**Meeting Abstracts**

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**4th International Meeting on Aortic Diseases: New Insights into an Old Problem**

Natzi Sakalihasan, MD, PhD *(course director)*

The main goal of The International Meeting on Aortic Diseases (IMAD) is to gather all cardiovascular clinicians and scientists to share their experiences on basic research, genetic aspects of aortic aneurysms, aortic dissections, aortitis, and their treatment as well as on the new pathophysiological concepts in bicuspid aortic valve, TAVI and surgical treatment of aortic valve diseases and also to provide information about the latest innovations in perfusion. Moreover, it is a great pleasure to share reflections with all worldwide scientists and clinicians interested in aortic diseases thanks to AORTA.

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**Scientific Program**

**Thursday, September 11 2014**

**Pathogenesis of AAA**

**Differences in the aneurysm wall could explain gender differences in prevalence rates and rupture risk**

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**Background:** The impact of gender on AAA is illustrated by both the difference in prevalence and the progression between the sexes. The male dominance in AAA prevalence suggests the aortic wall of men to be more prone to dilatation or the one in women to be resistant to it. The impact of gender on aneurysm formation might be related to an effect of sex hormones on the proteolytic activity, as illustrated in animal models.

On the other hand, the increased rupture risk in women with AAA, suggests the aneurysm wall of women to be less resistant. It is possibly related to biomechanical properties acquired during the course of the disease or an effect of “being female” on the continuous degradation.

The biomechanical properties of the aneurysm wall can be ascribed to its structural components: elastin, collagen and vascular smooth muscle cells (VSMCs). They are all susceptible to the degradation responsible for aneurysm disease, yet there is little knowledge of how these structural elements are altered in AAA of women and how it relates to the ones in men. A potential difference in these structural components of the aortic wall of men and women could help explain the difference in rupture risk between the sexes and possibly contribute to clarify if men are more susceptible to AAA formation or women more resistant.

**Note from the Editors:** The unedited abstracts from the 4th International Meeting on Aortic Disease are reproduced herein, as supplied by the organizers.

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**Methods:** Three different investigations based on biopsies of aneurysm wall from patients treated electively with open repair (n = 28, 32 and 40, respectively) and aortic wall from age- and gender-matched organ donors (n = 6) will be presented. Expression of elastin, elastolytic enzymes, collagen, collagen cross-linking (hydroxyl pyridinoline (HP) and lysyl pyridinoline (LP)) and markers of VSMCs and apoptosis, immunohistochemical, gene expression and western blot were analysed. HPLC were used for quantification of collagen and its crosslinking.

**Results:** The protein- and mRNA expressions of MMP-9 were greater in women compared with men (6.48 vs. 4.08, P = .037). Women had more LP than men (.14 vs. .07 vs. P = .005) and a lower HP/LP ratio (3.28 vs. 8.41, P = .003). Women with AAA had a greater proportion of apoptotic cells (.92 vs. .66, P = .005) and greater protein- and mRNA expressions of the apoptotic markers: tumor protein 53 (p53) and Bcl-2-associated X protein (BAX) (4.83 vs. 4.47, P = .045 and 4.55 vs. 4.10, P = .038).

**Conclusion:** The difference in rupture risk between men and women with AAA might be related to a less resistant aneurysm wall of women, due to more proteolytic enzymes, pronounced apoptosis and impaired collagen cross-linking in women with AAA. Analytical comparisons of aneurysm and aortic walls cannot solely explain the gender difference in aneurysm prevalence rates. The explanation to the different prevalence rates is dependent on further clarification of the pathogenic pathways of AAA, in both men and women.

**Novel mediators involved in oxidative stress and proteolysis in AAA**

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In the last years, there are evidences linking the presence of intraluminal thrombus (ILT) with the clinical evolution of AAA. The thrombus may participate in different pathological mechanisms, such as oxidative stress and proteolysis [associated to the presence of red blood cells (RBCs) and neutrophils], which could in turn induce a immune inflammatory, fibrotic and angiogenic response in the adventitia (associated to the presence of immune cells, fibroblasts and neovessels). Oxidative stress is defined as the balance of prooxidant and antioxidant proteins. A key mediator of oxidative stress observed in AAA is iron coming from RBC agglutination and lysis in ILT and/or neovessels in adventitia. We have observed that iron retention by phagocytes in AAA tissue could be associated to systemic increase in hepcidin and decrease in iron transport due to low transferrin levels. The subsequent functional iron deficiency leading to low haemoglobin levels is independently associated with AAA presence and clinical outcome. In the other hand, we have observed decreased antioxidant protein expression in RBC membrane of AAA patients (e.g. catalase and peroxiredoxin-2), further...
supporting a redox dysbalance in AAA. In addition, activated neutrophils releases different mediators of proteolysis, among them neutrophil gelatinase associated lipocalin (NGAL) which could favour aortic remodelling through neutrophil chemotaxis and/or by modulating matrix metalloproteinases (MMPs) stability and expression. In AAA patients, we observed increased NGAL levels in neutrophils and plasma, suggesting that NGAL could participate in AAA pathogenesis. On the whole, our data strongly suggest the involvement of RBC/iron dependent oxidative stress and PMN induced proteolysis as main mechanisms of AAA evolution.

Telomere shortening and oxidative stress in abdominal aortic aneurysm and varicose vein: comparing two dilative vascular pathologies

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Oxidative stress has been suggested as a key contributing factor for vascular diseases, but the exact mechanism underlying the alterations observed is not fully elucidated. The telomere is a simple repeating sequence of TTAGGG bases, located at the ends of chromosomes. Natural telomere shortening can be accelerated byiatrogenic or environmental factors including oxidative stress. Shorter telomere length (TL) is considered a good marker of cell aging and senescence, suggesting a key role in endothelial damage. We compared two vascular dilative pathologies such as Abdominal Aortic Aneurysm (AAA) and Varicose Vein (VV) in order to further evaluate the role of oxidative stress and telomere shortening in endothelial cell damage and vascular disease progression. AAA patients displayed shorter TL associated with increased oxidative stress not only in endothelial cells and vascular smooth muscle cells but also in circulating lymphocytes and keratinocytes suggesting the systemic nature of the disease. At vascular tissue level, VV patients had shortened telomere and high oxidative stress, similarly to AAA patients. Conversely, blood lymphocytes from VV patients had TL similar to healthy controls and significantly longer than the same cells from AAA patients. Moreover, oxidative stress in plasma from VV patients was significantly lower than from AAA group. Linear regression analysis showed a statistically significant inverse correlation between blood lymphocytes TL and plasma level of oxidative stress. Our results suggest that, unlike AAA, telomere attrition in VV tissue is not a systemic phenomenon but it may be attributable to tissue microenvironment conditions and possibly to high local oxidative stress.

Short communications from selected papers

Role of natural killer cell cytotoxicity pathway in human abdominal aortic aneurysms

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Objective: The goal of this study was to investigate the role of Natural Killer Cell Mediated Cytotoxicity Pathway in the pathobiology of human abdominal aortic aneurysms (AAAs).

Methods and Results: A genome-wide microarray expression profiling identified 3,274 differentially expressed genes between aneurysmal and control aortic tissue with False Discovery Rate (FDR) of < 0.05. Analysis of biological pathways, including Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG), indicated extreme overrepresentation of immune related categories. The enriched categories included the GO category Immune Response (GO:0006955; FDR = 2.1 × 10⁻⁹), and the KEGG pathways Natural Killer (NK) Cell Mediated Cytotoxicity (hsa04650; FDR = 5.9 × 10⁻¹⁰). In this pathway, 47/86 (55%) of the expressed genes were significantly different between AAA and the controls. We studied the protein expression of 9 different members of the NK Cytotoxicity Pathway in human AAA and compared the results to aortic tissue samples taken from the infrarenal aorta of age- and sex-matched controls. Eight (VAV1, VAV3, PLCG2, HCST, TYROBP, PTK2B, TNFA, and GZMB) of the corresponding mRNAs of these proteins had been shown to be significantly elevated and one (PLCG1) significantly decreased in AAA compared to non-aneurysmal aortae. Immuno-chemical analyses agreed with the mRNA results. Double staining was carried out with antibodies against CD68 or CD8 together with DAP10 (HCST), DAP12 (TYROBP), PTK2B or PLCG2. Many inflammatory cells, mainly in the adventitia and media in the AAA wall stained positive for PLCG2, but only a few of those cells expressed CD8. Double staining was also seen with anti-CD68 and anti-TYROBP as well as with anti-CD68 and anti-PLCG2 indicating that macrophages express TYROBP and PLCG2. PTK2B expression was seen in many cell types, including CD8-positive leukocytes.

Conclusions: These results provide strong evidence that the NK Cytotoxicity Pathway plays a role in human AAA. Based on our microarray and immunohistochemical studies, the pathway is activated in AAA. The data provide valuable insight for future studies to dissect the pathogenesis of human AAA.

Transglutaminase 2—a potential role in aneurysm progression?

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Abdominal aortic aneurysms (AAA) are dilatations of the abdominal aorta that are prone to rupture with fatal consequences. Although the pathogenesis of AAA is multifactorial, AAAs are characterised histologically by a reduced elastin:collagen ratio, thinning of the aortic media and elastin breaks. Elastin is cross-linked to accessory proteins, by the action of transglutaminase 2 (TG2) and this may provide a means of protecting elastin fibres from proteolysis. TG2 has been shown to be induced in experimental aneurysm development, has been implicated in arterial repair and may also play a distinct role after injury, and in line with this, we have seen intense immunohistochemical staining for TG2 in samples obtained from elective AAA surgery.

Mice floxed in the TG2 gene were crossed with transgenic mice expressing cre-recombinase in the germline to generate TG2+/− mice on a stable C57Bl/6 background. At 8-weeks of age these mice underwent laparotomy under anaesthesia and either normal saline, 0.25M CaCl₂ or 0.5M CaCl₂ was applied to the ventral surface of the exposed aorta. Vessel measurements pre-injury were obtained from calibrated captured images using Image Pro Software v7.0 (MediaCybernetics, USA) and were repeated at the time of euthanasia at either 6-weeks or 6-months post-surgery.

There was no difference between male control (C57Bl/6) and TG2+/− mice in pre-injury aortic diameter although the female control aortas were slightly larger (0.55 vs. 0.52 mm, p = 0.003). Neither group showed a significant increase in aortic diameter following saline application. Application of 0.5M CaCl₂ resulted in a larger % increase in aortic diameter than 0.25M CaCl₂ in both the control (74.4% vs. 36.5%) and the TG2−/− (91.8% vs. 25.0%) mice at 6-weeks. There was, however, no significant difference between the two genotypes at this time-point. At 6 months the mean aortic diameter in the C57Bl/6 group was 67.4% greater than at baseline, i.e. the dilatation was similar (or improved) compared to that at 6-weeks. In contrast, vessel diameter increased by 183.1% in the TG2−/− group indicating further progression. These initial data suggest that aneurysm initiation and progression may be distinct processes and that TG2 may have a role in the latter, possibly through its arterial repair function. Further work is planned to confirm these findings and to investigate the role of the homologous enzyme FXIII-A in aneurysm development.
Modulation of abdominal aortic aneurysm vascular smooth muscle cell function by pharmacological inhibition of the native Orai1 Ca^{2+} channel

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Introduction: Loss of medial vascular smooth muscle cells (VSMCs) is a key histopathological feature of end stage abdominal aortic aneurysm (AAA) disease. Maintenance of the VSMC population in early stage disease (e.g. at screen detection) is a potential therapeutic avenue to attenuate AAA progression. We have previously demonstrated that store operated calcium entry (SOCE) through the Orai1 Ca^{2+} channel can manipulate human VSMC function [1]. Here we investigate if beneficial functional modulation can be achieved in VSMC from human AAA by blocking the Orai1 channel with our novel, potent and specific small molecule inhibitor, JPIII.

Methods: VSMC were explanted and cultured from patients undergoing open AAA repair with ethical approval as previously described [2]. Gene expression was studied by rTPCR, calcium imaging using the ratiometric Ca^{2+} indicator dye, Fura-2AM with SOCE stimulated by thapsigargin (TG) or platelet derived growth factor (PDGF) and functional assays (proliferation, migration, apoptosis) by time lapse fluorescence microscopy with an IncuCyte FLR. The novel SOCE inhibitor JPIII was assessed for specificity (HEK Cells) and potency was assessed in the A7r5 VSMC cell line. JPIII responses were compared to vehicle control (dimethylsulfoxide) in all experiments using the AAA VSMC. The pharmacological studies were complemented by similar experiments comparing VSMC explanted from murine aortas of mice expressing a pore-dead, dominant-negative mutant of Orai1 (R97W) to littermate control explanted cells. Results were analysed for statistical significance using ANOVA with Bonferroni correction with a p < 0.05 taken to be statistically significant.

Results: The transcripts for the Orai1 channel and its Ca^{2+} store sensor, STIM1, were detectable in the human AAA VSMC. JPIII was potent and specific for SOCE in A7r5 cells. SOCE was observed in response to TG and PDGF in the AAA VSMC and could be blocked by JPIII. In the functional experiments JPIII inhibited PDGF driven migration into a linear wound (p < 0.05) and proliferation over 7 days (p < 0.01) compared to the vehicle control. In addition, JPIII protected the AAA VSMC from staurosporine induced apoptosis compared to vehicle control treatment (p < 0.01). Similar results were observed in the murine aortic VSMC expressing the dominant negative Orai1 mutant.

Conclusion: SOCE is present in human AAA VSMC and can be inhibited by the novel drug JPIII with beneficial functional effects on proliferation, migration and apoptosis. Inhibition of the Orai1 channel warrants further study as a potential therapeutic avenue for human AAA disease.

What’s new in the genetics of thoracic aortic aneurysm?

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Genome wide association studies (GWAS) have become a widely used tool for the identification of disease loci. To date, individual GWAS, combined with multi-centre followup validation, have identified six loci (CDKN2BAS1, DAB2IP, LRP1, IL6R, LDLR, SORT1) associated with abdominal aortic aneurysm (AAA). Combining individual GWAS using metaanalysis dramatically improves the statistical power to detect associations at genome wide significance.

A meta-genome wide association study was performed using six GWAS case-control cohorts from the United Kingdom (n = 1846 AAA cases / 5435 controls), Netherlands (n = 813/2790), United States (n = 725/1231), New Zealand (n = 608/612 & n = 397/387) and Iceland (n = 430/22000). Independent validation using additional cases and controls (~5000 of each) is currently being undertaken. The meta-GWAS identified all the previously reported loci as being amongst the most significant associations. The top hit was CDKN2BAS1 (lambda inflation adjusted p-value 5.8 x 10^{-12}). Other previously reported regions had values of; LDLR p = 2.8 x 10^{-12}, IL6R p = 7.4 x 10^{-10}, LRP1 p = 1.1 x 10^{-9}, SORT1 p = 4.5 x 10^{-9}, DAB2IP p = 4.6 x 10^{-7}. An additional 16 previously unreported AAA loci are currently undergoing independent validation. Of the 22 putatively identified AAA loci 7 are associated with coronary artery disease (CAD) in the CARDIOGRAM meta-analysis.

In conclusion, AAA meta-GWAS analysis appears likely to significantly increase the number of genetic loci associated with AAA. Importantly, several biologically plausible regions have not been previously associated with atherosclerotic arterial disease and may, therefore, represent AAA specific pathobiological mechanisms.

This work is presented on behalf of the AAA Meta-GWAS consortium.

Decision Making from Gene to Intervention for the Marfan Syndrome

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Background: Marfan syndrome (MFS) is an autosomal dominantly inherited connective tissue disease with a phenotype that involves many organ systems and that is caused by mutations in the gene coding for fibrillin-1, FBN1. Aneurysms of the aortic root give rise to the high mortality of MFS. Until today, prophylactic surgery with replacement of the aortic tissue is the single prophylactic measure that prevents patients from suffering acute dissection or rupture of the aorta. In Marfan patients timing of elective surgery hinges upon the aortic diameter, where operations are usually recommended at measurements between 4.5 and 5.0 cm. The problem is that the clinical presentation of Marfan is often indistinguishable from other genetic aortic syndromes (GAS). These GAS comprise syndromes such as the Loeys-Dietz syndrome (LDS) types 1-4, the vascular Ehlers-Danlos syndrome (vEDS), osteogenesis imperfect (OI) or familial thoracic aneurysm/dissections (TAAD).

Methods: We present international guidelines with specific recommendations for elective aortic root replacement according to different GAS and we review the diagnostic criteria of these GAS.

Results: Recommendations for timing of elective surgery depend on the diagnosis of a specific GAS. The firm diagnosis of these GAS requires demonstration of a specific mutation in the FBN1 gene for Marfan syndrome, in the TGFBR1, TGFBR2, TGFBR2, or SMAD3 gene for LDS, of COL3A1 gene for vEDS, or COL1A1, or COL1A2 genes for OI, and ACTA2, MYH11 or MYLK genes for TAAD.

Conclusion: Decision making for elective surgery in GAS should be based on clinical and molecular diagnosis of GAS.
Thoracic aortic aneurysm/dissection (TAAD) is an important cause of death in industrialized countries. TAAD often occurs in the young and many patients have a positive family history, which indicates that genetic factors significantly contribute to the etiology of TAAD. Up to now, several genes have been identified for both syndromic and non-syndromic forms of TAAD: FBN1 for Marfan syndrome, TGFBR1, TGFBR2, TGFBR2 and SMAD3 for Loey-Dietz syndrome, COL3A1 for vascular Ehlers-Danlos syndrome, EFEMP2 for autosomal recessive cutis laxa type 1, SLC2A10 for arterial tortuosity syndrome, SKI for Shprintzen-Goldberg syndrome, MYH11 for TAAD with patent ductus arteriosus, ACTA2 for TAAD associated with stroke, premature coronary disease and patent ductus arteriosus, NOTCH1 for calcified bicuspid aortic valve associated with TAAD, FLNA for the combination of periventricular nodular heterotopia and TAAD, and MYLK and PRKGI for non-syndromic TAAD. So far, the products of the non-syndromic genes (including ACTA2 and MYH11) all function in the contractile apparatus of the vascular smooth muscle cell, while several of the syndromic gene products are part of the TGFβ signalling pathway. The study of the pathophysiological mechanisms involved in the Marfan and Loey-Dietz syndromes has further emphasized the central role of TGFβ signalling in TAAD. Given the technological revolution that next generation sequencing has caused, many additional gene identifications are expected. It remains to be seen whether these new genes will also be part of the vascular smooth muscle cell contractile apparatus or the TGFβ signalling pathway, or that additional pathways will be revealed.

**Short communications from selected papers**

Genetic variants in SEPP1, SEL5, TXNRD2, GPX4 and SOD2 are associated with peripheral atherosclerosis and poor left-ventricular function in a comprehensive analysis of polymorphisms in selenoprotein genes in AAA and AIOD

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**Objectives and Aim:** Enhanced oxidative stress contribute to cardiovascular diseases. Selenium, as a component of selenoproteins, protects tissues from oxidative damage and thus have beneficial effects to cardiovascular system. In this study the role of common genetic variants in selenoprotein genes: SEPP1, SEL5, TXNRD1, TXNRD2, GPX4 and SOD2 gene in the development of abdominal aortic aneurysm (AAA) and aortoiliac occlusive disease (AOID) were evaluated.

**Materials and Methods:** In this case-control study patients with AAA, AOID, and controls were analyzed. Patients were characterized in terms of coronary and non-coronary atherosclerosis and its complications. Genotyping was performed using the TaqMan-based assays.

**Results:** The significantly decreased frequency of the homozygotes of the GPX4 variant allele in AAA, as compared to AOID was found (P < .05). This difference was enhanced by a two-loci interactions between GPX4 and SEL5, TXNRD2 or SOD2. The associations of SEPP1 coding sequence variant with decreased left-ventricular ejection fraction in patients (P < .01) and coexistence of peripheral atherosclerosis in AAA (P < .05) were also found.

**Conclusions:** This study identifies variant alleles of the selenoprotein genes and SOD2 gene as potential genetic markers that indicate stronger predisposition to occlusive types of vascular diseases and its complications, than to AAA. The work has been supported by the NSC in Poland under grant No. NN403250440.

Familial vascular Ehlers-Danlos syndrome caused by a mutation in COL5A1

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Different forms of Ehlers-Danlos Syndrome (EDS) exist, with specific phenotypes and associated genes. Vascular EDS, caused by heterozygous mutations in the COL5A1 gene, is characterized by a fragile vasculature with a high risk of catastrophic vascular events at young age. Classic EDS, characterized by fragile, hyperextensible skin and joint laxity, is caused by heterozygous mutations in the COL5A1 and COL5A2 genes. To date, vessel rupture in four unrelated classic EDS patients with a confirmed COL5A1 mutation was reported. We describe a familial case of clinically vascular EDS, diagnosed in a mother and her two sons, who all died at an early age from arterial ruptures. Diagnostic Sanger sequencing in the proband failed to detect aberrations in COL5A1, COL1A1, COL1A2, TGFBR1, TGFBR2, SMAD3 and ACTA2. Next, the proband’s DNA was analyzed using a next-generation sequencing approach targeting 554 genes linked to vascular disease (VASCULOME project). This revealed a novel heterozygous mutation in COL5A1, resulting in an essential glycine substitution in the triple helix domain, nearby the C-terminus of the protein (c.4610G>T; p.Gly1537Val). This mutation was also present in DNA isolated from autopsy material of the index’s brother. No material was available from the mother, but the mutation was excluded in her parents, siblings and in the father of her sons, suggesting that the COL5A1 mutation occurred in the mother’s genome de novo. This is the first report of familial clinical diagnosed vascular EDS with a mutation in COL5A1 displaying a similar phenotype to that caused by a COL3A1 mutation.

