reconstructions (endovascular and open surgical), and if extensive thoracic aortic coverage is planned extending form the subclavian to the celiac artery.

When planning TEVAR, particularly in emergent circumstances, the surgeon/ interventionist need to have a comprehensive understand of imaging; today CTA is most frequently used to evaluate patients with thoracic aortic emergencies and one has to be able to perform adequate measurements and select the appropriate stent grafts for TEVAR. Ruptured TAA limited to the descending thoracic aorta account for approximately one-third of all aortic emergencies and stent graft coverage of arch vessels, including the left subclavian and sometimes the left common carotid artery, which often require extra-anatomical carotid-subclavian and carotid-carotid bypasses. Furthermore, sometimes patients with ruptured TAA that have inadequate distal landing zones, and we need to evaluate the risks and benefits of celiac artery coverage to lengthen the distal stent graft landing zone. Data is scarce on this subject and recently we evaluated our single center findings of outcomes of planned celiac artery coverage during TEVAR for elective and emergent repair. (3) The study analyzed 228 patients that underwent TEVAR under elective (n=162, 71%) and emergent circumstances (n=66, 29%), of which 31 (14%) patients underwent planned celiac artery coverage during TEVAR. CTA was primarily used for a detailed evaluation of the gastroduodenal arcade with communicating collaterals between the celiac and the superior mesenteric artery (SMA), and intraoperative visceral arteriogram with selective celiac artery balloon occlusion for selectively used to identify the presence of these collaterals. The majority of patients had demonstrable collaterals between the celiac and the SMA (n=24, 77%), and postoperative complications included visceral ischemia in 2 (6%) patients, paraplegia in 2 (6%) patients, and death in 2 (6%) patients. All type 1b endoleaks (n=2, 6%) and type 2 endoleaks vial retrograde flow from the celiac artery (n= 3, 10%) were successfully treated by transfemoral coil embolization.

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## Perioperative Spinal Cord Protection During Thoracoabdominal Aortic Aneurysm Repair

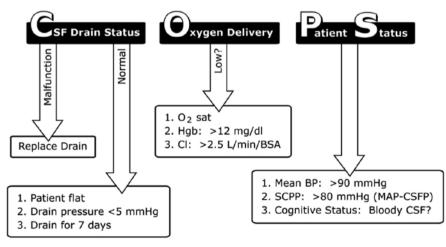
#### Anthony L. Estrera

Department of Cardiothoracic & Vascular Surgery, University of Texas Medical School Houston, USA

Thoracoabdominal aortic aneurysm (TAAA) repair remains one of the most challenging operative procedures in cardiovascular surgery. Although much advancement in this field has occurred over the past 2 decades, significant morbidity and mortality still remains. Since the 1960' s, TAAA repair in North America has evolved in its approach. Early in its inception, repair was originally undertaken using principles first used by E. Stanley Crawford. These included the reattachment approach of smaller vessels into larger vessels (inclusion technique) and the use of direct aortic cross clamping and direct repair using a Dacron graft. Although a great improvement since earlier repairs, significant morbidity remained with spinal cord injury being the most concerning. With paraplegia rates as high was 20-50% depending on the period of ischemia as well as the extent of the aneurysm, many sought ways to improve outcomes.

Using adjuncts of distal aortic perfusion and cerebrospinal fluid drainage, Hazim J. Safi, M.D. developed a program for TAA repair. Using these adjuncts as well as moderate hypothermia and aggressive intercostal artery reattachment, spinal cord injury incidence decreased to less than 1% for all TAAA and less than 4% for the most extensive of TAAA, the extent 2 aneurysm. As important, is the development of a post-operative protocol for the treatment of delayed paraplegia. (See Figure 1)

This lecture will provide details to our approach to TAAA repair and report on our outcomes.



#### TREATING DELAYED NEUROLOGICAL DEFICIT

Figure 1

**Fenestrated and Branched Experience.** 

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#### Eric L.G. Verhoeven

Department of Vascular and Endovascular Surgery, Klinikum Nürnberg, Germany

Endovascular aortic aneurysm repair (EVAR) has been established as an alternative to open surgical repair. One of the main limitations of EVAR is the need for a sufficient sealing zone below or above vital aortic branches. The last ten years, efforts have been made to overcome these limitations by incorporating fenestrations or branches in customized stent-grafts. First, short-necked infrarenal aneurysms were addressed. Later, juxtarenal- and suprarenal aneurysms were treated with the same technique. Finally, it became possible to treat thoraco-abdominal aneurysms by endovascular means. In addition, iliac branched devices allow us to treat (aorto) iliac aneurysms with preservation of flow into the internal iliac arteries.