Diagnostic and prognostic biomarker potential of miR-24 in abdominal aortic aneurysm disease and rupture

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MicroRNAs (miRNAs) have been identified as crucial posttranscriptional inhibitors of gene expression in response to stress and injury in cardiovascular disease (CVD) by regulating the expression levels of their target mRNAs. Lately, they have received much attention regarding their suitability as biomarkers for CVD. Aim of this current study was to explore the diagnostic and prognostic value of detecting circulating levels of miRNAs in AAs. Using a PCR-based array platform, we profiled the 168 most abundant blood miRNAs from 20 samples from an age, risk factor, and medication matched screening cohort without aneurysm. We were able to identify a total number of 12 miRNAs that were significantly altered in diseased patient samples as compared to controls. Next we investigated these 12 miRNAs in plasma (as well as in aortic tissue) from ApoE−/− mice with angiogenesis (AngII)-induced AAAs, in order to determine the potential prognostic value of miRNAs being released into circulation. Indeed we were able to detect that the expression of 4 out of the 12 miRNAs (miRs-126 and -668 both increased; miRs-24 and -210 both decreased), was substantially altered in

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plasma samples drawn from AAA mice immediately before rupture occurred between days 10 and 14 after AngII pump implantation compared to mice with AAA that did not rupture for the remainder of study (28 days), as well as saline-infused controls. Using the AngII model, as well as a second mouse model of AAA disease, the porcine-pancreaticelastase infusion model, we were able to show that overexpression of miR-24 protects from aneurysm progression (in the PPE model), as well as aortic rupture (in the AngII model) by repressing the expression of a target gene called chitinase3-like1 (Chi3l1), which regulates macrophage survival and cytokine release (from invading peritoneal macrophages). Finally, the expression of miR-24 was significantly and substantially different in plasma samples from human patients with acutely ruptured AAs (n = 7) compared to patients with non-ruptured AAs (abdominal aortic diameter between 55–78 mm; n = 7) undergoing surgical repair, as well as un-diseased controls (n = 7). The present study explores the diagnostic and prognostic biomarker potential of miRNAs being released into circulation during AAA propagation in mice and humans. The identification of miR-24 potentially offers great prognostic value to determine which patients present with increased risk of rapid AAA expansion and subsequent rupture.

Circulating microRNA expression signature in PET positive abdominal aortic aneurysms: new potential biomarkers
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Rupture of abdominal aortic aneurysm (AAA) is a cause of significant mortality and morbidity in aging population. Its prediction is a challenging issue in the field of vascular diseases. Recently, we showed that a positive uptake of fluorodeoxyglucose (FDG) in the aneurysmal wall observed by positron emission tomography (PET) was correlated with higher instability of the wall which could lead to its rupture [1]. Identifying circulating biomarkers correlated with a positive PET could help discriminating patients at higher risk of rupture. During last decade, small non-coding RNA, miRNA, that are potent post-transcriptional regulators of gene expression, were found to be present in blood and to represent valuable biomarkers for a variety of diseases, notably in cancers.

We evaluated the expression level of 372 miRNAs by using the miScript PCR system (Qiagen) in the plasma of 45 AAA patients among which 24 displayed no FDG uptake (A0) and 21 had a positive PET (A+). In a first approach, 4 pools of plasma samples from the A0 and the A+ groups were analyzed. 45 miRNA were found significantly modulated (p < 0.05) in A+ (26 downregulated and 19 upregulated) as compared to A0. Among them, miR-155 and miR-204 were found to be, respectively, upregulated and downregulated in A+ patients. A similar modulation of these two miRNAs was previously observed in the aortic tissue and blood of AAA patients compared to healthy donors [2,3].

This preliminary study identified a series of miRNAs as potential new biomarkers of PET+ AAA, at high risk of rupture. These results need to be validated on an individual basis and extended to a larger group of patients. However, by crossing data from transcriptomic analyses of aortic tissues from A0 and A+ patients (manuscript in revision) and known target genes of the modulated miRNAs, relevant signaling pathways involved in risky AAA progression will be soon identified.

References

Introduction: Since it has been shown that targeted ultrasound screening of persons at high risk allows reduction of AAA related mortality, a better risk prediction model based on clinical characteristics and biomarkers is needed to earlier identify persons at risk.

Methods: We aim to identify molecular markers for AAA by identifying genes, pathways and cellular mechanisms involved in remodeling of the vascular wall of the aorta in AAA. Structured family histories are obtained in an ongoing family study including all AAA patients from the Erasmus MC Vascular Surgery Clinic since 2009. Participants are offered information and aneurysm ultrasound family screening. WES, WGS and CN analysis are performed. To understand the effects of genetic variants and mechanisms predisposing to AAA, gene expression analysis in blood, fibroblasts and affected aortic tissue are studied. Mouse models and human cellular models are used to identify underlying pathways and molecular mechanisms predisposing to AAA.

Results: In our gene expression studies, we found genes which have been associated with AAA before, like COL11A1, Adiponectin, LPL. This underscores the validity of our screening approach. Using Ingenuity IPA we identified immune and fat metabolism related pathways. Interestingly also expression levels of genes involved in the Renin-Angiotensin System (RAS) and the TGFβ signal- ing were significantly changed. For the novel markers, pathways and key regulators we designed a flow chart to select genes based on their level of expression, potential as blood marker and possible relevance for aneurysmal disease. This will allow us to make selection of genes to be further studied in blood of AAA patients. As a next step, we will validate these markers in experimental models for aneurysmal disease. Via whole exome and genome sequencing in addition to linkage studies in structured AAA families we have identified a candidate pathogenic variant with dominant inheritance pattern for which we are currently performing functional testing.

Conclusions: Our gene expression profiling approach not only identifies genes and pathways previously associated with AAA genes, but also reveals novel genes and key regulators that will shed light on the processes involved in AAA formation and progression. Our approach of whole exome and genome sequencing with linkage analysis in structured families has been validated by the identification of a new candidate pathogenic variant that has not been associated with AAA before. Further validation experiments will be necessary to confirm our novel findings.

Reinventing pathophysiology of AAA: dystrophic changes
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Introduction: The abdominal aortic aneurysm (AAA) is a localized dilatation of the infrarenal aorta due to weakening of the vessel wall. Although the exact pathophysiologic mechanism is unknown it is generally accepted to be a chronic, inflammatory disorder coupled with an imbalance in matrix homeostasis. However, pharmacologic interventions targeting the immune system or matrix degradation have proven ineffective in humans. In fact, immunosuppression in the setting of solid organ trans-
plantation and treatment with protease inhibitor doxycycline leads to accelerated aneurysm growth. These findings suggest a role for additional pathophysiologic mechanisms most importantly impaired tissue repair.

Methods: Aortic aneurysmal vessel wall tissue was collected from 10 patients undergoing elective, open aneurysm repair. Control tissue from 10 multi-organ donors was obtained from the infrarenal aorta. Tissue samples were handled and processed for immunohistochemical and RNA analysis in accordance with local ethical guidelines.

Results: Evaluation of vascular tissue repair pathways show the uniform activation of the Hedgehog, Wnt, Notch, TGFβ, BMP and FGF pathways (p < 0.05) in mesenchymal AAA cells through increases in their downstream transcription factors. Immunohistochemical evaluation of mesenchymal cells responsible for vascular repair revealed a phenotypical shift of VSMC towards a synthetic cell type (p < 0.01), validated by the decreased expression of miR-143 (p < 0.001) and 145 (p < 0.05) as crucial regulators of the contractile VSMC phenotype. Gene expression of collagens I and III are increased 2-fold (p = 0.09) and 44-fold (p < 0.01) respectively combined with increased collagen presence in spectral imaging (p < 0.001) in AAA. Further evaluation shows the increased presence of PPARγ (p < 0.05), consistent with findings in dystrophic disorders.

Conclusion: Results from this study characterize AAA as a dystrophic disorder and implicate dystrophy as novel pathophysiological mechanism. These new findings could be responsible for the failure of pharmacologic interventions and simultaneously present new targets for pharmacological treatment of this chronic disorder.

Pioglitazone competes with EGR1 to suppress PKD1 in angiostin II-treated macrophages
Nicoletta Charolidi, Evelyn Torsney, Grisha Pirianov, Ken Laing, Axel Nothurfft, Gillian W. Cockerill
St. George’s, University of London, London, United Kingdom

Aims: Peroxisome proliferator-activated receptor γ (PPARγ) agonists have been shown to inhibit Angiostin II-induced experimental abdominal aortic aneurysms. Since increased macrophage infiltration in the vascular wall is a hallmark for initiation of aneurysmal pathology, we set out to explore the effects of the PPARγ agonist pioglitazone on Angiostin II-treated, phorbol-ester-differentiated monocytes, with the scope to identify molecular changes that may be responsible for the infiltrating phenotype of macrophages.

Approach and Results: Using microarray-based expression profiling of phorbol-ester-stimulated THP-1 monocytic leukemia cells, we found that Angiostin II (Ang II) or Ang II and pioglitazone were able to cause a number of aneurysm-related gene changes. Among those, polycystic kidney disease 1 (PKD1) was significantly up-regulated. Mutations that lead to changes in PKD1 expression are the main cause of autosomal dominant polycystic kidney disease, which is linked to increased incidence of aneurysms. Online-software analysis of the PKD1 proximal promoter revealed a putative Early Growth Response 1 (EGR1) binding site, which we confirmed by chromatin immunoprecipitation (CHIP) and quantitative real time (RT) PCR. Further analyses of publicly available ChIP-sequencing data (ENCODE project) revealed that this putative binding site in the PKD1 proximal promoter overlapped with a conserved EGR1-binding peak present in 5 other cell lines. Quantitative RT-PCR showed that EGR1 suppressed PKD1, while Ang II significantly up-regulated PKD1, an effect counteracted by pioglitazone. Conversely, in THP-1 cells that were lenti-virally transduced with EGR1 shorthairpin RNA, reduced EGR1 levels led to significant up-regulation of PKD1, especially after treatment with pioglitazone.

Conclusion: PKD1 is an EGR1-target gene that is suppressed during monocytic differentiation at the time of EGR1 expression. Ang II treatment up-regulates the expression of PKD1 and pioglitazone mediates the opposite effect by displacement of EGR1 from their shared binding site in the PKD1 proximal promoter through a mechanism that requires further investigation.

Fibrin clot structure in the angiotensin ii murine model of abdominal aortic aneurysm
Katherine Bridge, Fraser Macroe, Marc Bailey, Nadira Yuldasheva, Stephen Wheatcroft, D Julian Scott, Robert Ariens
University of Leeds, Leeds, United Kingdom

Background and Aims: Patients with AAA form denser clots which are resistant to fibrinolysis [1]. In-vivo modelling is commonly used for the assessment of disease states and the identification of potential therapies. The aim of this study was to assess the fibrin clot structure in a murine model of AAA, and in doing so develop assays which can be used to quantify changes in clot structure when novel therapeutics are tested in-vivo.

Methods: Male, ApoE−/− mice were infused with either Angiostin II (AngII) or 0.9% NaCl (control) using subcutaneous mini-osmotic pumps [2]. After 28 days, blood was collected from the IVC onto sodium citrate, and aortas photographed in situ. Fibrin clot structure was studied turbidity, turbidity/lysis, and confocal microscopy. Plasma levels of D-dimer were measured using ELISA. Aortic size and clot density were measured using Image-J. Results are presented as mean ± standard error of the mean.

Results: Fifteen mice (7 AngII and 8 controls) were included. The abdominal aorta, thoracic aorta and aortic ratio (abdo/thoracic) were all significantly larger in Ang II mice Ang II than controls (Abdominal aorta 1.9 ± 0.3 mm vs 0.6 ± 0.1 mm, p < 0.001, thoracic aorta 1.1 ± 0.1 mm vs 0.6 ± 0.1 mm, p = 0.003, ratio 1.7 ± 0.2 vs 1.0 ± 0.1, p = 0.001). Fibrin clots produced using plasma from Ang II mice tended to form quicker (11.1 ± 1.0 min vs 13.5 ± 0.8 min), have higher maximum absorbance (0.10 ± 0.03 vs 0.09 ± 0.01), and slower lysis (50.6 ± 8.8 min vs 41.2 ± 5.3 min) compared with controls, although these results failed to reach statistical significance. Fibre density was not significantly different between Ang II mice and controls (286.3 ± 130.2 vs 361.3 ± 88.7 fibres per 100 µm2), and D-dimer levels did not vary between the two groups (88.5 ± 133.8ng/ml vs 842.1 ± 62.2ng/ml).

Conclusion: Fibrin clot structure is not significantly altered by infusion of AngII and AAA formation in an in-vivo model, suggesting that the abnormal fibrin structure in patients with AAA may be due to more complex, chronic inflammatory-coagulation interactions.

References

Epidemiology of AAA

Five-year outcomes in men screened for AAA population-based cohort study
Sverker Svensjö, Martin Bjöck, Anders Wanhainen
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Acquiring contemporary data on prevalence and natural history of abdominal aortic aneurysms (AAA) is essential in the effort to optimize modern screening programs. Since the start of a AAA screening programme, targeting 65-year-old men, in Uppsala, Sweden, in 2006, a pending longitudinal population-based cohort-study was initiated offering all men in the County of Uppsala AAA-screening every 5-years, at the age of 65, 70, 75 and 80 years. This is a first analysis of that initiative.

Out of 2736 men screened at age 65 (2006–2007); 24 had completed AAA repair (6 died within 0–4 years), 239 had died, and 194 had moved, after 5 years (2011–2012). Thus, 2811 70-year old men were re-invited, and 2247 (79.9%) attended.
The AAA prevalence increased from 1.5% at age 65 to 2.4% at age 70. Of 2041 men with $<25$ mm at age 65, 0.7% had developed an AAA at age 70. Of 40 men with a sub-aneurysmal aorta (25–29 mm) at age 65, 52.5% progressed to AAA at age 70. In a Cox regression analysis; sub-aneurysmal aorta at age 65 (Hazard Ratio 59.78), and smoking (Hazard Ratio 2.78) were independent risk factors for AAA formation. Among 44 men with a screening detected AAA at age 65, 22 (50%) completed AAA repair with no 30-day mortality. During the 5-year follow-up period no ruptures occurred among those attending screening at age 65. Among 532 non-attenders at age 65, one had elective repair for an opportunistically detected AAA at age 66 and one had emergency repair for a ruptured 70 mm AAA at age 69 and died during surgery.

In conclusion, AAA screening in a contemporary setting is safe at 5 years, with a single AAA rupture among non-attenders. AAA formation was common among men with subaneurysmal dilatation, indicating a possible need for surveillance of this group.

10-Year follow-up of the Western Australia randomized trial of AAA screening
Paul Norman
University of Western Australia, Fremantle, Australia

**Background:** The Western Australian randomised controlled trial of screening for abdominal aortic aneurysm (AAA) began in 1996 and the mid-term results were reported in 2004. The long-term (12 year) results are now available. Although the original trial included men aged 65–83, the latest update focusses on men age 65–74 years. The latest update focusses on men age 65–74 years. The latest update focusses on men age 65–74 years.

**Methods:** Men aged 65–74 years were identified through the electoral roll and randomised to Invitation for screening (n = 13,266) and Control (n = 13,239) groups. Screening using ultrasound was under taken in 1996–9 and subsequent AAA procedures and mortality were monitored using record linkage of Health Department records from 1996–2010.

**Results:** The attendance rate was 68% and the prevalence of AAAs $\geq 3$ cm was 6.6% and $\geq 5.5$ cm was 0.4%. At a median follow-up of 12 years, 48 men in the Invitation for screening group and 52 in the Control group died from AAA — a rate ratio of 0.92 (95%CI 0.61 – 1.38).

**Conclusions:** Using the Australian electoral roll to identify and invite men aged 65–74 years for screening for AAA, results in a relatively small reduction in mortality from AAA.

Characteristics and outcomes of men screened vs not screened for AAA in Sweden
Rebecka Hultgren
Dep Vasc Surgery, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden

**Background:** The rationale and cost effectiveness of screening for AAA in elderly men has been thoroughly investigated. Based on these results; screening for AAA in elderly men started in some selected counties in Sweden in 2005, and by 2013 screening was offered to most elderly men nationally. Sweden has a population of 9.7 million inhabitants, and only the smallest county (57000 inhabitants) has chosen not to screen. The nationally. Sweden has a population of 9.7 million inhabitants, and only the smallest county (57000 inhabitants) has chosen not to screen.

In conclusion, AAA screening in a contemporary setting is safe at 5 years, with a single AAA rupture among non-attenders. AAA formation was common among men with subaneurysmal dilatation, indicating a possible need for surveillance of this group.
References

Surveillance of small AAA
Simon Thompson
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The international RESCAN project collated individual data for patients under surveillance for small AAA (diameter 3.0–5.4 cm). The aims were to assess the determinants of growth and rupture rates, and to provide evidence on the cost-effectiveness of different surveillance intervals. A total of 18 studies provided data with repeated ultrasound measurements of AAA diameter over time in 15,471 patients [1].

For each 0.5 cm increase in AAA diameter, growth rates increased by about 0.6 mm per year and rupture rates approximately doubled. To limit the risk of rupture between surveillance scans to less than 1%, surveillance intervals of 2 years for aneurysms measuring 3.0–3.9 cm, 1 year for 4.0–4.9 cm, and 6 months for 5.0–5.4 cm, would suffice [2]. These intervals would also limit the risk of reaching the 5.5 cm surgical threshold before the next scan to below 10%, but are longer than those currently used in most countries. If adopted, they would reduce the number of surveillance scans undertaken and their associated costs, but could slightly increase rupture rates. In an evaluation of the surveillance intervals used by the UK national screening programme, we have shown that increasing the surveillance interval for 3.0–4.4 cm aneurysms from 1 to 2 years is likely to be cost-effective, while increasing the interval for 4.4–5.4 cm aneurysms from 3 months is not similarly cost-effective [1].

Growth rates of small AAA are increased in smokers, but decreased in patients with diabetes. Rupture rates in the small AAA range are almost fourfold higher in women than men, are doubled in smokers, and increase with higher blood pressure [3]. While such factors could theoretically be taken into account to tailor surveillance intervals for each individual, the effects are generally not substantial enough to justify the consequent organisational difficulties. An exception is the sex difference in rupture rates. In an evaluation of the surveillance intervals used by the UK national screening programme, we have shown that increasing the surveillance interval for 3.0–4.4 cm aneurysms from 1 to 2 years is likely to be cost-effective, while increasing the interval for 4.4–5.4 cm aneurysms from 3 months is not similarly cost-effective [1].

Do hernias contribute to increased severity of aneurysmal disease among abdominal aortic aneurysm patients?
Mariana Estrelinha¹, Florian Corvinus², Carolin Zimmermann³, Diane T. Smelsey⁴, Helena Kuivaniemi⁵,⁶, Irene Hinterseher⁶
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Introduction: Some published studies have suggested that patients with abdominal aortic aneurysm (AAA) have a high prevalence of abdominal wall hernias. Based on the current knowledge that generalized connective tissue disorders play a role in the pathogenesis of both of these entities, this study tested the hypothesis that hernias in AAA patients contribute to increased severity of AAA.

Material and Methods: The information about inguinal and incisional hernias from 195 AAA patients was collected through a questionnaire. The patients were divided into 4 groups based on the severity of the aneurysmal disease: 1) survivors of ruptured AAA (n = 22); 2) patients after elective open repair (n = 90); 3) patients after elective endovascular repair

Aortic Aneurysms in the young (below 40 years age)
Tripathi Ramesh K, Verma Himanshu, Vora Simit, Robbie K George
Narayana Institute of Vascular Sciences, Narayana Hospitals Healthcare, Bangalore, India

Purpose: To describe the pattern of Aortic Aneurysms treated in a tertiary care hospital in India and the special significance of aortic aneurysms in patients below 40 yrs.

Methods: A retrospective review of hospital records revealed 154 patients treated for Aortic Aneurysms from January 2011 to June 2014. The mean age was 53 ± 3 with a male: female ratio of 7.3. Forty eight (31.2%) patients below the age of 40 were identified and further studied for presenting symptoms and signs, type of aneurysms, treatments offered and their outcomes.

Results: Of the 48 patients in the age group ≤ 40 yrs, risk factors identified were hypertension, tuberculosis and past history of typhoid. All patients presented with abdominal pain and 13 (27%) patients had rupture. Aetiology included idiopathic non-specific aortitis 29 (60.4%), Tuberculosis 7 (14.5%), Takayasu Disease 6 (12.5%), Salmoneilllosis 3 (6.25%), Connective tissue disorders 2 (6.25%) and Kawasaki disease 1(2%). Treatment strategies included 11 EVARs, 7 TEVARs, 26 Hybrid repairs, 1 Covered stent and 14 open repairs. There were 7 peri-operative deaths (14.5%), 2 in Hybrid repair group and 5 in open repair group. Overall actuarial 1-year survival was 77%.

Conclusion: Aortic Aneurysms in the young in India form a clustered group of inflammatory aneurysms and represent challenging anatomy and pathology. Open surgery is hazardous due absence of tissue planes and encasement of vessels by severe inflammatory tissues. Endovascular or hybrid treatments are suitable and have good outcome over a short-term follow-up.

Short communications from selected papers
Preliminary data from the Liège Screening programme suggests the reported decline in AAA prevalence is not global.

Georgios Makrygiannis1, Mounia El Hachemi1, Philippe Labalue1, Jean-Olivier Defraigne2, Jes S. Lindholt3, Natzi Sakalihasan1

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Background: Population based studies have shown evident benefit in terms of mortality from screening for Abdominal Aortic Aneurysm (AAA) among men aged over 65. However, recent studies from USA, UK and Sweden suggest a decrease in the prevalence of AAA in the general population. These results confirm previous observations on the high prevalence of abdominal wall hernias in AAA patients but suggest that hernias do not contribute to increased severity of the aeurysmal disease.

Recent advances and future directions of AAA

Medical treatment for AAA: past and future
Jonathan Golledge

James Cook University & The Townsville Hospital, Townsville, Australia

Medical management of patients with small abdominal aortic aneurysms is needed to reduce cardiovascular events, limit aneurysm rupture, reduce requirement for surgical intervention and improve outcome after interventions if needed. Current guidelines suggest that patients with small abdominal aortic aneurysms in which surgery is being considered should receive aspirin, a statin, adequate blood pressure control and a smoking cessation programme where appropriate to minimise the risk of cardiovascular events and improve perioperative outcome. Currently there is no indicated therapy to limit the requirement for surgical intervention in patients with small abdominal aortic aneurysms. Over the last decade there has been a large number of studies examining the pathogenesis of abdominal aortic aneurysms mainly employing animal models. There are also a growing number of randomised trials in patients aimed at identifying therapies able to limit AAA expansion. In this presentation current work being undertaken to identify a therapy to limit AAA expansion will be discussed.

The IMPROVE trial: results of a randomized trial of open vs endovascular repair for ruptured AAA
Janet T. Powell

Charing Cross Hospital, London, United Kingdom

Background: Ruptured abdominal aortic aneurysm is a common vascular emergency and an important cause of sudden death, with about 6000 deaths per annum in the United Kingdom. Repair of the rupture by open surgery has a mortality of 40–50% but mortality from endovascular repair may be much lower.

Objectives: To assess whether a strategy of endovascular repair (if aortic morphology suitable, open repair if not) versus open repair reduces 30-day and mid-term mortality (and costs) for unselected patients with suspected ruptured abdominal aortic aneurysm.

Design: Randomised controlled trial with telephone randomisation, with computer-generated assignment of patients in a 1:1 ratio, using variable block size and stratified by centre.


Participants: 613 eligible patients (480 men) with a clinical diagnosis of ruptured aneurysm made at the trial centre.

Interventions: 316 patients were randomised to the endovascular strategy (immediate computerised tomography followed by endovascular repair if anatomically suitable and open repair if not) and 297 to open repair (with computerised tomography being optional).

Main outcome measures: The primary outcome was 30-day mortality, with 30-day costs and time and place of discharge as early secondary outcomes as well as the influence of clinical parameters and aortic morphology on 30-day mortality. The outcomes of 1 year and 3 year mortality, costs, quality of life and cost-effectiveness as well as individual patient metaanalysis of 3 European trials will follow.

Results: 30-day mortality was 35.4% in the endovascular strategy group and 37.4% in the open repair group, Odds Ratio 0.92 [95%CI 0.66 to 1.28], p = 0.62 and after adjustment for age, sex and Hardman index Odds Ratio 0.94 [95%CI 0.67 to 1.33]. Women may benefit more than men (interaction test p = 0.02) from the endovascular strategy Odds Ratio 0.44 [95%CI 0.22 to 0.91] versus 1.18 [0.80 to 1.75]. More patients in the endovascular strategy (94%) versus open repair group (77%) were discharged directly home, p < 0.001. Average 30-day costs were similar between the randomised groups, with an incremental cost saving for the endovascular strategy versus open repair of £1,186 [95%CI, -625 to +2997]. The 30-day mortality was inversely proportional to lowest systolic blood pressure and aneurysm neck length and mortality after endovascular repair was 4-fold lower when local (versus general) anaesthesia was used.

Conclusions: The 30-day operative mortality, including those who died before repair, was similar in the 2 randomised groups. For those who received endovascular repair, it took longer to reach the operating theatre but their mortality was 25% versus 37% for those who received open repair. Since patients receiving endovascular repair are more often dis-
charged directly to home (and sooner), the 12 month outcomes may still show the superiority of an endovascular strategy.

The RAVI-study and the TicAAA-trial
Anders Wanhainen
Dep. of Vascular Surgery, Uppsala University, Uppsala, Sweden

The RAVI-study (Improved Reproducibility of Abdominal Aortic Aneurysm (AAA) measurements using Volumetric Imaging). Current assessment of AAA size and growth is based on ultrasound (US), a measurement technique limited by high variability. This has consequences on clinical decision-making as well as on science, for example sample size calculations for an intervention study to prevent AAA growth. The RAVI-study investigates the reproducibility of AAA measurement by means of volumetric technique by MRI and 2-dimensional ultrasound technique. 30 patients with an AAA of 30–45 mm are examined by means of ultrasound and MRI at baseline, 6 months, 1-year and annually thereafter up till 5 years. An interim analysis (1-year) indicates that the reproducibility of AAA measurements can be improved by MRI compared with ultrasound and volumetric assessment of the AAA rather than just anterior-posterior aortic diameter measurements.

The TicAAA-trial (Does Ticagrelor inhibit growth of small AAA? A randomised controlled trial). A key limitation of contemporary treatment strategies of AAA is the lack of therapy directed at reducing expansion. Platelet activation and intraluminal thrombus renewal are key events in AAA progression, and clinical and experimental data suggests that antiplatelet treatment with aspirin may be associated with reduced growth rates for AAAs. The TicAAA-trial is an ongoing investigator sponsored multi-centre randomized controlled trial investigating whether treatment with Ticagrelor (Brilinta, Brilique) inhibits growth of small AAA. A total of 140 ASA-naïve patients with an AAA of 35–49 mm are randomized to Ticagrelor or placebo (1:1). Ticagrelor is a potent antiplatelet drug that acts by a selectively and reversibly binding to the platelet P2Y12 receptor, blocking the actions of the platelet agonist adenosine diphosphate (ADP). The primary efficacy variable is difference in log-transformed AAA-volume determined by MRI at 12 months vs. log-transformed volume at baseline. The study is powered to detect a 20% reduction in growth rate.

HIV associated aneurysms
Martin Veller
University of the Witwatersrand, Johannesburg, South Africa

The HIV epidemic in Southern Africa has unearthed a number of conditions that are caused by this pathogen. In the vascular field an association with occlusive and aneurysmal arterial disease on the basis of an arteritic process has been described.

Arterial aneurysms associated with HIV have clinical and histological characteristics that differ from the other known cause of aneurysms. The majority of patients presenting with this condition have low CD4 counts with other manifestations of the infection. For this reason we believe this to be an AIDS defining condition.

HIV associated aneurysms have been found in most major arteries and are usually saccular in nature as a result of a localized region of cytotoxic activity in all layers of the arterial wall. Patients tend to present with multiple aneurysms. Treatment of the aneurysm is based on the usual principles of care for aneurysms but because of the poor health of many of these patients, endovascular modalities are favored.

Should patients with CAD be screened for aortic aneurysms?
Rodolphe Durieux1, Hendrik Van Damme1, Nicos Labropoulos2, Alsev Yazici1, Victor Legrand1, Adelin Albert1, Jean-Olivier Defraigne1, Natzi Sakalihasan1

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We studied the association between abdominal aortic aneurysm (AAA) and coronary artery disease (CAD) in a large contemporary series of patients undergoing coronary angiography. Over an 18-month period, abdominal aortic ultrasound was performed on 1,000 patients undergoing coronary angiography for suspected or known CAD, or prior to valve surgery.

The overall number of previously repaired, already diagnosed, and new cases of AAA in the study population was 42, yielding a prevalence of 4.2%. Among the patients with newly detected AAAs, only two had an
**Table 1. Characteristics of screened patients, globally and according to absence or presence of AAA**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All patients (N = 1000)</th>
<th>No AAA (N = 958)</th>
<th>AAA (N = 42)</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean ± SD</td>
<td>64 ± 11.6</td>
<td>63.8 ± 11.6</td>
<td>70.3 ± 8.94</td>
<td>&lt; 0.001</td>
<td></td>
</tr>
<tr>
<td>Age ≥ 65</td>
<td>490 (49%)</td>
<td>462 (48.2%)</td>
<td>28 (66.7%)</td>
<td>0.007</td>
<td>0.003</td>
</tr>
<tr>
<td>Male gender</td>
<td>699 (69.9%)</td>
<td>658 (68.7%)</td>
<td>41 (97.6%)</td>
<td>0.004</td>
<td>0.005</td>
</tr>
<tr>
<td>Family history</td>
<td>79 (7.9%)</td>
<td>73 (7.6%)</td>
<td>6 (14.3%)</td>
<td>0.12</td>
<td>0.01</td>
</tr>
<tr>
<td>Smoker ever</td>
<td>703 (70.3%)</td>
<td>666 (69.5%)</td>
<td>37 (88.1%)</td>
<td>0.03</td>
<td>0.005</td>
</tr>
<tr>
<td>Past smoker</td>
<td>434 (43.4%)</td>
<td>414 (43.2%)</td>
<td>20 (47.6%)</td>
<td>0.22</td>
<td></td>
</tr>
<tr>
<td>Current smoker</td>
<td>269 (26.9%)</td>
<td>252 (26.3%)</td>
<td>17 (40.5%)</td>
<td>0.003</td>
<td></td>
</tr>
<tr>
<td>Coronary profile</td>
<td></td>
<td></td>
<td></td>
<td>&lt; 0.0001</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>No significant lesion</td>
<td>267 (26.7%)</td>
<td>263 (27.5%)</td>
<td>4 (9.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 vessel disease</td>
<td>361 (36.1%)</td>
<td>350 (36.5%)</td>
<td>11 (26.2%)</td>
<td>0.47</td>
<td></td>
</tr>
<tr>
<td>2 vessel disease</td>
<td>238 (23.8%)</td>
<td>228 (23.8%)</td>
<td>10 (23.8%)</td>
<td>0.18</td>
<td></td>
</tr>
<tr>
<td>3 vessel disease</td>
<td>134 (13.4%)</td>
<td>117 (12.2%)</td>
<td>17 (40.5%)</td>
<td>&lt; 0.001</td>
<td></td>
</tr>
<tr>
<td>Mean number of affected coronary arteries ± SD</td>
<td>1.2 ± 1.0</td>
<td>1.2 ± 1.0</td>
<td>2 ± 1.0</td>
<td>&lt; 0.0001</td>
<td></td>
</tr>
<tr>
<td>Aortic diameter (mm), mean ± SD</td>
<td>18.1 ± 6.02</td>
<td>17.3 ± 3.50</td>
<td>41.9 ± 13.2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* after exclusion of the 10 patients with previous AAA repair.

Data are presented as mean ± standard deviation (SD), number of patients (N), or percentages.

AAA diameter of > 54 mm and were therefore treated surgically. In men aged > 65 years, the prevalence reached 8.6%, while in men with three-vessel CAD it was 14.4%. Multivariate analysis showed that age > 65 years (p = .003), male gender (p = .003), family history of AAA (p = .01), current smoking (p = .002), and three-vessel CAD (p < .0001) were significantly associated with a higher prevalence of AAA.

Although the association between AAA and CAD has been described previously, this is the first study that clearly correlates the frequency of AAA with the severity of CAD. Despite the fact that some recent epidemiologic studies suggest a decrease in the prevalence of AAA in the general population, we demonstrate that the disease remains widespread in the population of patients with three-vessel CAD.

The majority of patients with a diagnosis of CAD will continue to have routine follow-up visits with the cardiologist and previous studies have shown the feasibility and accuracy of a rapid evaluation of the abdominal aorta during routine transthoracic echocardiography.

While our findings do not prove the cost-effectiveness of screening for AAA in these high risk patients, they do support the usefulness of a quick ultrasound examination of the abdominal aorta during routine transthoracic echocardiography in such patients.

**Optimal preparation using simulation both in elective and ruptured case**

Isabelle Van Herzelee, Liesbeth Desender, Heidi Maertens, Frank Vermassen

Ghent University Hospital, Ghent, Belgium

Recent advancements in simulation science permit patient-specific rehearsal of endovascular repair of an infrarenal abdominal aortic aneurysm (EVAR).

By incorporating patient-specific imagery into endovascular simulations, real patient cases can be practiced before treatment of the actual patient.

Evidence is emerging that this rehearsal may be valuable to improve case planning by selecting the appropriate patients and correct devices.

Furthermore, rehearsals may influence the treatment plan by identifying the optimal introduction side, by adjusting the position of the contralateral limb to facilitate cannulation or by spotting pitfalls. The contrast use and the radiation dose for the patient, physician and the endovascular team may be decreased by the identification of the optimal C-arm angulation (proximal and distally) in advance to eliminate the parallax. Patient-specific rehearsals may optimize the preoperative preparation of the endovascular team by providing unlimited practice, using a variety of endovascular devices and techniques leading to a more efficient use of the hybrid angiosite.

Furthermore, research has suggested that patient-specific rehearsal may also enhance human factor skills such as decision-making, coordination, leadership, communication and confidence during the real procedure. These cognitive and interactive skills complement technical competency are vital in the efficient and safe execution of complex tasks, especially in crisis situations. In ruptured cases, this patient-specific rehearsal may be used preoperatively (in stable cases) and postoperatively for debriefing or to increase the experience of the various endovascular teams with the overall management of ruptured aortic aneurysms.

**Minimizing radiation exposure during endovascular aortic procedures**

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Utilization of endovascular procedures has become exceedingly popular amongst vascular specialists. Endovascular aortic repair (EVAR) represents one of the most complex endovascular procedures today. EVAR exposes patients and staff to significant doses of ionizing radiation. Medical imaging studies now represent the greatest man-made source of ionizing radiation to the general population and patients undergoing EVAR are a prime example. Virtually all patients undergoing EVAR have a pre-op CT scan, intraoperative fluoroscopic imaging and lifelong surveillance imaging. Furthermore, knowledge basics about radiation has not been developed and incorporated into training, while appropriate behavior in the interventional suite is very often ignored, leading to unnecessary radiation exposure. Exposure to ionizing radiation has both stochastic and deterministic effects on the human body. Stochastic effects occur without a threshold dose of ionizing radiation. After ionizing radiation causes damage to DNA, the error-prone process of DNA repair is just the catalyst necessary for neoplastic processes to occur. On the contrary, deterministic effects of ionizing radiation are dose-dependent. Before the threshold dose is reached, no damage to the exposed tissue will occur. An example of a deterministic effect of radiation exposure is skin erythema. Variation in technique, screening and surveillance protocol along with the equipment used for patients undergoing EVAR used may affect the dose of radiation exposure to the
patient and staff involved. There is a large variation in the dose of radiation to the patient. This is indicative of variation in technique of the user. The effective dose in the studies included ranged from 5.8mSv to 11.968mSv. While sometimes specified, not all studies specified which type of EVAR was being evaluated. Thoracic EVAR (TEVAR) resulted in lesser effective dose (mSv) than abdominal aortic repair. Not all studies commented on the specific type of equipment used. The use of a hybrid angiography suite (ceiling mounted interventional imaging system) resulted in less radiation exposure to users and patients than rooms with portable C-arms. The largest percentage of radiation exposure in patients undergoing EVAR is represented by the pre-op and post-op surveillance imaging. Follow up CT imaging represents >80% of total radiation exposure after 1 year which is over 90% at 5 years and gets higher in a lifetime. To reduce the effective dose of radiation to the user, the C-arm should have the least amount of obliquity as possible. The AP shot had the lowest exposure (4.53–4.98mSv/hr) to the user while the 90 degree lateral had the greatest exposure (69mSv/hr). The ends of the head to toe axis had the least exposure while the lateral edges of the angio table had the greatest amount of radiation recorded. The distance from the tube and the importance of magnification cannot be overstated. It has been recommended to reduce or avoid the use of CT for following-up the patients. The use of special drapes and the development of newer equipment have led in a significant reduction in the radiation exposure without reducing the image quality. Despite of what has been traditionally taught there is no safe dose of radiation. The level of the radiation repair genes is variant and currently, there is no test for the repair genes. There is a lack of awareness and education on radiation safety. With the increasing use of such procedures the risk is likely to increase and therefore preventive measures both for the patients and the staff are essential.

Can the FEM be used as a predictor for rupture risk in clinical practice? Method and validation so far
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Based on a large number of interventions, a maximum transverse diameter of, on average, 55 mm appears to be the best indicator for elective abdominal aortic aneurysm (AAA) repair. In addition to aneurysm size, other rupture risk factors such as asymmetric geometry, gender, family history, fast aneurysm expansion, a thick intra-luminal thrombus layer etc., should also be considered for the decision to perform elective AAA repair. Specifically, diameter-based (static) and growth-based (dynamic) effects should also be considered for the decision to perform elective AAA repair. A biomechanical post processing of CT-A scans at moderate costs could significantly improve the management of AAA patients.

References

Figure 1. Biomechanical rupture risk assessment by relating the individual patient to the average AAA patient. The Rupture Risk Equivalent Diameter (RRED) expresses the size of an aneurysm in the average patient population, which is at the same risk of rupture than the individual case.
Results: Both the media and adventitia of infra-renal AAA samples demonstrated a significantly greater number of ST sol +, cKIT+ and CD34+ cells when compared with matched non-aneurysmal control aortic tissues. Furthermore, double immunofluorescence staining identified that AAA SCs express the macrophage marker CD68 but not the SMC marker SM22 or the fibroblast marker FSP1. CD68+ cells within the aortic wall co-localized with the cellular marker of proliferation Ki67.

Conclusions: SCs are significantly elevated in infra-renal AAA tissue compared to matched control aortic tissue. Our data also demonstrate that AAA SCs express macrophage surface antigens but not SMC or fibroblast markers. Furthermore, CD68+ cells within the aortic wall co-localized with the cellular marker of proliferation Ki67. These findings suggest an inflammatory/immune role of stem cells during AAA pathogenesis and raise the possibility of localized replenishment within the aneurysm wall.

Screening of microRNAs expressed in isolated cells of human abdominal aortic aneurysm for the identification of potential biomarkers

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MicroRNAs are stable biomarkers which have only been studied in experimental abdominal aortic aneurysms (AAA). Macrophages M1 and M2 and vascular cells, essentially smooth muscle cells (SMC) are found in the complex AAA tissue.

In our study, these cells were isolated by laser microdissection from 20 human AAA biopsies obtained during surgical repair and control SMC from 14 healthy aortic biopsies harvested during organs multiretrieval. RNA from 2 samples of each isolated cells was screened on human miRNAs microarray. Differential expression of selected miRNAs was evaluated by quantitative RT-PCR between healthy SMC and aneurysmal SMC, between M1 and M2 macrophages and common aneurysmal cells and healthy SMC. In order to select miRNAs, a detection value threshold was chosen to be the detection value of miR-29b, described in experimental AAA to be a potential biomarker. Moreover, miRNAs were selected when the detection value on microarray was at least of 2-fold change. Differential expression of miR-21 and miR-29b, two potential biomarkers identified in experimental models of AAA, was also evaluated between aneurysmal and healthy SMC.

Out of the 850 human miRNAs tested for each samples, 92 were found to be present in AAA after normalization of the detection values. Forty-seven miRNAs were common to each tested cells; 54 miRNAs were found in SMC, of which 35 were common to AAA and control aortas and 12 specific to AAA; 85 miRNAs were found in macrophages of AAA, of which 37 were common to M1 and M2 macrophages and 5 specific to M1 macrophages, 28 to M2 macrophages. Ten miRNAs were selected by these means to be evaluated by quantitative RT-PCR. We found miR-199a-3p to be overexpressed in M1 macrophages compared to M2 macrophages. We also found an overexpression of miR-21 and miR-1207-5p in M2 macrophages. MiR-29b was found less expressed and let-7f overexpressed in aneurysmal SMC.

In conclusion, we confirm the results of experimental models of AAA in human. The analysis of isolated cells allows to find additional differential expression of miRNAs as potential biomarkers of AAA.

The ectopic adventitial adipocytes of abdominal aortic aneurysm

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Background: Abdominal aortic aneurysm (AAA) is a common manifestation of cardiovascular disease among the elderly [1]. The molecular mechanisms that underlie the pathogenesis of AAA remain unknown [2,3]. We utilized comprehensive matrix-assisted laser desorption/ionization imaging mass spectrometry (MALDI-IMS) of intraoperative dissected human AAA samples to visualize compositional changes in cellular metabolites related to AAA.

Material and Methods: We studied 30 patients who underwent elective open surgery to repair infrarenal AAAs at the Division of Vascular Surgery, Hamamatsu University School of Medicine. The localization of each lipid molecule in the aortic wall was assessed by MALDI-IMS [4-6]. Conventional and immunofluorescence staining were performed for histopathologic examination. The total lipid content in the homogenized aortic tissue was determined.