The evolution of fenestrated and branched endovascular techniques is now enjoying increasing widespread. Many presentations and articles, albeit mainly from expert centres, have discussed technical feasibility, durability, limitations, and results. The results as reported are encouraging. Mortality and morbidity in fenestrated grafts for complex abdominal aortic aneurysms are in the range of standard EVAR, and remarkably consistent. Fenestrated grafts have proven to be stable and durable, provided technical success was achieved. Indeed most complications reported were due to incorrect technical outcome. Long term renal function deterioration remains a concern, but is probably induced by repeated contrast exposure due to yearly CTA follow-up. For Branched grafts in thoraco-abdominal aortic aneurysms, reported mortality is between 5 and 10%, which seems acceptable in view of the high-risk population treated. Indeed, every published series includes patient cohorts with 50-70% refused for open surgery. However, other (serious) complications including paraplegia and dialysis have been reported in low percentages. Late (unrelated) mortality is a concern and reminds us that not all high-risk patients should be treated.

My personal global experience (Groningen University Hospital, 2001 to 2009, and Klinikum Nurnberg, from 2009 onwards) now includes more than 350 fenestrated and branched cases. This experience has grown over the years in terms of more complex cases, but also in numbers per year. This has been made possible as a result of technical evolution of both stent-grafts and ancillary products, and further technical refinements. More difficult anatomy and thereby more patients can now safely be offered an endovascular solution.

The main limitation of these techniques is (extreme) tortuosity. Correct positioning of the main graft and catheterization of target vessels and positioning of the bridging stent-grafts are both tedious with unfavorable tortuous anatomy. Other important factors include the diameter and quality of the target vessels and their take-off angle.

These and other relative contra-indications need to be taken into account before offering these complex techniques to patients. However, it is clear that the major impact of open surgery, even in specialized centers and in selected patients, will continue to thrive fenestrated and branched endovascular techniques forward.

## TRANSAPICAL TRANSCATHETER AORTIC VALVE IM-PLANTATION - INFLUENCE OF A LEARNING CURVE ON CLINICAL OUTCOMES

## Matthias Thielmann<sup>1</sup>, D. Wendt<sup>1</sup>, S. Pasa<sup>1</sup>, P. Kahlert<sup>2</sup>, T. Konorza<sup>2</sup>, R. Erbel<sup>2</sup>, H. Jakob<sup>1</sup>

<sup>1</sup>Department of Thoracic and Cardiovascular Surgery, West German Heart Center, Essen, NRW, Germany, <sup>2</sup>Department of Cardiology, West German Heart Center, Essen, NRW, Germany

**Objectives** – Transapical transcatheter aortic valve implantation (TA-TAVI) has been suggested as an alternative to aortic valve replacement in high-risk patients with aortic stenosis. We describe our TA-TAVI learning curve by evaluating clinical outcomes in our entire experience with this novel procedure.

**Methods** – One-hundred-forty-eight consecutive high-risk patients (age:  $80.3 \pm 5.1$  years, logistic Euro-SCORE:  $34 \pm 15\%$ , STS-score:  $12 \pm 9\%$ ), representing our entire TA-TAVI experience between 10/2007 and 03/2011 were evaluated and stratified by the first (n=75) and the second half (n=73). Perioperative outcomes were used to evaluate the learning curve of TA-TAVI procedure, including operative and procedural time, as well as short-term morbidity and mortality.

**Results** – TA-TAVI was performed in a hybrid-OR using the balloon expandable Edwards-SAPIEN <sup>TM</sup> and SAPIEN XT <sup>TM</sup> (Edwards Lifesciences, Irvine, CA, USA) prosthesis, as well as the self-aligning Symetis Acurate TA <sup>TM</sup> prosthesis. Valve implantation was successful in all but one patient. Intraoperative mortality was 0.7% for the entire TA-TAVI group. There was no coronary artery obstruction or migration of the prosthesis. By comparing the first and second half of the TA-TAVI cohort, operative time (139 ± 30minversus 92 ± 21min, *P*<0.001), procedural time (55 ± 35min versus 31 ± 15min, *P*<0.001), and valve positioning and implantation time (8 ± 5min versus 2 ± 1min, *P*<0.001) as well as fluoroscopy time (6.8 ± 1.9min versus 3 ± 1min, *P*<0.001) decreased significantly between the first and second half, respectively. Contrast media could be reduced (226 ± 76mL versus 112 ± 28mL; *P*<0.001), leading to a lower incidence of renal failure (8% versus 2%). Predicted 30-day mortality for the first half was 40 ± 16% (logistic EuroSCORE) and 16.5 ± 9.8% (STS-score) compared to 26 ± 8% (logistic EuroSCORE) and 8 ± 5% (STS-score) for the second half (*P*<0.001). The observed 30-day mortality fell from 16% of the first half to 4% of the second half.

**Conclusion** – This single centre experience underlines that outcomes of this novel TA-TAVI procedure can improve significantly after a procedure specific learning curve.