Results: MALDI-IMS revealed a characteristic distribution of triglyceride (TG) specifically in the aneurismal adventitia of distended aorta (fig.1A,B)[7]. Pathological analysis revealed that characteristic TG distribution was derived from ectopic appearance of adipocytes in adventitia (fig.1C). Accumulated adipocytes were found to locally produce proinflammatory cytokines and matrix metalloproteinases, with subsequent disruption of the local collagen network (fig.2A). Peroxisome proliferator-activated receptor gamma 2 was expressed in not only these adipocytes, but also in fibroblast-like cell marker positive cells (fig.2B)[8,9].

Conclusions: We propose that ectopic adventitial PPAR-y2 expression in fibroblast-like cells contributes to mechanical weakening of the AAA wall via two pathways. One is transformation from fibroblast-like cells into adipocytes. The other is the decrease of collagen production.

Figure 1.
References

**The actual bomb in abdominal aortic aneurysm (AAA) disease ticks. . .**
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**Introduction:** The presence of an AAA has a substantial negative effect on a patient’s life expectancy. Although the focus in AAA treatment is on rupture, cardiac death is the principal cause of excess mortality in these patients. This controversy largely reflects a sharply increased vascular risk in AAA patients. It has been argued that AAA patients are at high risk for cardiovascular disease and should be treated accordingly. We developed a model to test whether and to what extent cardiovascular disease (CVD) risk management can improve survival of AAA patients. In addition we used data from the PHAST trial to explore the current level of risk management in AAA patients.

**Methods:** A Monte Carlo-Markov decision model is constructed with data derived from an extensive literature review and the patient cohort of the PHAST trial, a randomized, multicentre trial evaluating the effect of doxycycline on AAA progression (NTR 1345). The impact of AAA management, measured in quality adjusted life years (QALYs), on the occurrence of CVD will be investigated for three strategies; optimal cardiovascular risk management, aneurysm repair, and a combination of the first two. Additionally, data of the PHAST trial is used to assess current practice of AAA management in the 286 participating patients.

**Results:** The Monte Carlo analysis showed that in AAA patients, aneurysm repair alone (open and EVAR for AAA > 5.5 cm) resulted in an improved life expectancy of 0.63 QALYs. Optimal cardiovascular risk management alone for AAA resulted in a gain of 1.00 QALYs. Data from the PHAST trial showed that 70% of patients received statins, 66% was on antihypertensives and 40% used anti-platelets. Yet, the majority of patients was undertreated as 39% had apolipoprotein B levels over 0.9 g/L, and 60% of the patients exhibited blood pressure values over the target value of 140/90 mmHg. Furthermore, 65% of patients was overweight (BMI > 25), 17% was obese (BMI > 30), and 33% of patients was still smoking.

**Conclusion:** This study shows a high potential gain for strict cardiovascular risk management in patients with AAA disease. An inventory in the PHAST population shows that 30% of the AAA patients is not receiving risk management, and that those receiving risk management are generally undertreated.

**Promising first experience of endovascular treatment of ruptured abdominal aortic aneurysms**
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**Objectives:** To describe the implementation and evaluate short-term outcome of the first Danish experience of endovascular repair of ruptured abdominal aortic aneurysm (rAAA).

**Design:** Historical prospective cohort study including all patients at OUH (DK) treated for rAAA and/or iliac artery aneurysms rupture from 1st of October 2012 until December 2013.

**Results:** 53 patients were treated due to rAAA or iliac aneurysms at our institution in this period. Of these, 27 (51% 95% confidence interval (CI): 0.38–0.64) patients were treated with EVAR and 26 (49%) by open repair.

**Figure 1.** 67 year male with heart failure and EF 30% came with ruptured 7 cm big AAA.

**Figure 2.** Inflammatory cytokine TNF-α and PPARγ2 expression in fibroblast-like cell marker positive cells

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*Meeting Abstracts 225*

4th International Meeting on Aortic Diseases
Two patients (7%, 95% CI: 0.01–0.22) died within the first 30 days post-operatively in endovascular group. One patient died peri-operatively due to myocardial infarction verified by autopsy. The other one died due to massive coagulopathy and multiorgan failure shortly after the procedure. In the group with open repair, 7 patients (30.7%) died within the 30 days. Consequently, the mortality of all patients treated for rupture at our institution was 19% compared to 32% in Denmark.

**Conclusion:** Endovascular treatment of rAAA is feasible and overall post-operative mortality and morbidity of rAAA can probably be reduced by its implementation.

**References**


**Figure 2.** Occlusive aorta ballon due to hemodynamic unstable condition and angiography.

**Figure 3.** Control angiography after placement of aortouniiliakal stent graft and additionally aortic cuff because of endoleak type 1A with intentional covered right renal artery. No endoleak. Underwent crossover bypass after EVAR.

Two patients (7%, 95% CI: 0.01–0.22) died within the first 30 days post-operatively in endovascular group. One patient died peri-operatively due to myocardial infarction verified by autopsy. The other one died due to massive coagulopathy and multiorgan failure shortly after the procedure.

**Prevention of incisional hernia after midline laparotomy for abdominal aortic aneurysm treatment: a randomized controlled trial**

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The incidence of incisional hernias (IH) after open abdominal aortic aneurysm (AAA) repair is high. Prophylactic mesh augmentation (PMA) during laparotomy closure has been proposed in high-risk patients.

Methods: A multicenter prospective randomized controlled study was conducted on patients undergoing elective repair of AAA through midline laparotomy (Clinical.Trials.gov: NCT00757133). In the study group a retro-muscular PMA was performed with a large-pore polypropylene mesh (Ultrapro™, width 7.5 cm). The primary endpoint was the incidence of IH at 24 months.

Results: Between February 2009 and January 2013, 120 patients were recruited at 8 Belgian centers. Patients’ characteristics at baseline were similar between the groups. Operative and postoperative characteristics showed no difference in morbidity or mortality. A highly significant reduction of IH incidence was found after PMA compared to conventional closure, respectively 0% (CI: 0%–5.5%) versus 27.6% (CI: 16.7%–40.9%) (p < 0.0001; Fisher’s exact test). The estimated “freedom of IH” curves (Kaplan-Meier estimate) were significantly different across study arms (X2 = 18.93, p < 0.0001; Mantel-Cox test). No adverse effects were observed, apart from an increased mean (SD) time to close the abdominal wall for PMA: 46.2 min (18.6) versus 29.6 min (18.5) (p < 0.001; Mann-Whitney U test).

Conclusion: Prophylactic retro-muscular mesh augmentation of a midline laparotomy in AAA patients is safe and effectively prevents the development of IH, with an extra time investment of 17 minutes.

**SCIENTIFIC PROGRAM**

**Friday September 12**

**Clinical management and treatment of thoraco-abdominal and abdominal aortic diseases**

Short and intermediate outcome of EVAR with the use of new generation endografts

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Effective proximal sealing in EVAR remains the cornerstone of this kind of intervention and failure to achieve it has serious consequences. The refinements in the design of the new generation endografts were mostly aiming to provide active fixation and deployment in difficult anatomic situations eliminating the defects of the past generations in the proximal fixation. We conducted this multicenter study to assess the short (1-month) and intermediate (1-year) outcome with the use the new generation endografts implemented in endovascular repair (EVAR) over the last years.

Retrospective analysis of prospectively collected data of 400 EVARS from four centers from January 2009 to February 2012 was undertaken. Endografts utilized in the period of the study were the Endurant (Medtronic), Zenith LP (Cook), Excluder and Excluder C3 (Gore), Anaconda (Vascutek) and Ovation (Trivascular). Patients’ demographic data, risk factors, type of operation (elective vs. urgent), type of endograft used (supra- vs. infra-renal fixation, bifurcated vs. uni-iliac) and aneurysm morphological characteristics (proximal neck diameter, length, angle, calcification and thrombus and sac diameter) were analysed in respect to endoleak presence and sac expansion during the first post-operative year. All cases as per protocol were investigated with CT scanning on the 1st month and 1st year. Multivariate and logistic regression analysis was used for associations.

The mean age was 71.3 years (SD 7.9), 381 were males, in 349 cases (87.25%) the intervention was elective, the mean AAA sac diameter was 57.1mm (SD 12.54), the mean proximal neck length and diameter were 29 mm (SD 12.93) and 24.6 mm, SD 3.1, respectively. Only in 32 cases (8%) the proximal neck angle was >60°. Type 1a endoleak was present in 13 cases (3.25%) in 1-month, but in 1-year only 4 of them were present and 2 more developed. In logistic regression, initial sac diameter > 55 mm (p = 0.031) and proximal neck diameter > 30 mm (p = 0.032) had significant association with type 1a endoleak. Neck angle > 60° and length < 15 mm had no significant association. Type 2 endoleak was present in 75 cases (18.75%) in 1-month which all persisted in 1-year with the addition of 6 new accounting for a total of 81 cases (20.25%). No significant association was found for the development of type 2 endoleak. Sac expansion in 1-year was detected in 18 cases and in logistic regression it was associated only with the presence of any type of endoleak (p = 0.019). No rupture occurred during the first year after EVAR.

New generation endografts appear to perform satisfactorily even in difficult anatomic conditions. Risk of type 1a endoleak is low, and it is associated only with the initial sac and proximal neck diameter, while the 1-year sac expansion is associated only with the presence of endoleak.

**Ruptured aortic aneurysm: experience in Thong Nhat hospital**

Que Do Kim

Thongnhat hospital, Ho Chi Minh Ville, Vietnam

Ruptured abdominal aortic aneurysm (AAA) and Thoracoabdominal aortic aneurysm (TAAA) is one of the most fatal surgical emergencies, with an overall mortality rate of 90%. Most AAAs rupture into the retroperitoneal cavity, which results in the classical triad of pain, hypotension, and a pulsatile mass. However, this triad is seen in only 25–50% of patients, and many patients with ruptured AAA are misdiagnosed. It is likely that different sites of rupture of AAA determine a variety of common and uncommon clinical presentations, the recognition of which can save many lives. The reduced physiological impact of endovascular aneurysm repair (EVAR) compared with conventional open repair has been demonstrated. The overall anatomic suitability rates for EVAR is about 50% to 80%. The average post-operative mortality rate was 24%, ranging from 9 to 45%. The overall mortality rate of 90%. Most AAAs rupture into the retroperitoneal cavity, which results in the classical triad of pain, hypotension, and a pulsatile mass. However, this triad is seen in only 25–50% of patients, and many patients with ruptured AAA are misdiagnosed. It is likely that different sites of rupture of AAA determine a variety of common and uncommon clinical presentations, the recognition of which can save many lives. The reduced physiological impact of endovascular aneurysm repair (EVAR) compared with conventional open repair has been demonstrated. The overall anatomic suitability rates for EVAR is about 50% to 80%. The average post-operative mortality rate was 24%, ranging from 9 to 45%.

Keywords: abdominal aortic aneurysm; ruptured aneurysm; aortic rupture; rupture; emergency; surgery; endovascular aneurysm repair.

**Short communications from selected papers**

Outcomes of persistent intraoperative Type 1a endoleak following standard endovascular aneurysm repair (EVAR)

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Objective: The aim of this study was to analyse outcomes for patients with persistent intraoperative type 1a endoleaks following standard EVAR.

Method: The study group was identified from a consecutive cohort of 209 patients undergoing EVAR (2011–13). Post-operative imaging and case notes were reviewed. Primary outcome measures: freedom from type 1a endoleak and survival. Secondary outcomes: freedom from sac expansion and secondary interventions.
Results: 33 patients (16%) (Median [Range]; Aneurysm Diameter: 63mm [53 – 98], Neck Length: 21mm [12 – 55], Neck Diameter: 25 [20 – 36]) had persistent type 1a endoleak, despite intraoperative adjunctive manoeuvres in 30 cases. One patient was lost to any follow-up. At first post-operative CT angiogram (Median; 33 days [3 – 61]), 31 patients (94%) demonstrated resolution of the endoleak without secondary intervention. Overall survival = 85% (median follow-up 27 months [9 – 41]). At median follow-up 23 months [2 – 38] 30 patients (91%) had a stable/shrinking aneurysm. One patient had successful secondary intervention 8 days post-EVAR with Onyx embolization. No recurrence of the endoleak was noted in any patient.

Conclusion: Despite adjunctive intra-operative manoeuvres, persistent type 1a endoleaks can be relatively common. This short-term study indicates that they may be observed and will usually seal spontaneously without significant sac expansion or adverse event.

Functionality and biological response of the Multilayer Flow Modulator implanted in the abdominal aorta of adult miniature swine
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Objective: In vivo pre-clinical testing offers the opportunity to evaluate the Multilayer Flow Modulator (Cardiatis, Isnes, Belgium) by means not readily available with in vitro methods. The purpose of this preclinical animal study was to evaluate the performance of the device in an in vivo environment prior to its clinical application. The study was intended to evaluate device functionality (accurate deployment of the device) and vessel biological response to the implanted device.

Methods: Thirteen animals were implanted with the study device in the abdominal aorta, seven animals for thirty days and six animals for six months. Device functionality and immediate thrombosis were assessed during implantation. Upon completion of the study period, each animal underwent a necropsy to examine how the implanted device had affected the artery and surrounding tissue. Neointima and stenosis formation were recorded via morphometry, and endothelialization via histopathological analysis.

Results: At thirty days and at six months, all of the explants were widely patent. Histopathological finding showed the MFM caused little mural damage at thirty days and mild mural damage at six months. In most areas, flattened, endothelium like cells lined the luminal surface of the neointima (Figure 1). Scanning electron microscopy also showed the device was well tolerated, inciting only a minimal neointimal covering and little fibrin or platelet deposition. The histologic appearance of those cells did not change significantly from thirty days to six months. The device was well tolerated with minimal inflammation response, and healing response was good. Neointimal thickness of 239.7 ± 55.6 μm and 318.3 ± 130.4 μm, and percentage area stenosis of 9.6 ± 2.6% and 12.6 ± 5% were recorded at thirty days and six months respectively. No statistical differences were found between these results at thirty days and six months.

Conclusion: This study aimed to evaluate the MFM device for functionality in terms of deployment and biocompatibility of the implanted device. The MFM devices were delivered to their respective implantation sites without difficulty. The MFM also incited little neointimal and stenosis formation in the aorta. The values of stenosis, which were less than 50% are judged to be not significant when compared to circumstances for vascular reintervention of a stented artery.

Management of aortitis and mycotic aneurysms

Mycotic Aneurysms. Is endovascular treatment the way to go? Experience from India
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Purpose: Mycotic aneurysm of the aorta and paravisceral aorta is a life threatening condition. Endovascular options have been explored as repair by either in situ replacement or extra-anatomic reconstruction can be quite challenging. We review our experience of surgical and endovascular management of mycotic aortic aneurysms.

Method: From January 2011 to June 2014, a total of 154 patients with aneurysms of the thoracic and abdominal aorta underwent surgery for aortic at our institution. Nineteen (12.3%) of these patients (mean age, 61.4 years; MF: 9:1) were treated for mycotic aneurysms of the descending and thoracoabdominal (n = 9), suprarenal (n = 6), and infrarenal (n = 4) aorta. Eleven (57.9%) patients had sepsis history. There was an increased white cell count, C-reactive protein and procalcitonin levels in 68.4% patients. Clinical presentation included fever in 57.9%, abdominal pain in 84% of the patients. There were 5 (26.3%) contained and 3 (15.7%) free ruptures. Common pathogens from blood cultures were Staphylococcus aureus, Salmonella and acenatobacter species. Careful debridement of all infected tissue was essential. Endovascular stent grafting was used in 3 patients, hybrid repair in 7 patients and open repair with in situ graft in 9 cases. No extra-anatomic procedures (axillobifemoral or femorofemoral crossover bypass graft) were carried out. All patients had peri-operative antibiotics that were extended to a minimum of 6 months post-peratively.

Results: Total mortality was 7/19 (36.8%). Peri-operative mortality was 5/26.3%. Patients presenting with rupture had high mortality at 50%. There was no demonstrable difference in the outcomes for hybrid versus open repair, perhaps due to small and heterogeneous nature of the two groups. Medium-term follow-up (mean, 12 months; range, 1–40 months), showed a infection free survival of 63.1%.

Conclusions: Mycotic aortic aneurysms remain a life-threatening condition more so if the patient presents with rupture. Endovascular/hybrid surgeries are as effective as open surgery in non-ruptured cases. Lower virulence of offending organisms and long-term antibiotics may be the key to long-term survival.

Takayasus’s aneurysms
Martin Veller
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Takayasus’s arteritis is a T-cell driven, non-specific granulomatous inflammation of all layers of the vessel wall. In response to the inflammation, cellular proliferation in the intima and media may lead to occlusion and stenosis of the artery, or weakening of the media and adventitia which can result in dilation and aneurysm formation. The most frequently affected vessels are the subclavian arteries, carotid arteries and the aorta, including...
the origin of its visceral branches. Dilation or aneurysm formation is usually only found in the aorta.

The diagnosis is most frequently made on the basis of the clinical manifestations an elevated ESR and CRP are during the active phases of the disease. Imaging is essential to delineate the full extent of the vascular involvement. PET may play a role. Treatment consists of immunosuppression usually using high doses of prednisone in the acute phase. This regime is usually effective in addressing the inflammation in the vascular wall and abating the constitutional symptoms but two thirds of patients with Takayasu’s arteritis experience relapses of symptoms or progression of vascular disease. Methotrexate and some other agents are used without prednisone during phases of remission in order to minimise the corticosteroid side effects. Agents such as infliximab have shown promise but are usually unaffordable in the countries in which this disease predominates.

Surgical and endovascular interventions play an important role in treating occlusive and aneurismatic manifestations. The indications for intervention are the same as they are for other pathologies, usually only when life or limb sparring. Fortunately, few interventions are required in the acute phase, as failure rates for procedures performed when acute inflammation is present, are high. Revascularisation in our practice is deferred, if at all possible, until pharmacological therapy has completely suppressed the inflammation, which we believe to be indicated by a normal CRP and ESR.

Endovascular aortic repair in aortobronchial and aortoesophageal fistulas

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Aortobronchial fistula (ABF) and aortoesophageal fistula (AEF) are rare but potentially life-threatening complications of both treated and untreated aortic disease due to exsanguinating hemorrhage. By classification, primary fistulas occur as communications between the untreated aorta and the bronchial tree/esophagus due to aneurysm rupture, penetrating aortic ulcer, advanced esophageal or lung cancer, or ingestion of foreign body. Secondary fistulas originate from reconstructed aorta (prosthetic graft) or develop secondary to complications of a visceral surgical procedure (anas-tomotic insufficiency). Compared with results of open surgery for thoracic aortic aneurysm (TAA) with a mortality of 14%, open aortic surgery in ABF and AEF is endowed with a significantly increased mortality of 24 and 50%, respectively, clearly reflecting the complexity of these lesions. Therefore, less invasive concepts to reduce perioperative mortality have been evaluated with special attention on thoracic endovascular aortic repair (TEVAR).

Placement of esophageal stents has emerged as a valuable tool, however, they were not able to seal the lesion completely and therefore cannot exclude risk of mediastinitis. Definitive surgical correction seems vital to obtain a reasonable long-term perspective and possible techniques include esophageal resection with gastric pull-up, esophagoplasty, or the “Thal” fundoplication.

Aortoduodenal Fistulas: An aortoenteric fistula is an abnormal communication between the aorta and the bowel lumen. It is usually caused by previous aortic surgery and involves the duodenum (ADF) in most cases. The treatment of this high-mortality condition is based on the correction of enteric and vascular defects.

The enteric procedure was described as: duodenorraphy, duodenal resection/reconstruction, antibiotic or abdominal. Vascular treatment was described as: extraanatomic bypass, in situ graft, direct closure of the aortic defect, endovascular procedures and arterial reconstructions. The most common cause of death was ADF recurrence (41.8%), which was significantly high in the patients who underwent simple duodenorraphy. Delayed or avoided enteric repair after endovascular treatment emerged as an option, but needs additional supporting research.

Challenging cases in aortic pathology

Failure of stent-graft at long-term follow-up

Sonia Ronchey, Stefano Fazzini, Andrea Esposito, Nicola Mangiagardi

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An 83 years old woman, previously operated for colon cancer, was treated for a pararenal aneurysms on march 2013. The procedure consisted in a double chimney for the SMA (advanta 9-58+protegè 9-80) and LRA (viabahn 6-100+protegè 6-80) and a home made fenestration (Cook TFFB 32–125) for the RRA (advanta 6–22) with good immediate result. The 3 months CT scan confirmed the good result of the procedure and the 6 months duplex scanner too. The 12 months duplex demonstrated a type one endoleak and an increase in sac diameter of more than one centimeter. The subsequent CT scan showed a dilatation of the distal portion of the proximal neck, a distal migration of the stent graft with consequent partial disconnection of the fenestration. The two chimney reman in stable position. The patient was treated by proximal extension of the stent graft (gore C-TAG 34–100) extension of the two chimneys (SMA; advanta 9-59+protegè 9–80 - LRA: viabahn 6-50+protegè 6–80) and relining of the fenestration for the RRA (advanta 6-22+zilver 7–30). The one months CT scan control shows the good results of the procedure. The case underline the need for a close follow-up especially in complex procedure like this one because the risk of type one endoleak due to gutters or evolution of the proximal neck is relatively high and exposes the patient to the risk of rupture.

Endovascular techniques first to treat an increasing aneurysm post-EVAR

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Introduction: An increasing aneurysm post-EVAR (endovascular repair of infrarenal abdominal aortic aneurysm) is most often due to a proximal attachment and sealing problem, and represents the most common reason for secondary intervention. Although the incidence of EVAR failure seems to decline, owing to advancements in graft-technology and better understanding of the technique, recent reviews still report crude annual secondary intervention rates ranging from 1.7–4.3% [1]. We present endovascular options to address primary EVAR failure.

Management of Type I endoleak: Type I endoleaks result from an inadequate initial proximal/distal sealing zone, but can also develop due to progression of disease. In the presence of an adequate proximal landing zone, a proximal cuff placement is the obvious solution. In case of a distal type I endoleak a limb extension can easily be applied. A highly angulated proximal neck poses an additional problem for many stent-grafts. The use of endostaples can secure the position of the primary stent-graft to the aortic wall or the proximal cuff [2]. When shorter proximal neck length prohibits the use of a standard cuff, fenestrated stent grafts (F-EVAR) can provide a safe and effective solution. In our experience, F-EVAR represents a less morbid alternative than open repair, with a high technical success rate, and a high target vessel patency and durability in mid-term follow-up [3]. Management of Type II endoleak: Type II endoleaks are common if one looks hard enough, with an incidence of 10–25% in published series [4,5]. Their course is benign in the majority of cases, with 75% resolving spontaneously, at least on standard imaging techniques. A conservative approach to type II endoleaks is generally accepted when the aneurismatic sac does not increase. Transarterial coil or onyx embolization is the first line treatment modality in case of aneurysm expansion. Recent series confirm the efficacy of the technique, but stress the need for continued surveillance in this patient cohort [6]. Translumbar fluoroscopy-guided
embolization can offer another minimal invasive technique, before moving towards conventional open techniques such as laparotomy with ligation of lumbar/inferior mesenteric arteries, or conversion.

Management of Type III endoleak: Type III endoleaks originate either from fabric tears or an inadequate seal between endograft components. Reported incidence ranges from 0.1% to 6.4%. An endovascular approach with the deployment of an additional stent-graft to bridge the defect or so-called “endolining” is generally well accepted. The procedure is usually straightforward, but can be more cumbersome in case of complete limb separation or severe vessel tortuosity.

**Endotension:** An increase in aneurysm size after EVAR without evident endoleak poses a diagnostic and therapeutic problem. The incidence of endotension is 1.5–5% [2]. In this setting, a thorough diagnostic algorithm including contrast enhanced ultrasound, CT angiography with delayed contrast phase and possibly a digital subtraction angiography is required, to exclude endoleaks. Treatment is individualized according to the general condition of the patient and the underlying cause for aneurysm expansion. An initial “relining” with strict follow-up is justified in some cases, but open conversion may be the only way to identify the cause and prevent eventual aneurysmal rupture.

**Conclusion:** Endoleaks and aneurysm increase are considered the Achilles heel of EVAR. Despite decrease of such complications in contemporary practice, secondary interventions remain needed in a considerable percentage of patients. Whenever safely possible, endovascular techniques should be attempted.

**References**

**Aortic root and thoracic aortic aneurysms**

**Managing the aortic root during pregnancy**

*Julie De Backer*

University Hospital Ghent, Ghent, Belgium

In patients with known aortic disease, pregnancy entails a risk for aortic dissection/rupture, which is related to both hemodynamic and hormonal changes. The risk for pregnancy-related complications is determined by several factors, including:

1. the underlying disease,
2. the aortic diameter,
3. previous surgical interventions.

The risk stratification depends on these factors and may vary from low-risk to very high-risk where pregnancy may even be contra-indicated. Management of women with known aortic disease should be initiated prior to pregnancy with adequate counseling regarding the risk of the pregnancy for the mother and fetus as well as the inheritance risk. Prophylactic surgery may be indicated in certain instances and medical treatment to decrease the rate of aortic growth is mandatory in all cases. Careful monitoring of aortic diameters and blood pressure throughout pregnancy is necessary and the mode of delivery is also dictated by the history and actual size of the aorta. In this presentation, underlying diseases, counseling and management throughout pregnancy will be systematically addressed.

**Practical ascending aneurysm genetics for the surgeon**

*John A. Elefteriades*

Aortic Institute at Yale-New Haven Hospital, Yale University School of Medicine, New Haven, CT, USA

Genetic studies over the past several decades have helped to better elucidate the inheritance patterns and specific genomics of thoracic aortic diseases. Seminal work from various researchers has identified several genetic factors and mutations that predispose to aortic aneurysms. Syndromic aneurysms have been associated with Marfan disease, Loeys-Dietz syndrome, aortic aneurysm osteoarthritis syndrome, arterial tortuosity syndrome, cutis laxa syndrome, Ehlers-Danlos syndrome, and TGFβ2 mutations. Mutations in MYH11, TGFβ1, TGFβ2, MYLK, SMAD3, TGFβ2 and ACTA2 genes have been linked to familial non-syndromic cases. This presentation will focus on key genetic and genomic factors that are associated with thoracic anortic diseases. The presentation takes a common sense approach suitable for surgeons and other non-genetics practitioners.

**References**

**Combined coronary artery bypass grafting (CABG) and hybrid repair of arch of aorta aneurysms**

*Ramesh K Tripathi1, Himanshu Verma1, Praveen Kumar2*

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**Purpose:** To report our initial experience of CABG combined with concomitant endovascular Hybrid repair of Aortic Arch Aneurysms.

**Methods:** A retrospective review of 23 consecutive patients with Aortic Arch Aneurysm treated by a cardiac and vascular team at a tertiary hospital was carried out. Of these 9 patients (8 Males, 1 Female; median age 59 years, range 48–80 years) had an arch aneurysm > 5.5 cm and > 2 vessel coronary artery disease. In the Hybrid OR, this subgroup underwent CABG (All off-pump) followed by Ascending Aorta to Innominate and Left Common Carotid and Subclavian Bypass and Thoracic Endovascular Aneurysm Repair (TEVAR).

**Results:** Success rate of all combined procedures under a single general anaesthesia and midline sternotomy was 100% with a mean Fluoroscopy time of 6 minutes (range 2–14 minutes) and a surgical duration time of 399 minutes (range 268–589). Median Intensive Therapy Unit stay was 5 days (range 1–9 days), while hospital stays were 11 days (range 8–19 days).
Redo surgery after Type A aortic dissection repair
John A. Elefteriades
Aortic Institute at Yale-New Haven Hospital, Yale University School of Medicine, New Haven, CT, USA

In late follow-up after Type A aortic dissection repair, dilatation of the residual dissected aorta can occur, distal to the end of the original repair. This usually involves the aortic arch and the proximal third of the descending aorta. Reoperation under such circumstance is challenging. We present results for this scenario from our center, as well as reviewing important technical principles for surgeons, including the following:

- **Safe Re-entry**
  - Femoral artery exposure before sternotomy
  - “Towel Clip” Bail Out
  - CPB rarely req’d before sternotomy
  - Retrosternal sponge technique

- **Limited Tissue Dissection**
  - Ao (surround)
  - RA

- **“No Touch” for SVGs**

- **Myocardial protection/Systemic Hypothermia/Retrograde**

- **Methods of Brain Protection**

- **Elephant Trunk Options**
  - Four methods to gain control of elephant trunk
  - “Finger-thumb” technique
  - Arch clamp
  - Adenosine asystole
  - Deep hypothermic arrest.

Reference

Yale data on appropriate criteria for intervention for the ascending aorta
John A. Elefteriades
Aortic Institute at Yale-New Haven Hospital, Yale University School of Medicine, New Haven, CT, USA

This presentation reviews the current general concepts and understandings of the natural history of thoracic aortic aneurysms and their clinical implications. Our database has now expanded from hundreds to thousands of patients followed, permitting more powerful statistical conclusions. Our studies show that the normal aorta in the general population is very small (3.2 cm for the ascending aorta). Aortas greater than 5 cm are rare in the real world. The aneurysmal aorta grows at a mean of 0.2 cm/year, and larger aneurysms grow faster than smaller ones. Size continues to be a strong predictor of natural complications and a suitable parameter for intervention. The dissection size paradox (which shows some aortic dissections occurring at small aneurysm sizes) is explained by the huge number of patients with small aortas in the general population. As we enter the era of personalized aneurysm care it is likely that specific genetic mutations will facilitate determination the appropriate size criterion for surgical intervention in individual patients.

References

Short communications from selected papers

Lessons learned from using the multilayer fluid modulator outside of indications for use in 38 cases
Niarn Hynes, Mohammed Sultan, Sherif Sultan
Western Vascular institute, Galway, Ireland

The purpose of this study is to scrutinize 38 cases of Thoraco-abdominal aortic aneurysm (TAAA) treated with a Multi-layer Flow Modulator (MFM) out side the indication for use (IFU) which were identified during collecting data for the independent MFM global registry “MFM GR”. All of the cases were performed on a compassionate basis in continental Europe, for patients in whom co-morbid disease severity precluded more invasive treatment alternatives.

Patients and Methods: There were 30 males with mean age 70.8 years and 8 females with mean age 67.8 years. The mean TAAA diameter was 7.1 cm. 10 patients presented with rupture TAAA. 23 patients had previous intervention; 20 of whom had Thoracic Endovascular Aortic Repair (TEVAR) with commercially available thoracic endografts and three had open repair. One patient had a combined procedure in which both commercially available endografts and an MFM were deployed at the same primary setting. 13 patients had chronic Stanford Type B Aortic Dissection with aneurysmal dilatation of more than 6 cm. Six patients had Myotic aneurysms. Four patients had saccular aneurysms, while the number with TAAA Crawford type I, II, III, IV were 1, 7, 5, 2, respectively.

Results: No incidence of death, paraplegia, cerebrovascular accident, renal or visceral compromise was documented during the periopeative hospital stay. During a mean follow-up of 10.03 +/- 6.96 months, total mortality was 89.5% (34 patients), of which 27 (71.1%) were aneurysm-related. All cause survival, freedom from aneurysm related death and rupture-free survival were 17.5%, 25%, 31.5% respectively at 18 months. There were 8 visceral branch complications, (6 Superior Mesenteric Artery (SMA) and 2 renal arteries). 14 endovascular secondary interventions (37.8%) in 11 patients were required during follow-up. None of the dissecting aneurysms treated achieved complete thrombosis and remodeling of the false lumen during follow-up. All treated aneurysms showed a mean aortic diameter growth of 0.71 cm +/- 0.65 cm (range 0–2.61 cm) with a mean growth rate of 0.12 +/- 0.16 cm. Factors having a significance influence on risk of aneurysm related death included maximum aneurysm diameter (p = 0.035, HR = 0.73, 95%CI [0.55–0.96]), Previous TEVAR (p = 0.03, HR = 0.41, 95%CI [0.18–0.91]), the number of MFM devices deployed (p = 0.05,
Background: The present prospective registry is aimed at clarifying the results of elective frozen elephant trunk (FET) surgery using the Evita Open Plus hybrid endoprosthesis (Jotec Inc., Hechingen, Germany) for the treatment of extensive chronic aortic disease.

Methods: Sixteen centers distributed evenly in the French territory participated in the registry; a total of 73 patients received elective FET using the Evita Open Plus device and were included. Pre- and intraoperative data, as well as early clinical results were prospectively stored in an electronic database. Follow-up was conducted by scheduled outpatient visits and control contrast-enhanced CT scans before hospital discharge, at 3 and 12 postoperative months, and every year thereafter. Although minor changes may exist among the participating centers, surgical strategy included circulatory arrest under moderate hypothermia (24–26°C) and antegrade selective cerebral perfusion.

Results: Average age was 63.6 ± 11.3 years. Indications to surgery were true aneurysm (44%), post-dissection aneurysm (20%), chronic dissection (26%) and pseudoaneurysm (10%). Selective cerebral perfusion time was 75.7 ± 39.7 min. Operative mortality was 8.2% (one due to aortic causes). Most frequent morbidities were renal failure (18%), pulmonary complications (15%) and revision for bleeding (8%). Cerebral stroke occurred in 4.1% of cases and spinal cord injury in 6.8%; nonetheless, the latter were permanent in only 2 cases (2.7%). Actuarial survival at 20 months was 85.9% ± 5.2 (3 late deaths). During follow-up, we observed 2 aortic reoperations, 2 endoleaks, 1 pseudoaneurysm, no cases of endotension, and a 51.9% rate of false lumen thrombosis (dissection cases only). The registry included 4 patients who received concomitant FET and distal endovascular completion for extensive descending aortic aneurysm (Figure 1).

Conclusion: The FET procedure for chronic aortic disease using the Evita Open Plus device is reproducible and characterized by acceptable operative mortality/morbidity and contained rates of neurological complications. Continued follow-up will be required in order to detect the occurrence of late aortic complications.

References

Dilation of the ascending aorta: collagen analysis in tissue obtained from patients with bicuspid aortic valve disease compared with tricuspid aortic valve
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Background: Dilation of the ascending aorta is a common occurrence in the elderly and patients with bicuspid aortic valve (BAV) disease. The aim of the current study was to characterize collagen content in advanced...
glycation end products (AGEs) of dilated aortic tissue from BAV patients and control tricuspid aortic valve (TAV) patients.

Materials and Methods: Dilated aortic specimens were collected from 11 BAV patients (mean age, 52.5 ± 17.0 years) and 6 TAV patients (mean age, 68.0 ± 6.8 years). Collagen from 100 mg diluted aortic tissue was isolated by enzymatic digestion using pepsin (PEF) and the non-digested material was further digested using cyanogen bromide (CNBr; CNBr fraction), whereas insoluble collagen was extracted by HCl hydrolysis (HF). The AGE content in the different collagen fractions was analyzed by measuring AGE fluorescence. The AGE-modified carboxymethyllysine (CML), pentosidine, and argpyrimidine in the CNBr fraction were immunologically analyzed via slot blot analysis. The immunological detection of carbonyl groups introduced into proteins by oxidative reactions was analyzed in the CNBr fraction using the Oxyblot protein detection kit. The collagen content in the different fractions was quantified using the 4-hydroxyproline assay.

Results: Samples of TAV tissue showed diminished fluorescence of the pepsin extracted fraction compared to BAV tissue (129.8 ± 53.1 vs 90.6 ± 22.2 μg, p = 0.02). CML and pentosidine content in BAV tissue was significantly higher in comparison to that in TAV tissue (0.355 ± 0.337 vs 0.127 ± 0.151, p = 0.007).

Conclusion: Collagen analysis of AGE content in thoracic aortic dilation is critical to understand the nature of early BAV-associated aortopathy.

Keywords: Bicuspid aortic valve, Advanced glycation end products, Aortopathy.

Bicuspid aortic valve: molecular tissue factors identified prognostic for future aortopathy

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Objective: The clinical course of many patients with a bicuspid aortic valve (BAV) is complicated by ascending aorta dilation. Unfortunately, aortic diameter, which is currently the only selection criterion for surgery, is insufficient for identifying patients that are prone for aortic dilation. Some patients with a non-dilated aorta during concomitant cardiac surgery may still develop aortic dilation in future, while others will never. We investigated structural differences between the aortic wall of BAV and tricuspid aortic valve (TAV) with and without dilation. Furthermore for a possible patient-tailored risk stratification we studied molecular biological markers which might be predictive for aortopathy in BAV.

Methods: Ascending aorta biopsies of BAV (n = 36) and TAV (n = 23) both without and with (>44 mm) dilation were investigated immunohistochemically for the expression of markers for: differentiating and mature smooth muscle cells (SMCs), myoblast differentiation (lamin A/C), cardiovascular aging (progerin), vascular remodeling (TGF-β, phosphorylated Smad2, MMP9) and cellular dedifferentiation (c-Kit, phosphorylated-c-Kit, HIF1α and eNOS).

Results: All BAVs showed significantly less inflammation (p < 0.001), less expression of mature SMC markers (p < 0.01), lamin A/C (p,0.05) and progerin (p < 0.05) as compared to all TAVs. Based on the signaling pathway characteristic for cellular dedifferentiation, exemplified by the marked expression of c-Kit, phosphorylated-c-Kit and HIF1α, the diluted BAV group was comparable to only a subgroup of the non-dilated BAV (BAb). Whereas the remainder of the non-dilated BAV group (BAa) was significantly distinct. This difference between the diluted BAV and BAa was also apparent for expression of the vascular remodeling factors studied.

Conclusion: All BAVs show a less well differentiated aortic wall as compared to TAV. Using a panel of molecular tissue markers the non-dilated BAV can be divided in a susceptible (BAb) and a non-susceptible (BAa) group for aortic dilation.

SCIENTIFIC PROGRAM
Saturday September 13

The treatment of Type B dissection

Prognostic impact of new information from functional imaging (4d-MRI)

Rachel Clough

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Aortic dissection is associated with significant morbidity and mortality [1]. Computed tomography is usually used for rapid radiological evaluation, replacing catheter-based angiography as the most commonly used pre- and post-operative imaging modality for the aorta [2]. Functional imaging methods such as magnetic resonance (MR) have evolved considerably in

Figure 1. These are mesh plots of the velocity of blood flow in the true and false lumens at different timepoints in the cardiac cycle. Red demonstrates high velocity and blue low velocity flow.

Figure 2. These are four dimensional phase contrast MR images. Helical flow evolves over time and is shown with the large white arrow. The true and false lumens are indicated by the red and white arrows respectively.
recent years and are able to provide clinically relevant information regarding the anatomy, and underlying haemodynamics and biomechanics [3-5]. (Figure 1, Figure 2). These features can be used for accurate diagnosis, risk stratification and selection of the appropriate treatment for individual patients [6-8]. Advanced MR image acquisition expertise and equipment is becoming available at a growing number of institutions worldwide and this will greatly enhance existing imaging and treatment strategies for patients with aortic dissection.

References

The new criteria of risk in clinically silent type B dissection
Falko Tillwich
Rostock, Germany

Acute aortic dissection is a multi-faceted disease often associated with fatal outcome. The common denominator of aortic dissection is disruption of the media layer of the aorta with possible complications like sidebranch compromise malperfusion, neurological impairment, pericardial tamponade and cardiogenic shock depending on location and expansion of the dissection. An undelayed diagnostic and therapeutic management are key to successful treatment.

Patients with acute aortic dissection often present with a variety of symptoms. Prognosis is clearly related to undelayed and appropriate individualized treatment depending on the absence or presence of complications in addition to a variety of early signs of impending complications.

Genetics and pathology of bicuspid aortic valves

Comparative biology of progressive dilatation (aneurysm) versus acute intraparietal rupture (dissection) of the human ascending aorta
Jean-Baptiste Michel
Inserm Unit 1148, Paris, France

Whatever their etiologies, monogenic disease, associated to bicuspid aortic valves, or degenerative, all TAAs and dissections share common pathophysiological pathways involving proteolysis of insoluble extracellular matrix [1], allowing dilation and finally rupture [2]. The arterial wall of conductance arteries is structured as a spatial multi-layered tissue: endothelium, media and adventitia from inside to outside, in which all the interstitial signalling are unidirectional from inside to outside (convection) as a teleonomic consequence of species’ evolution [3]. Analysis of interactions between outwardly convected plasma proteins within the arterial wall components has never been studied in TAA. Since plasminogen-derived plasmin is a serine protease able to injure adhesive glycoproteins of the extracellular matrix, to release TGF-beta of its storage sites and to activate MMP’s proforms, we have recently focused on the ability of plasminogen:
- to produce active plasmin during outward convection through TAA walls [4],
- by interaction with vascular Smooth Muscle Cell (vSMC) [5],
- to degrade fibronectin and fibrillin [6],
- to provoke pericellular proteolysis and vSMC anikis [7],
- to release TGF-beta [8],
- to be inhibited by Protease Nexin-1(PN-1) expressed by vSMC [9],
- a Smad2-dependent tissue serpin expression [10],
- to be cleared as a Plasmin/PN-1 complex by vSMC in human TAA.

Therefore plasmin activation could be an interesting target for functional diagnostic and therapeutic option in TAAs and dissections.

References

Novel flow-mediated gene expression signature in patients with bicuspid aortic valve
Per Eriksson
Atherosclerosis Research Unit, Center for Molecular Medicine, Department of Medicine, Karolinska Institutet, Stockholm, Sweden

Bicuspid aortic valve (BAV) is the far most common congenital disorder of the aortic valve and is believed to result from abnormal cusp formation during valvulogenesis. It has been estimated that BAV is present in 1–2% of the population. The presence of BAV predisposes for progressive dilation of the ascending aorta and thereby constitutes an increased risk of aortic aneurysm that can eventually lead to fatal rupture or dissection of the aorta. The prevalence of aortic dilatation (thoracic aortic aneurysm,
BAV is a common disorder (1–2% population) with a high risk of aortic valve deterioration and ascending aorta dilatation. TTE is usually the primary imaging technique for diagnosing BAV and it is usually adequate to assess the aortic root and proximal ascending aorta. Visualization of the mild-distal ascending aorta, the most frequent dilated segment in BAV, may be difficult in adults, and MRI or CT is an option.

Yearly TTE surveillance is recommended in patients with a diameter greater than 40 mm and a baseline MRI or CT scan can be indicated. If there are no significant disparities between measurements, TTE will be used to follow-up valvular dysfunction and ascending aorta dilatation until the diameter reaches 45 mm. In cases with significant disparities (>3 mm) due to difficulties in the visualization of the tubular part of the ascending aorta or asymmetry in the aortic root, annual MRI or CT is mandatory. Surgery is recommended when the aorta reaches a diameter of 55 mm, or 50 mm when there are risk factors. A growth rate of the aorta diameter >3 mm/y, correctly measured, in end-diastole, side by side, using the same imaging technique, should also be considered an indication for surgical treatment. In cases with non-standard body-size, indexation of diameters by BSA is recommended. An index value >30 mm/m² can be accepted as a recommended cut-off value for surgical indication. Valvular dysfunction should be followed-up just as other valvular diseases are.

After surgery, depending on the type: supracoronary replacement with/without aortic valve surgery, Bentall’s procedure or only valvular repair, imaging control by TTE/TOE should be performed before discharge and a TTE annually from then on. In cases with an ascending aorta diameter >45 mm MRI or CT should be performed every 2-3 years. When the aorta diameter is over 50 mm these imaging test are indicated annually. The maximum diameter to indicate a reintervention is not well established (55 mm–60 mm) and should be decided considering the age, risk factors and morbidities. An aortic index 35 mm/m² or a annual growth rate >5 mm are also taken into account for surgical reintervention indication.

References
Aortic dissection in BAV patients: the IRAD experience and beyond
Marco Di Eusanio1, Linda Pape2, Alan C. Braverman3, Marek P. Ehrlich4, Patrick O’Gara5, Truls Myrme6, Reed E. Pyeritz7, Eric M. Isselbacher14, Daniel G. Montgomery11, Arturo Evangelista12, Kim A. Eagle11, Alessandro Della Corte8, Andrea Ballotta9, Kristian Bartnes6, Ehrlich4, Patrick O’Gara5, Truls Myrmel6, Reed E. Pyeritz7, Andrea Ballotta9, Kristian Bartnes6, Ehrlich4, Patrick O’Gara5, Truls Myrmel6, Reed E. Pyeritz7

Background: Bicuspid aortic valve (BAV) is a congenital condition that predisposes patients to ascending aortic aneurysm and dissection. We aimed to characterize patients with acute aortic dissection (AAD) and BAV to improve our understanding of this disease.

Methods and results: We examined 3393 AAD patients enrolled in the International Registry of Acute Aortic Dissection. Among 113 patients with BAV (3.3%), 93 (82.3%) presented with type A AAD while 20 (17.7%) had type B AAD. Compared to tricuspid aortic valve (TAV) patients, those with BAV were younger (mean age: 53.6 ± 16.3 vs. 63.5 ± 13.5 years; p < 0.001). BAV patients demonstrated more known aortic aneurysms (25.5% v. 13.1%; p < 0.001) and prior aortic valve replacement (14.7% vs. 3.1%; p < 0.001). Compared to the TAV population, AAD in BAV patients more frequently involved the aortic root (46.2% v. 34.7%; p = 0.016) and/or arch vessels (41.6% v. 28.6%; p = 0.014). Furthermore, these patients demonstrated less extension to the abdominal aorta (28.6% vs. 44.6%, p = 0.002). In addition, BAV subjects were more likely to present with larger aortas (Sinauses of Valsalva: 5.0 v. 3.9 cm, p < 0.01; ascending: 5.3 v. 4.5 cm, p < 0.001), and aortic valve insufficiency (52.1% v. 39.3%; p = 0.013). Consequently, BAV patients more frequently underwent aortic valve replacement (56.8% vs. 21.7%; p < 0.001) and/or root replacement (66.7% vs. 28.4%; p < 0.001) replacement. Despite their younger age, BAV patients did not show superior hospital survival rates (80.5% v. 86.7%; p = 0.096).

Conclusions: AAD BAV patients present with distinct morphological and clinical characteristics. These findings may expand our understanding of this aortic malformation and improve management.

References

Meeting Abstracts
Future research on BAV will need to be of multidisciplinary and translational nature, research objectives should be pursued taking into adequate account the heterogeneity and complexity of the disease and within multi-specialty, multi-center registries, so that, ultimately, the adequate account the heterogeneity and complexity of the disease and translational nature, research objectives should be pursued taking into account the disease and its relative weight in guiding the indications can vary case by case according to other prognostic factors? The accumulating body of literature, trying to suggest which the other risk markers could be, will be appraised in this lecture: beside the already available phenotypic markers, also markers of altered aortic function and/or abnormal aortic flow and even possibly circulating biomarkers are currently being appraised in this lecture: beside the already available phenotypic neural crest cells with cardiovascular development, particularly that of the semilunar valves. Anat Embryol (Berl). 1990;182:263–72.

The clinical and basic research on bicuspid aortic valve (BAV) and associated aortopathy is an exponentially expanding field. Nevertheless, the current knowledge of BAV, particularly its causes, pathogenetic mechanisms, and pre-clinical history, is probably more limited than generally believed. These persistent gaps of knowledge have affected the surgical treatment of BAV aortopathy with both a lack of guiding criteria for treatment individualization and important divergences in practice among the different surgeons and centers. BAV aortopathy today is over-treated in a proportion of patients undergoing valve surgery with a mildly or moderately dilated aorta, by the addition of aortic resection procedures that are generally at low risk but may not be really needed. Another proportion of BAV patients may be exposed to a significant risk of acute aortic complications that can go overlooked, in the absence of an overt aortic dilatation at the time of aortic valve surgery.

The official recommendations for surgical indication in BAV aortopathy have remarkably changed over the last few years. Akin to the indications for aortic surgery, the criteria for the extent of resection are also currently subject to wide variations according to the individual surgeon or center's policies. However, no other stratification criteria than the aortic diameter are today considered in the surgical decision making process. Does the aortic diameter need to be integrated into a more complex system of stratification including other risk markers, so that its relative weight in guiding the indications can vary case by case according to other prognostic factors? The accumulating body of literature, trying to suggest which the other risk markers could be, will be appraised in this lecture: beside the already available phenotypic markers, also markers of altered aortic function and/or abnormal aortic flow and even possibly circulating biomarkers are currently being focused on in research.

Future research on BAV will need to be of multidisciplinary and translational nature, research objectives should be pursued taking into adequate account the heterogeneity and complexity of the disease and within multi-specialty, multi-center registries, so that, ultimately, the surgical approach to BAV aortopathy will hopefully be based on the concepts of phenotypic and genotypic stratification and treatment individualization.

**Management of aortic valves: conventional surgery and TAVI**

**Pre and post TAVI imaging evaluation**

Luc Pierard

Professor of Medicine, Head, Department of Cardiology, University Hospital Sart Tilman, Liege, Belgium

Multimodality imaging is helpful for the management of patients treated by TAVI. The first step is to ensure the severity of aortic stenosis (AS). Echocardiography is the cornerstone of the assessment but some pitfalls exist. Accurate assessment is challenging in severe AS with low gradient and low flow. Low-dose Dobutamine echocardiography is useful for distinguishing severe vs pseudo-severe AS. The degree of calcification using cardiac computed tomography is a complementary technique.

When the patient is considered for TAVI, severe answers should be provided. Aortic valve annulus sizing is crucial to avoid aortic regurgitation or aortic annulus rupture. Three dimensional imaging is required. Multi-detector CT is the technique of choice and the perimeter and/or the area of the annulus should be measured. Although bicuspid valve has been considered as a relative contra-indication, TAVI is feasible and safe, but this condition needs to be identified and the degree of calcification as well. Concomitant mitral regurgitation is frequent and usually improves after TAVI if it is functional without pulmonary hypertension. Choosing the most appropriate access route is important and CT is the best method to measure the size of femoral and iliac diameters and to assess the presence and severity of vessel tortuosity and calcification.

Echocardiography monitoring of the TAVI procedure is usually not mandatory.

After the procedure, the presence and severity of eventual aortic regurgitation (AR) – a relatively frequent complication –is important as it has prognostic importance. Quantification is difficult. Using echocardiography, the ratio of regurgitation jet width and LV outflow tract diameter and the extent of the circumference of the prosthesis covered by AR are the most useful measurements which could however underestimate AR. Cardiac MR may be interesting for a better quantification. Prosthesis-patient mismatch should be avoided: it is however frequent and associated with a worse outcome.

In conclusion, appropriate imaging evaluation using several modalities is mandatory before and after TAVI.

**Update of the Belgian TAVI registry**

Joelle Kefer

Cliniques Saint-Luc, université catholique de Louvain, Brussles, Belgium

TAVI was first performed in France in 2002 and in Belgium at the end of 2007. The Belgian TAVI registry is a medical community initiative which collected the data of 861 consecutive patients treated with this technique in our country. Despite all the limitations due to the lack of reimbursement of this (relatively) new technique, the data presented during this meeting will show interesting and encouraging results, supporting the technique.

The **PROACT trial: valve choice has changed**

Marc Gerdisch⁴, Dennis Nichols⁵, Allen Greave², John Puskas³

¹Franciscan St. Francis Heart Center, Indianapolis, IN, United States; ²Tacoma General Hospital, Tacoma, WA, United States; ³Mount Sinai Hospital, New York, NY, United States

Introduction: The Prospetive Randomized On-X Anticoagulation Clinical Trial (PROACT) is a multicenter trial designed to determine whether it is safe and effective to manage patients with alternative anticoagulation...
therapy after implantation of the On-X mechanical valve prosthesis rather than the currently recommended societal guidelines. Methods: In the PROACT trial, patients requiring aortic (AVR) who were high risk (HR) or mitral valve replacement (MVR) were randomized to receive either lower dose warfarin (AVR HR) test INR1.5–2.0 and MVR test INR 2.0–2.5 or to continue standard dose warfarin therapy (control INR 2.0–3.0 AVR and 2.5–3.5 MVR). The low risk (LR) AVR group was randomized between an aspirin / clopidogrel regimen and standard dose warfarin, three months after surgery. INR was adjusted by home monitoring and a daily aspirin was given to all patients. Adverse events were independently adjudicated according to the AATS/STS guidelines for valve studies. Results: 749 AVR patients were randomized into control (378) and treatment (371) groups between September 2006 and February 2013. These groups break down to test – 185 HR, 90 LR and 96 MVR; control – 190 HR, 90 LR and 98 MVR. Follow-up is adequate for analysis in the AVR HR patients averaging 3.82 years (755.7 pt-ys control and 675.2 pt-ys treatment). Adverse event data seen in the table for the AVR high risk group show that the treatment group experienced significantly lower major and minor bleeding event rates in %/ptyr. There was no significant difference in incidence of stroke, transient ischemic attack (TIA), total neurological events or mortality. Follow-up in the other groups is shorter but data are trending toward the same conclusion in MVR and toward no difference in AVR LR. Conclusions: INR may be maintained in the range of 1.5–2.0 in AVR patients after implantation of the On-X bileaflet mechanical prosthesis. In combination with low-dose aspirin, this therapy resulted in significantly lower risk of bleeding than customary INR 2.0-3.0, without significant increase in TE.

OnX valve conduit: from table-made to off-the-shelf, a single surgeon experience
Marc Gerdisch
Franciscan St. Francis Heart Center, Indianapolis, United States
Objective: To evaluate the performance of a novel, valved ascending aortic prosthesis for replacement of the aortic root with or without the ascending aorta and/or hemiarch in patients with aortic valve (AV) disease of heterogenous etiology. Methods: Charts were reviewed for all patients who underwent replacement of the aortic root with or without the ascending aorta and/or hemiarch with a novel, valved ascending aortic prosthesis. In early cases, the prosthesis was hand-fabricated by sewing an On-X mechanical aortic heart valve (On-X Life Technologies, Austin, TX) to a Valsalva graft; later, a commercially available, prefabricated, valved ascending aortic prosthesis (On-X) was used. All operations were performed by a single surgeon (MWG).
Results: Between May 2008 and June 2014, 62 consecutive patients underwent the procedure. Baseline characteristics and risk factors are detailed in Table 1. The first 14 patients received the hand-fabricated prosthesis and the subsequent 48 received the prefabricated valved ascending aortic prosthesis. The median valve size implanted was 25 mm (range 21 to 29 mm). Circulatory arrest was employed in 37 patients (average 16.2 ± 6.33 min). Implantation of the valved prosthesis was isolated in 42 cases. Average crossclamp time for isolated-procedure patients was 125 ± 29.4 min in patients with circulatory arrest (n = 23) and 129.2 ± 36.9 min in patients without circulatory arrest (n = 19). Concurrent procedures were performed in 20 patients and included Cox-Maze (n = 5), CABG (n = 11), MV procedures (n = 6), TV procedures (n = 2), removal of an infected PPM (n = 1), and ASD closure (n = 2). Early postoperative adverse events included anemia requiring transfusion (n = 4), renal injury or failure (n = 6), and tamponade (n = 1). There were no early thromboembolic events or MI. PPM and/or ICD were placed in a total of 10 patients. Of these, 6 were necessary after complex cases that included concomitant MAZE for persistent AF (n = 3), redo valve replacements (n = 2), redo or primary valve repairs (n = 4), and/or infected PPM replacement (n = 1). There was one intraoperative death (emergent attempted salvage of an acute ascending aortic dissection; one in-hospital death 13 days postop-

<table>
<thead>
<tr>
<th>Event</th>
<th>Control N (%/ptyr)</th>
<th>Treatment N (%/ptyr)</th>
<th>Rate Ratio</th>
<th>Confidence Limits</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major bleed</td>
<td>25 (3.31)</td>
<td>10 (1.48)</td>
<td>0.44</td>
<td>0.19 – 0.97</td>
<td>0.027</td>
</tr>
<tr>
<td>Minor bleed</td>
<td>26 (3.44)</td>
<td>8 (1.18)</td>
<td>0.34</td>
<td>0.13 – 0.78</td>
<td>0.006</td>
</tr>
<tr>
<td>Total bleed</td>
<td>51 (6.75)</td>
<td>18 (2.67)</td>
<td>0.39</td>
<td>0.22 – 0.69</td>
<td>0.0004</td>
</tr>
<tr>
<td>Stroke</td>
<td>5 (0.66)</td>
<td>5 (0.74)</td>
<td>1.12</td>
<td>0.26 – 4.86</td>
<td>0.859</td>
</tr>
<tr>
<td>TIA</td>
<td>5 (0.66)</td>
<td>7 (1.03)</td>
<td>1.31</td>
<td>0.38 – 4.70</td>
<td>0.630</td>
</tr>
<tr>
<td>Neurological Events</td>
<td>10 (1.32)</td>
<td>12 (1.78)</td>
<td>1.34</td>
<td>0.53 – 3.47</td>
<td>0.489</td>
</tr>
<tr>
<td>Overall Mortality</td>
<td>11 (1.46)</td>
<td>10 (1.48)</td>
<td>1.02</td>
<td>0.39 – 2.64</td>
<td>0.968</td>
</tr>
</tbody>
</table>

Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Valuea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>50.4 ± 10.4</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>44 (71%)</td>
</tr>
<tr>
<td>Body surface area, m²</td>
<td>2.0 ± 0.29</td>
</tr>
<tr>
<td>Aortic valve anatomy</td>
<td></td>
</tr>
<tr>
<td>Bicuspid</td>
<td>44 (71%)</td>
</tr>
<tr>
<td>Unicuspid</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>Trileaflet or other</td>
<td>16 (26%)</td>
</tr>
<tr>
<td>AV endocarditis</td>
<td></td>
</tr>
<tr>
<td>Native</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>Prosthetic</td>
<td>3 (5%)</td>
</tr>
<tr>
<td>Prosthetic valve failure</td>
<td></td>
</tr>
<tr>
<td>Tissue (2 homograft; 3 pericardial)</td>
<td>4 (6%)</td>
</tr>
<tr>
<td>Mechanical</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>AV pathology</td>
<td></td>
</tr>
<tr>
<td>Insufficiency</td>
<td>23 (37%)</td>
</tr>
<tr>
<td>Stenosis</td>
<td>27 (44%)</td>
</tr>
<tr>
<td>Combined AS/AI</td>
<td>7 (11%)</td>
</tr>
<tr>
<td>Other/not applicable</td>
<td>5 (8%)</td>
</tr>
<tr>
<td>Aortic diameter &gt; 5.0 cm</td>
<td>22 (35%)</td>
</tr>
<tr>
<td>NYHA Class</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>17 (27%)</td>
</tr>
<tr>
<td>II</td>
<td>27 (44%)</td>
</tr>
<tr>
<td>III</td>
<td>9 (15%)</td>
</tr>
<tr>
<td>IV</td>
<td>9 (15%)</td>
</tr>
<tr>
<td>EuroSCORE (median, range)</td>
<td>4.7% (1.4 to 72%)</td>
</tr>
</tbody>
</table>

Risk Factors
| Procedure, any | 13 (21%) |
| Persistent AF  | 7 (11%) |
| Prior MI       | 7 (11%) |
| Stroke or TIA  | 2 (3%) |
| Diabetes       | 11 (18%) |
| COPD           | 4 (6%) |
| Urgency        | | |
| Elective       | 46 (74%) |
| Urgent         | 11 (18%) |
| Emergent       | 5 (8%) |

aData are presented as mean ± SD or n (%) unless otherwise noted.
eratively (supermorbid obese patient with emergent preoperative AV endocarditis, septic emboli, ARF, and acute MI with cardiogenic shock); and one in-hospital death 32 days postoperatively (s/p emergent operation for infected prosthetic AV, MV, and PPM). Two late deaths occurred: one 4 months postoperatively from a recurring pseudomonas infection of a PPM combined with AV/MV endocarditis; and one sudden death 20 months postoperatively from a suspected rupture of a descending aneurysm. Long-term, patients show acceptable valve and hemodynamic function. In patients with preoperative AS, average gradients decreased from 39.1 ± 16.6 mmHg preoperatively to 10.0 ± 4.1 postoperatively (n = 30).

There was one late reoperation to repair a periaortic leak following a redo-AVR/MVR replacement in a patient with history of intravenous drug abuse and double prosthetic valve endocarditis. There was 1 lower-extremity thrombotic event, 1 TIA in a patient with subtherapeutic INR, and no incidence of stroke.

Conclusions: In this small series, the novel valved ascending aortic pros thesis yielded acceptable results when used for aortic root, ascending aorta, and proximal arch replacement, without an apparent elevated risk of complications.

Short communications from selected papers

Aortic complications in bicuspid aortic valve and Marfan syndrome: a histologic comparison

Nimrat Grewal1, Romy Franken1, Barbara J.M. Mulder1, Marie-José Goumans2, Johannes H.N. Lindeman2, Monique R.M. Jongbloed2, Marco C. DeRuitter2, Robert J.M. Klautz2, Robert E. Poelmann2, Ad J.C. Bogers2, Adriana C. Gittenberger-de Groot2

1Academic Medical Center, Amsterdam, The Netherlands; 2Leiden University Medical Center, Leiden, The Netherlands

Objective: Patients with bicuspid aortic valve (BAV) and Marfan syndrome (MFS) have an increased susceptibility for development of ascending aorta dilation and dissection compared to persons with a tricuspid aortic valve (TAV). In this study we compared the histopathological substrate of their aortopathy, in order to demonstrate intrinsic defects and to elucidate pathways of a distinct clinical course.

Methods: Ascending aorta wall biopsies were divided in five groups: BAV (n = 36) and TAV (n = 23) both without and with (>44 mm) dilation and non-dilated MFS (n = 8). General histologic features and expression of vascular smooth muscle cell maturation markers were investigated. Furthermore expression of fibrillin-1 known to be mutated in MFS was also studied.

Results: In most aspects MFS was comparable to BAV showing a less differentiated media of the aortic wall with significantly lower expression of alpha smooth muscle actin, SM22alpha, smoothelin and lamin A/C. The fibrillin-1 level was decreased in all BAVs and MFS as compared to the TAV. Unlike TAV, MFS and BAV further did not exhibit markers for degeneration and ageing like inflammation and progerin expression. However similar to the TAV, MFS showed medial cytolytic necrosis and degradation of the elastic lamellae, which was not seen in BAV.

Conclusions: In MFS a fibrillin-1 deficiency accompanies immaturity of the aortic wall like in BAV. This is ameliorated in MFS by the genetic mutation leading to also structurally abnormal fibrillin-1 explaining a multiple hit theory, which leads to severe aortopathy at a younger age in MFS.

New approach in the treatment of aneurysm of Sinus of Valsalva

Andranik Petrosyan, Patrice Bergeron
Department of Thoracic and Cardiovascular Surgery, Clinique "Residence du Parc", Marseille, France

Objective: is to reduce the operation time and the risks of complications related of coronaries’ implantation in high risk population by using a new approach and a new technique of treatment of aortic aneurysm in sinus of Valsalva segment.

Methods: Were selected and operated 15 patients (11 male), mean age 81 ± 8.2 years old, with aortic dilatation in sinus of Valsalva (the mean diameter 50.5 ± 7.38 mm) without aortic annulus dilatation. The major criteria of selection were the dilatation of non-coronary and right coronary cusps of the sinus of Valsalva, with intact left-coronary cusp. Surgical steps included the resection of dilated non-coronary cusp, then dilated aorta 1 cm above of right and left coronary arteries orifices. Next step was a duplication of the aortic wall by polypropylene suture in the middle of right-coronary cusp by reducing the surface approximately equal to unchanged left-coronary cusp. The suture was started from outside to inside and from the end of sinus of Valsalva (sino-tubular junction side) to the annulus of aorta by stopping 1-1.5 mm above of the annulus. The running type of suture was used. With the same stitch and same needle was doubled the suture by coming back to the end of sinus of Valsalva: finishing the node in outside of aorta. A tailored Dacron tube was used to

Figure 1. CT scanner of dilated non-coronary and right coronary side and not dilated left coronary side of sinus of Valsalva.

Figure 2. The reconstruction on picture of the suture on the right coronary side of SV (view from outside).
replace the resected aorta according to David technique. The mean cardiopulmonary bypass time and cross-clamp time were 96 ± 19.4 and 73.4 ± 11.1 minutes respectively. Results: The maximum follow-up was 30 months, mean 12 months. There were no death and stroke in perioperative and early post-operative periods. In one case patient presented low cardiac output syndrome and long cardiopulmonary bypass was needed (140 minutes). One case of TIA was detected. Late complications include one aortic arch dilatation, one left-coronary cusp dilatation, one infective endocarditis of aortic native valve at 18th months and one death at 10th month of follow-up. During the re-operation for infective endocarditis the full visual revision of aortic wall, the added suture of the right coronary cusp and the right coronary orifice revealed the presence of the suture, no involvement in infective endocarditis, no thrombus on the suture, no distortion of the aorta, no occlusion or kinking in right coronary

**Table 1. Preoperative characteristic of 15 patients**

<table>
<thead>
<tr>
<th></th>
<th>N (%)</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>11 (73.3)</td>
<td>5 (6.6)</td>
</tr>
<tr>
<td>Female</td>
<td>4 (26.6)</td>
<td>2 (13.3)</td>
</tr>
<tr>
<td>Diabetic</td>
<td>2 (13.3)</td>
<td>1 (6.6)</td>
</tr>
<tr>
<td>CKD</td>
<td>4 (26.6)</td>
<td>2 (13.3)</td>
</tr>
<tr>
<td>HTN</td>
<td>8 (53.3)</td>
<td>5 (33.3)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>5 (33.3)</td>
<td>1 (6.6)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>2 (13.3)</td>
<td>1 (6.6)</td>
</tr>
<tr>
<td>Smoker</td>
<td>5 (33.3)</td>
<td>1 (6.6)</td>
</tr>
<tr>
<td>COPD</td>
<td>3 (20)</td>
<td>1 (6.6)</td>
</tr>
<tr>
<td>Carotid severe stenosis</td>
<td>2 (13.3)</td>
<td>1 (6.6)</td>
</tr>
<tr>
<td>TIA</td>
<td>2 (13.3)</td>
<td>1 (6.6)</td>
</tr>
</tbody>
</table>


**Table 2. Preoperative data**

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>%</th>
<th>Mm (mean) ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sinus Valsalva dilatation</td>
<td>15</td>
<td>100</td>
<td>50.5 ± 7.38</td>
</tr>
<tr>
<td>Ascending aorta dilatation</td>
<td>11</td>
<td>74.8</td>
<td>53.5 ± 16.7</td>
</tr>
<tr>
<td>Atypical placement of right coronary artery orifice</td>
<td>4</td>
<td>26.6</td>
<td></td>
</tr>
<tr>
<td>Bicuspid aortic valve</td>
<td>4</td>
<td>26.6</td>
<td></td>
</tr>
<tr>
<td>Aortic insufficiency (sever and moderate)</td>
<td>8</td>
<td>53.3</td>
<td></td>
</tr>
<tr>
<td>Left ventricular ejection fraction (mean)</td>
<td></td>
<td>60</td>
<td></td>
</tr>
</tbody>
</table>

SD - standard deviation.

**Table 3. Perioperative data**

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>%</th>
<th>Time minutes (mean) ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVR</td>
<td>10</td>
<td>66.6</td>
<td></td>
</tr>
<tr>
<td>Femoral cannulation</td>
<td>5</td>
<td>33.3</td>
<td></td>
</tr>
<tr>
<td>ECC</td>
<td>15</td>
<td>100</td>
<td>96 ± 19.4</td>
</tr>
<tr>
<td>Cross clamp</td>
<td>15</td>
<td>100</td>
<td>73.4 ± 11.1</td>
</tr>
<tr>
<td>Dacron tube</td>
<td>15</td>
<td>100</td>
<td>30 ± 2.5</td>
</tr>
</tbody>
</table>

*ECC - Extracorporeal circulation, AVR - aortic valve replacement, SD - standard deviation.*

**Table 4. Postoperative complications**

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection of sternum</td>
<td>1</td>
<td>6.66</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>1</td>
<td>6.66</td>
</tr>
<tr>
<td>Arch dilatation</td>
<td>1</td>
<td>6.66</td>
</tr>
<tr>
<td>Left coronary cusp dilatation</td>
<td>1</td>
<td>6.66</td>
</tr>
<tr>
<td>Death</td>
<td>1</td>
<td>6.66</td>
</tr>
</tbody>
</table>
Impact of obesity on the risk of aortic dilatation in patients with bicuspid aortic valve

Marianna Buonocore, Ciro Bancone, Sabrina Manduca, Franco E. Covino, Marco V. Montibello, Giovanni Dialetto, Alessandro Della Corte

Dept of Cardiothoracic Sciences, Second University of Naples — Cardiac Surgery, V Monaldi Hospital, Naples, Italy

Introduction: The impact of obesity on the association between congenital bicuspid aortic valve (BAV) and ascending aorta dilatation is currently poorly defined.

Methods: By analysing a database containing anthropometric, echocardiographic and clinical information of 715 adult BAV patients, we assessed the relation between obesity and aortic diameter at both root and ascending level and between obesity and presence of aortic aneurysm (diameter ≥5 cm), also stratifying with respect to other factors affecting the aortic phenotype, including gender, hypertension, valve function, and cusp fusion pattern.

Results: Obesity was found, according to WHO definition, in 20% patients. The rate of obese patients increased from the third to the fifth decade of age, to remain stable thereafter (p < 0.001). Patients with a body mass index (BMI) ≥30 had a significantly greater mean diameter of the aorta at the ascending tract (4.4 ± 0.7 cm) compared to non-obese patients (4.1 ± 0.8 cm; p < 0.001), whereas aortic root diameter was only slightly larger (3.6 ± 0.6 cm versus 3.7 ± 0.5 cm; p = 0.10).

Conclusion: Obesity was an independent predictor of the ascending diameter in multivariable linear regression analysis (p = 0.004) and of ascending aortic aneurysm in multivariate logistic regression (OR 2.1; 95%CI 1.04–4.16; p = 0.035). The difference in ascending diameter was greater than predicted based on age differences, and obese patients showed no significant correlation between age and diameter unlike the other patients. When stratifying for gender, the difference in aortic diameter between obese and non-obese patients did not reach significance in the female subpopulation (p = 0.06). Obesity was significantly associated with hypertension (p = 0.005), however in non-hypertensive patients the association with larger ascending aorta was confirmed. The difference in ascending diameter between obese and non-obese patients was greater in the subgroup with normal valve function, also showing a stronger correlation of diameter with BMI (Figure 1). There was a significant association between obesity and aortic aneurysm (diameter ≥5 cm), both in the general cohort and in the subgroups with: right-noncoronary cusp fusion pattern (p = 0.007), normal blood pressure (p < 0.001), normal valve function (p = 0.002).
Conclusions: This is to our knowledge the first study observing a significant impact of BMI on the presence and severity of aortopathy in BAV patients. The obesity factor is likely to have complex interactions with other known modifiers of the aortic phenotype: this study suggested which BAV patient profiles could benefit more from dietary and medical interventions aiming at preventing or controlling BMI increase.

PARALLEL SESSION | Innovation in perfusion

COAGULATION MANAGEMENT
Update in coagulation management
Gregory Hans
CHU of Liege, Liege, Belgium

Coagulopathy is frequent after cardiothoracic surgery involving the use of cardiopulmonary bypass. It can lead to excessive bleeding, require the administration of allogenic blood products and adversely affect patients’ outcome. The fact that worldwide 20% of allogenic blood products are transfused in the setting of cardiothoracic surgery further highlights the importance of this problem [1]. With respect to blood products utilization, the use of a transfusion protocol has been shown superior to transfusion based on clinical judgment alone [2]. Consequently, most hospitals have developed their own transfusion protocol for treating bleeding after cardiothoracic surgery. Many of these protocols rely on viscoelastic point-of-care tests like thromboelastometry to guide the administration of blood products. Specific tests for platelet aggregation also become increasingly popular and are particularly helpful in the assessment of patients treated with anti-platelet agents. Despite the broad availability of point-of-care tests, standard laboratory coagulation tests also remain useful. Preoperatively, they inform about the patient’s “coagulation” reserve. Fresh Frozen Plasma (FFP) and platelet concentrates (PC) have long been the cornerstones of treatment of postoperative bleeding. Many recent, the critical importance of maintaining an adequate level of fibrinogen has been recognized [3]. Prothrombin complex concentrates, activated factor VII, factor XIII and desmopressin also appear in many transfusion algorithms although their exact place remains to be determined. There is little doubt that in the near future, these transfusion algorithms will be considered as part of an integrated and patient-centered management of excessive post-operative bleeding particularly relevant to patients undergoing major aortic surgery under cardiopulmonary bypass.

References

TEMPERATURE MANAGEMENT
Deep hypothermia: the gold standard?
John A. Elefteriades
Aortic Institute at Yale-New Haven Hospital, Yale University School of Medicine, New Haven, CT, USA

Effective cerebral protection remains a principle concern during aortic arch surgery. Deep hypothermic circulatory arrest (DHCA) has been entrenched as the primary neuroprotection mechanism since the 70s, as it slows injury-inducing pathways by limiting cerebral metabolism. However, excessive DHCA duration has been associated with poorer neurological outcomes, necessitating the adjunctive use of antegrade (ACP) and retrograde cerebral perfusion (RCP). ACP has superseded RCP as the preferred perfusion strategy as it most closely mimics physiological perfusion. Even with ACP, there exists uncertainty regarding several vital technical details, such as unilateral versus bilateral perfusion, flow rate and temperature, perfusion site, undue trauma to head vessels, and risks of embolization. We believe that for the vast majority of aortic arch operations, the convenience, simplicity and effectiveness of straight DHCA justify its sole use, without necessity for ACP or RCP perfusion adjuncts. This presentation offers a historical and clinical comparison of the DHCA with other techniques of cerebral protection. The safety of straight DHCA for up to 50 minutes of brain protection is documented with detailed neurocognitive testing results.

References

TEMPERATURE MANAGEMENT
Modern temperature management in aortic arch surgery
Maximilian Luehr, Friedrich-Wilhelm Mohr, Christian D. Etz
Department of Cardiac Surgery, Leipzig Heart Center, University of Leipzig, Leipzig, Germany

Arch surgery is undoubtedly among the most technically and strategically challenging endeavours in aortic surgery, requiring thorough understanding not only of cardiovascular physiology, but also in particular, of neurophysiology (cerebral and spinal cord), and is still associated with significant mortality and morbidity. In the late 1980s, when deep hypothermic circulatory arrest (HCA) had gained widespread acceptance as the standard approach for arch surgery, antegrade selective cerebral perfusion (SCP), as an adjunct to deep HCA, began its triumphal march, offering excellent neuroprotection and improved overall outcome. This encouraged the use of antegrade SCP in combination with steady increasing body core temperatures-a trend culminating in the progressive advocacy of moderate-to-mild temperatures up to 35°C, and even nontherm-mia. The impetus for progressive temperature elevation was the limitation of adverse effects of profound hypothermia and the most welcome side
effect of significantly shorter cooling and rewarming periods on cardiopulmonary bypass (CPB), and thereby, potentially, the alleviation of the systemic inflammatory response and, in particular, the risk of severe postoperative bleeding (and other organ dysfunctions). The safe limits of prolonged distal circulatory arrest, particularly with regard to the ischemic tolerance of the viscera and the spinal cord, have not yet been clearly defined. Adverse outcomes due to inappropriate temperature management (core temperatures too high for the required duration of distal arrest) are probably highly underreported. Complications historically associated with hypothermia, namely excessive bleeding, are possibly overestimated. Trading effective neuroprotection and excellent outcomes for the risk of prolonged ‘warm’ distal ischaemia might constitute a significant step back, jeopardizing visceral and, in particular, spinal cord integrity, with unpredictable consequences for long-term outcome and quality of life, particularly affecting those in need of more complex surgery or with previous neurological deficits.

**VENTILATION MANAGEMENT**

**Prophylactic NIV: does it improve patient’s outcome?**

Alastair Glossop

Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, United Kingdom

Noninvasive ventilation (NIV) is a form of respiratory support that has become an established treatment for acute respiratory failure (ARF) over the last 20 years, with mortality benefits demonstrated in patients with RF due to COPD, cardiogenic pulmonary oedema and in the immunocompromised [1]. More recently it has been used prophylactically to prevent progression to respiratory failure in susceptible and high risk patient groups, including patients following major surgery. Development of respiratory failure in post operative patients is associated with a number of adverse patient outcomes including prolonged critical care and hospital stay, increased incidence of infective complications and - in certain patient groups - increased mortality.

The effects of using NIV to prevent respiratory complications following major vascular surgery have been studied in two large RCTs to date [2,3]. They concluded that the prophylactic use of NIV, compared to standard medical therapy, resulted in significant reductions in rates of hypoxaemic respiratory failure, respiratory complications and hospital length of stay. These findings have been replicated in several other patient groups at risk of developing respiratory complications following major surgery including abdominal [4], cardiac [5] and thoracic surgery [6]. In addition a recent meta analysis of studies suggested a mortality benefit with the use of NIV compared to standard medical therapy in general post operative populations [7].

Therefore the use of prophylactic NIV is associated with better outcomes for patients, with reduced morbidity and mortality demonstrated across a range of surgical specialties. The use of NIV is recommended in patients following major vascular procedures to reduce the risk of pulmonary complications that are associated with significant morbidity and worse patient outcomes.

References


**VENTILATION MANAGEMENT**

An innovative approach of CRF treatment: low flow CO₂ removal

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Introduction: As with any therapy, mechanical ventilation has side-effects, and may induce lung injury (ventilator-induced lung injury (VILI)) because of overdistention, repeated stretch to the alveoli and increased inflammatory mediator levels [1]. In order to reduce these deleterious effects, protective ventilation strategies have been developed. However, beneficial effects resulting from protective lung ventilation are counterbalanced by deleterious hemodynamic effects. Indeed, hypercapnia resulting from ventilation at lower tidal volume enhances pulmonary hypertension and is associated with right ventricular failure. In order to supplement or replace the lung function and to avoid ventilator-induced lung injury, gas exchange via an extracorporeal device has been developed. Such a device may make it possible to avoid mechanical ventilation altogether in selected patients. Extracorporeal membrane oxygenation (ECMO) allows blood oxygenation and carbon dioxide (CO₂) removal but requires high blood flow and, as a result, placement of large cannulas. Less invasive veno-venous devices, called “low flow extracorporeal veno-venous CO₂ removal therapy (ECCO₂RT)”, have been specifically designed for CO₂ removal with high gas exchange efficiency at relatively low blood flow rates [2]. The aim of our study was to determine if ECCO₂RT used at early stage of ARDS could have beneficial hemodynamic effects on pulmonary circulation and improve RV function.

Methods: Our study was performed on an experimental model of ARDS obtained in 8 pigs. After sedation, analgesia and endotracheal intubation via a cervical tracheostomy, the pigs were connected to a volume-cycled ventilator. A micromanometer-tipped catheter was inserted into the main pulmonary artery and into the left atrium. A conductance micromanometer-tipped catheter was inserted into the right ventricle. ARDS was obtained by repeated bronchoalveolar lavage (0.9% saline solution). Protective ventilation at lower tidal volume was then achieved. Animals were connected to a pump-driven extracorporeal membrane oxygenator (PALP, MAQUET, Germany) in order to achieve CO₂ removal therapy.

Results: ARDS induced severe hypercapnic acidosis (PaCO₂ = 82.5 ± 10.8 vs. 46.3 ± 10.7 mm Hg and pH = 7.14 ± 0.07 vs. 7.46 ± 0.07, p < 0.01). Systolic pulmonary artery pressure (PAPs) significantly increased from 27.4 ± 4.3 to 43.0 mm Hg, p < 0.01. After the PALP was started, PAP (mm Hg)
aciddosis was corrected (pH = 7.39 ± 0.08) and normocarbia was maintained (PaCO₂ = 41.9 ± 12.6 mm Hg, p < 0.01) despite protective ventilation (tidal volume = 6 vs. 10 mL/kg). At the same time, PAPs significantly decreased to 30.8 ± 5.0 mm Hg, p < 0.01.

Conclusions: Veno-venous removal therapy enabled protective ventilation while maintaining normocarbia during ARDS. CO₂ removal decreased pulmonary hypertension and improved right ventricular function. This technique may be an effective lung- and right ventricular- protective adjunct to mechanical ventilation.

References

ePosters

Transcriptional (ChiP-Chip) analysis of ELF1, ETS2, RUNX1 and STAT5 in human abdominal aortic aneurysm

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Background: The purpose of this study was to investigate the transcriptional control of gene expression in human abdominal aortic aneurysm (AAA). We previously identified 3,274 distinct differentially expressed genes in human AAA tissue compared to non-aneurysmal infrarenal control aorta samples using microarrays. In silico approach found common transcriptional elements in the promoter regions of these genes. Methods and Results: Four transcription factors (ELF1, ETS2, STAT5 and RUNX1) known to be expressed in human AAA were chosen for the study. Chromatin immunoprecipitation with human aortic tissues from AAA patients and controls and antibodies against the four transcription factors followed by hybridization to 2.1 M promoter chips (NimbleGen) was carried out. The results demonstrated enrichment in transcription factor binding in the AAA tissue to a large number of genes which were also differentially expressed in AAA. Functional classification of the genes containing transcription factor binding sites was carried out using Gene Ontology (GO), KEGG, and Network Analysis. The results revealed enrichment in several biological processes including “leukocyte migration” (FDR = 3.09e-05) and “intracellular protein kinase cascade” (FDR = 6.48e-05). In the control aorta, the most significant GO categories differed from those in the AAA samples and included “cytoskeleton organization” (FDR = 1.24e-06) and “small GTPase mediated signal transduction” (FDR = 1.24e-06). When we analyzed the target genes separately based on their mRNA levels in the AAA tissue, genes upregulated in AAA tissue showed a highly significant enrichment for GO categories “leukocyte migration” (FDR = 1.62e-11), “activation of immune response” (FDR = 8.44e-11), “T cell activation” (FDR = 4.14e-10) and “regulation of lymphocyte activation” (FDR = 2.45e-09). The genes downregulated in AAA enriched in completely different GO categories including “cytoskeleton organization” (FDR = 7.84e-05), “muscle cell development” (FDR = 1.00e-04), “organ morphogenesis” (FDR = 3.00e-04) and “cell junction assembly” (FDR = 3.00e-04). Quantitative PCR assays were used to confirm a sub-set of the transcription factor binding sites including those in MRCh1, DUSP10, ITGAM, MRACH1, HDAC8, MMP14, MAG1, THBD and SPOCK1.

Conclusions: This genome-wide analysis provides evidence of involvement of transcription factors ELF1, ETS2, STAT5 and RUNX1 in AAA pathogenesis through transcriptional control.

Does time to theatre affect outcome in the management of ruptured abdominal aortic aneurysms?

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Background: A ruptured abdominal aortic aneurysm (rAAA) is a surgical emergency associated with a high level of mortality [1]. Evidence suggests that the outcome of patients presenting with vascular emergencies is better when managed in high volume centres by specialist surgeons [2]. It is also known that delay to definitive surgery may affect outcome [3]. The Solway Basin Vascular Network (UK) covers a large geographical area with a relatively low population density with the Cumberland Infirmary in Carlisle as its designated vascular centre [4]. Low population density areas like that of the Solway Basin have the predicament therefore of balancing the risk of delay with the benefits of access to a high volume centre. The primary objective of our study was therefore to examine the relationship between time to theatre and outcome.

Methodology: We performed a five year retrospective observational study of all rAAs managed in North Cumbria between October 2008 and October 2013. 101 patients were identified by the electronic search of which 12 sets of notes were unattainable and 27 patients excluded (reasons including diagnosis made at post mortem, incorrect coding, not primary reason for presentation, poor documentation etc). 62 patients were therefore included in the study. We carried out a detailed case-note analysis.

Results: 39 patients presented in the first instance to Carlisle directly, 17 to Whitehaven and 6 to Dumfries. The majority of patients had had symptoms for greater than one hour but less than 24 hours prior to presentation. Over 60% had cardiovascular co-morbidities. 19 of the 62 patients were known to vascular services already and of these 17 were known to have an AAA >5.5 cm, with elective treatment planned and awaited in 4. 43 patients had a mean time to CT from initial presentation of 254 minutes (median 166, range 25–1740). Time from presentation to transfer was poorly documented (11 transferred), of the 6 times recorded a mean of 188 minutes (range 145–315)

Table 1. Time to CT and time to theatre in survivors vs deceased

<table>
<thead>
<tr>
<th></th>
<th>Patients who died</th>
<th>Patients who survived to discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number</td>
<td>37</td>
<td>25</td>
</tr>
<tr>
<td>Time to CT (mins) mean</td>
<td>314 of n = 25</td>
<td>185, 100 of n = 24</td>
</tr>
<tr>
<td></td>
<td>(total who had CT)</td>
<td></td>
</tr>
<tr>
<td>Time to KTS (mins) mean</td>
<td>240, 135</td>
<td>338, 217</td>
</tr>
<tr>
<td></td>
<td>n = 18</td>
<td></td>
</tr>
<tr>
<td>P-possum mean physiology score</td>
<td>32</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>for n = 24</td>
<td></td>
</tr>
<tr>
<td>GAS mean</td>
<td>102</td>
<td>86</td>
</tr>
<tr>
<td></td>
<td>for n = 25</td>
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was reported. 42 patients gave a mean time from presentation to knife-to-skin (KTS) of 296 minutes (median 192.5, range 40–1410). 5 patients died intraoperatively. Overall survival to discharge was 40%, with a calculated mean P-possum predicted mortality of 68% and a mean Glasgow Aneurysm score of 95. Table 1 shows the break down of times to CT and times to theatre for the two distinct groups - those who survived versus those who died.

Discussion: Limitations lie in the nature of the study (retrospective), missing notes and gaps in documentation. We extrapolated from our data however that patients who died had on the whole a much more rapid KTS time (median 135 minutes) when compared to those who survived (median 217 minutes). This is likely to be somewhat attributable to a heightened sense of urgency with patients who are inherently unstable. Interestingly despite a significant mean time to theatre, overall survival was higher than predicted by the P-possum score. (Tables for this abstract can be viewed in the PDF Abstract Book).

References

Evaluation of the multilayer flow modulator in aneurysm repair using porcine animal models
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Purpose: To examine with porcine test animals whether the Multilayer Flow Modulator (Cardiatis, Isnes, Belgium) (Figure 1) can successfully treat abdominal aortic aneurysms (AAA) through intra-arterial hemodynamic modulation without substantial parent or small branch artery compromise.

Methods: The MFM was evaluated in 8 porcine test animals with AAA experimentally induced by grafted venous tissue. The planned study period was 1 month, at which point all animals were to be euthanized and explanted for final examination of devices and vessels. The MFM delivery system underwent a separate evaluation with planned deployment of 8 devices in 1 pig without an induced aneurysm.

Results: In the delivery system evaluation, navigation, placement, deployment, and withdrawal were without complication. In the evaluation of MFM performance in induced aneurysms, angiographic follow-up at 8 days showed 3 aneurysms reduced in size and 1 totally excluded. Collective examination upon final angiography and explantation showed an overall trend of reduction in aneurysm size. In 2 explants, the aneurysm opening was nearly occluded with thrombus and the venous graft wall had thickened significantly, suggesting an evolution into an arterial type vessel wall. No intimal hyperplasia was observed in any of the explants. The visceral arteries covered by the device remained patent, and the device was found to be adhering to the arterial wall with endothelialization clearly visible.

Conclusion: In this in vivo study, the MFM was implanted without intra-arterial compromise and aneurysms were stabilized while adequate blood flow was preserved to collateral arteries. Further studies are needed to assess the MFM.

Changes in thread design of the multilayer flow modulator and the effects on biocompatibility
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The Multilayer Flow Modulator (MFM) (Cardiatis, Isnes, Belgium) is a self-expandable mesh of cobalt alloy wires used for the treatment of aortic aneurysms. We assessed the impact of design thread count and duration of implantation on the biocompatibility of the MFM in porcine animal models. Eight mini-piglets received 26 MFM (12 with 56 thread design, 14 with 80 or 96 threads) in iliac, carotid, and renal arteries. Animals were sacrificed/explanted at 1, 3, and 6 months, when histological and ultra-
structural analyses were conducted. The MFM was successfully deployed in 25 of 26 cases. The 56 thread devices were well tolerated locally and yielded fewer signs of inflammation and neointimal hyperplasia. Percentage stenosis was 16.9% ± 5.1% for the 56 thread devices versus 33.4% ± 10.2% for the 80–96 thread devices (p = 0.001) at 3 months, and 21.7% ± 9.9% for the 56 thread devices versus 33.6% ± 12.4% for the 80–96 thread devices (p = 0.004) at 6 months. The 5 devices selected for Scanning Electron Microscopy (SEM) examination were well deployed, integrated into the vessel wall and endothelialized (Figure 1), and had patent side branches. Further preclinical and clinical studies will extend assessment of the long-term safety and effectiveness of the MFM.

Endothelization kinetics of multilayer versus single layer intra-arterial stents
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The multilayer flow modulator (Cardiatis, Isnes, Belgium) is a self-expandable mesh of braided cobalt alloy wires used for treatment of aortic aneurysms. Because the endothelialisation kinetics of the device are poorly understood, they were investigated and compared with those of two single-layer control stents in porcine animal models.

A total of 19 stents were implanted in the left and right iliac and carotid arteries of 5 adult pigs, with each animal receiving two multilayer flow modulator devices plus a balloon-expandable stainless steel stent and a self-expandable nitinol stent. An animal was sacrificed every week for up to five weeks for device explantation, at which time analyses were conducted on the explants and/or vessels by gross examination, histology, scanning electronic microscopy, and immunohistochemistry.

All 19 stents were successfully delivered. At 1 week, endothelisation and neointimal covering were slightly more advanced for the multilayer flow modulator device than for the two control single-layer stents. For all devices, non-significant traces of inflammation or thrombosis were noted, and there were no signs of local intolerance. Through 5 weeks, the proximal and distal edges of the multilayer flow modulator device were often not fully integrated into the artery wall, indicating that the endothelialization process was not totally complete (Figure 1).

Overall, the multilayer flow modulator device was found to develop a thin layer of endothelial cells sooner and was associated with less significant neointimal development than the two single-layer control stents. At 1 and 2 weeks, surface cell proliferation confirmed the positive integration of the multilayer flow modulator device into vessels, with continuing neointimal development over the duration of the study.

Off label use of Valiant graft for treatment of complete endograft migration with major endoleak
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Background: In this case report we describe the off label use of Valiant graft to treat endograft migration with major endoleak.

Figure 1. Scanning electron microscopy showing endothelialization of the MFM.
Method and Material: A 71-year-old Caucasian man with history of nephrectomy and paraaortic lymphadenectomy presented at approx. 15 years after their initial endovascular abdominal aortic aneurysm repair. He had separation of a proximal aortic cuff from a migrated main body device resulting in a type I endoleak. He was treated with an aortouniiliac endovascular graft with cross-over bypass from right to left common femoral artery.

An infrarenal aneurysm, originating 26 mm below the renal arteries with separation of a proximal aortic cuff from a migrated main body device, was revealed by means of CT and angiography (Fig. 1-2). The maximum outer diameter of the aneurysm was 9 cm. It was decided that a thoracic aortic graft, with a cranial diameter of 40 mm and a length of 152 cm, should be implanted. The stent graft (Valiant, Medtronic, Minneapolis, USA) was inserted via a right femoral arteriotomy over an extra-stiff guidewire (Amplatz extra stiff, William Cook Europe, Bjaeverskov, Denmark). A Reliant® Ballon catheter was used to mold the two graft’s coaxial aortic segments. A patent aortouniiliac stent graft and absence of leakage was shown by means of postoperative angiography. There was technical success with no postoperative complications. On CT-angiography follow-up after 4 days shows subtotal obstruction of aortic stent and the cross-over graft (Fig. 3-4). A transfemoral thrombectomy via right femoral approach was done. Finally a CT-angiography shows rest thrombosis in the Endograft that we decided to treat with oral anticoagulation (Marcumar®, active substance: Phenprocoumon) (Fig. 5).

Conclusion: To perform this technique, there must be a sufficient distance between the proximal landing zone and the flow divider of the migrated endograft to allow deployment. If applicable the treatment with Valiant thoracic endograft has advantages over the use of an open reconstruction upside from off label use due to its lower intra- and post-operative complications.

Conflict of Interest (COI): no conflict

Uptake of FDG detected by positron emission tomography in the abdominal aortic aneurysm is correlated with endoleaks and predicts the adverse outcome of AAA after endovascular aortic repair

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Endovascular aortic repair (EVAR) has been applied to abdominal aortic aneurysms (AAA) to decrease and prevent morbidity and mortality due to open surgery. However, this approach may lead to complications such as occurrence of endoleaks which may result in aneurysm rupture. Decisions for complementary treatment after EVAR to prevent aneurysm rupture are based on endoleak characterization and aortic diameter expansion. These two parameters are however not always predictive of rupture. Recent reports support the view that 18F-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) provides unique information on cellular metabolic activity thought to drive aneurysm expansion and rupture [1]. We evaluated here if FDG/PET could predict the outcome of aneurysms repaired by endoprostheses.

A cohort of 56 AAA patients (55 male; mean age of 74.6 years), treated by EVAR, underwent one or several PET/CT before and/or after surgery with a total number of 108 examinations. When the PET was positive before EVAR, 50% of these patients presented symptoms, such as increasing diameter of the aneurysmal sac, while only 12.5% of PET0 patients were symptomatic. Furthermore, two patients PET+ before EVAR underwent conversion for open surgery for rapid growth and rupture with leaking. Such outcome did not occur among the PET0 patients. No significant difference in the occurrence of endoleak could be found between the two groups of patients. The circulating levels of MMPs inhibitors, TIMP1 and TIMP2, were negatively correlated to the level of FDG uptake measured before EVAR suggesting possible alterations of the extracellular matrix remodeling leading to instability of the wall in this group of patients. A positive FDG uptake occurring after EVAR was not correlated to the AAA diameter but 54% of these patients presented endoleaks versus 22% in PET0. The circulating level of IL6 was also correlated with this FDG uptake after EVAR. When comparing globally the group of patients presenting endoleaks to those without endoleak, significantly increased circulating levels of the fibrinolytic factors D-dimers, and of the inflammatory markers...
cytokine IL8 were observed whereas that of the collagenase MMP1 was largely decreased.

Altogether, these results suggest that PET positivity before EVAR might predict a negative outcome of the endoprosthesis repair and could represent a beneficial tool for patient management.

Reference

Hemodynamic assessment of endoleak using time-resolved phase contrast magnetic resonance imaging
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Background: Endoleak is defined as persistent blood flow within the aneurysm sac but outside the stent-graft [1] and reported to account for >45% of all post endovascular aortic aneurysm repair (EVAR) reintervention complications [2]. Computer tomography (CT) surveillance has been often performed for endoleak detection, but recently the superiority of magnetic resonance angiography (MRA) to detect endoleak has been reported [3–5]. More recently, time-resolved phase contrast magnetic resonance imaging (4D-Flow) has been introduced and demonstrated the utility in hemodynamic analysis of the heart, thoracic aorta, abdominal aorta, branch vessels of abdominal aorta, and intracranial vasculature [6–10]. The purpose of this study is to investigate the usefulness of 4D-flow for assessment of post-EVAR endoleak.

Material and Methods: From January 1, 2013 to April 30, 2014, MRA/4D-Flow and CT were performed in 24 patients within 10 days after EVAR in Hamamatsu University School of Medicine, Japan. MRA/4DFlow date set were transferred to a personal computer in DICOM format, and post-processed with a flow analysis software (Flova, Renaissance Technology, Hamamatsu, Japan). Several sectional planes of the abdominal aorta, inferior mesenteric artery (IMA), and lumbar arteries (LAs) were selected and analysed.

Results: CT identified endoleaks in 12 patients (50%) and MRA/4D-flow identified endoleaks in 18 patients (75%). According to 4D-flow analysis, type I, II, III, IV endoleaks were 8.3, 75, 16.7, and 8.3%, respectively. 7 patients among the 18 patients with endoleak (38.9%) showed concomitant multiple types of endoelak. Hemodynamic analysis with 4D-flow demonstrated that type II endoleak could be further classified into the 3 distinct subtypes according to the flow patterns of the aortic side branches (fig.1). Type Ila endoleak is to-end-fro solitary leak in which branch vessels of abdominal aorta show periodical changes in blood flow direction from between retrograde and antegrade without connecting to any other branch arteries. Type Iib endoleak is inflow-and-outflow connection type leak in which there is a connection between the inflow and outflow aortic branches. Type Iic endoleak is one-way solitary flow type leak in which there is a leaking branch with continuous inflow or outflow, but there is no recognized counterpart.

Conclusions: Hemodynamic analysis using 4D-Flow provides more detailed information about endoleak. This novel modality helps to classify endoleaks and might be useful to decide strategy for treatment of endoleaks for preventing aneurysm rupture.

References

Volume growth of abdominal aortic aneurysms is predictable and correlates with increasing biomechanical rupture risk.
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Introduction: The growth of abdominal aortic aneurysm (AAA) diameter is unpredictable and the use of different measurements that could increase the accuracy is debated. Volume has been proposed as a more sensitive measurement of growth [1,2]. Finite element modeling (FEM)-derived peak wall stress (PWS) and the maximal wall stress/wall strength ratio, called peak wall rupture risk (PWR) has previously been shown to be
Figure 1. Illustration of growth and change of estimated biomechanics in abdominal aortic aneurysms. Red color represents areas with high ratios between wall stress and wall strength. Abbreviation; CT-A: computed tomography angiography.

superior to diameter at predicting rupture [3,4]. In this study, we wanted to test whether growth of AAA volume is predictable and how it correlates with biomechanics as estimated by FEM.

Methods: Forty-one patients (9 women, 32 men) with baseline AAA diameters of 40-60 mm and two computed tomography angiographies (CTA) performed within 8–17 months were retrospectively identified. Digital 3D models of the AAAs were reconstructed from all CTAs and the models were subsequently subjected to FEM. Annual rates of geometric growth and biomechanical change were calculated from the differences in geometry, PWS and PWRR between CTAs. Correlation was determined by Spearman’s rank and predictability was assessed with receiver operating characteristic (ROC) curves.

Results: Mean growth rates for diameter and volume were 3.1 mm (12%) and 21 cm³ (14%) per year, respectively. As expected, baseline diameter correlated with baseline volume (r = 0.71, p < 0.0001) and diameter growth rate correlated with volume growth rate (r = 0.55, p = 0.0002). However, in our small cohort with limited range of AAA diameters, diameter growth could not be predicted by baseline diameter (r = 0.22, p = 0.33, ROC: area < 0.65, p > 0.17). On the other hand, volume growth was predicted by baseline volume (r = 0.56, p = 0.00014, ROC: area > 0.82, p < 0.0020). Volume growth correlated with increasing PWS/PWRR in whole sample (r > 0.3, p < 0.05) and in aneurysms with growth rate higher than the sample median (r > 0.5, p < 0.018), whereas diameter growth did not (whole: r < 0.2, p > 0.29; median: r < 0.3, p > 0.25).

Conclusions: Volume growth was predictable from baseline measurements and correlated with increasing biomechanical rupture risk, in contrast to diameter growth. These results support other recent reports on the possible increased accuracy in growth and rupture risk estimations by considering the volume of the aorta rather than only its maximum diameter.

References

Simultaneous orthotopic liver transplantation with abdominal aortic aneurysm repair
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Introduction: Concomitant abdominal aortic aneurysms (AAA) and liver cirrhosis that need surgical treatment are rare. There are still controversies regarding the timing of AAA repair and liver transplantation as well as optimal treatment of AAA [1]. However, it has been observed that these aneurysms expand more rapidly in transplant recipients than in non-transplant individuals [2]. Furthermore, transplant patients show higher rates of AAA ruptures with the considerable risk for surgery-related ischemic injury [3].

Case presentation: We present a case of a 70-year-old white male presented with end-stage liver disease secondary to chronic hepatitis C with a solitary hepatocellular carcinoma measuring 5 cm in diameter in a right liver lobe. A 6.7 cm abdominal aortic aneurysm (AAA) was also discovered during preoperative evaluation. The decision was made to perform an orthotopic liver transplantation with simultaneous aneurysm repair. The patient was initially explored through median laparotomy. The liver transplant was performed first with the liver graft prepared on the back table in the standard fashion. The liver graft was transplanted using “piggyback” technique with end-to-side caval and end-to-end portal vein anastomosis. The arterial anastomosis was performed with end-to-end anastomosis between the donor proper hepatic artery and the recipient common hepatic artery. The bile duct was anastomosed with an end-to-end anastomosis. Midline incision was extended to the pubis. After proximal and distal vascular control of infrarenal aorta, resection of AAA was performed and reconstruction with prostheses Intervascular 22 mm with 3.0 Prolene in a running fashion. The patient remained well during 1-year follow up.

Conclusion: Although rare, in a patient with end-stage liver disease and AAA, a simultaneous liver transplantation and aneurysm repair represent the safest treatment solution.

References

Long term results after retroperitoneal repair for AAA. Single center experience
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Introduction: The increasing use of endovascular procedures has significantly reduced the number of open surgical repairs for abdominal aortic aneurysm (AAA). The retroperitoneal approach, less invasive than the transperitoneal approach, is characterized by better postoperative outcomes but is still less commonly performed [1]. The purpose of this study
was to describe the postoperative outcomes and survival rates after abdominal aortic aneurysm repair through the retroperitoneal approach.

Methods: A retrospective analysis from consecutive patients electively treated for AAA in our Unit from 1996 to 2011 was performed. In 280 cases the patients received endovascular repair (EVAR), whereas 560 underwent surgical treatment through either a transperitoneal (group TP: 193) or retroperitoneal approach (group RP: 367). The two groups were compared for postoperative outcomes and survival rates at 12 and 180 months after surgery. Oral feeding, mean length of hospital stay, stay in the ICU were shorter in the RP group. Respiratory and cardiac complications were higher in the TP group. 12 and 180 months survival rate in the RP group appeared significantly higher compared with the TP group. From 2008 an enhanced recovery protocol is being applied for all AAA patients undergoing retroperitoneal repair showing additional improvements in postoperative outcomes.

Conclusions: Surgical retroperitoneal approach has still a place in the repair of AAA. Application of enhanced recovery protocols may further contribute to improve postoperative outcomes in patients unsuitable for EVAR techniques. Surgical training and competence should be maintained in order to select the more appropriate therapy for each patient.

Reference

Endovascular treatment of type B aortic dissection with aortic coarctation

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Introduction: Uncomplicated type B aortic dissection has traditionally been treated by medical therapy. Recently endovascular repair has been suggested as an alternative to get better anatomical remodeling of dissected aorta. Association of type B aortic dissection with coarctation is rare. We report one case of uncomplicated type B aortic dissection associated with isthmic coarctation and treated by stent-graft.

Case report: A 63-year-old man was admitted to our emergency room for sudden precordial pain irradiated in the shoulders and later in the epigastrium. He had past history of obesity and asymptomatic isthmic coarctation and treated by stent-graft.

Discussion: Acute aortic dissection distal to isthmic coarctation is rare. Endovascular and surgical treatment are preferably reserved for complicated type B aortic dissections. Recently it was suggested that covering the entry tear of uncomplicated type B aortic dissection by a stent-graft can lead to thrombosis of the false lumen, expansion and remodeling of the true lumen, and prevention of late complications. D-imer level and uptake of 18F-FDG could be determinants of unfavorable outcome in uncomplicated acute type B aortic dissection. Endovascular treatment of type B aortic dissection complicating coarctation is feasible and safe. More follow-up and randomized studies are mandatory to prove the efficacy of such treatment.
determine the feasibility and limitations of endovascular treatment and to outline directions of future development.

Material and Methods: The assessment of images from CT angiography of 100 patients qualified for the invasive treatment of infrarenal AAA was carried out. The average age of the patients was 69 years old. The maximum diameter of the aneurysm was 64 mm. The analysis of the images was performed using Osirix program with 3D-MPR mode. The morphology of the proximal neck was evaluated (diameter, length, angulation, shape, presence of thrombus and calcification) along with the diameter of the distal neck, diameters and course of common iliac arteries, iliac external and internal arteries. Optimal morphological criteria were defined as follows: proximal neck with cylindrical shape with calcification and thrombus, which do not exceed 50% of the neck circumference, diameter 18–28 mm, 15 mm in length and the angle between the aneurysm and the axis of the aorta $< 60\%$, distal neck with a diameter $\geq 20$ mm, distal landing zone of the common iliac arteries with a length of $\geq 10$ mm and $\geq 20$ mm in diameter, iliac external arteries with a diameter of $\geq 7$ mm.

Results: Only 23% of the AAA met all the optimal morphological criteria. The most common deviations from the optimal criteria related to the morphology of the proximal neck was conical shape of the neck, the diameter $> 28$ mm, the angle between the aneurysm and the axis of the aorta $> 60\%$, and also the distal landing zone of the common iliac arteries.

Conclusion: The majority of patients with infrarenal AAA who were qualified for invasive treatment do not meet the optimal criteria for endovascular treatment. The introduction of the systems capable of effective and durable endovascular treatment of AAA with conical, angulated, wide necks and wide common iliac arteries would extend the optimal morphological criteria.

References

Elevating plasma high-density lipoproteins reduce experimental abdominal aortic aneurysm — investigating the therapeutic potential

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Background: We have shown that elevating plasma high-density lipoproteins (HDLs) before aneurysm induction reduces AAA formation in the AngII-induced hypercholesterolemic mouse model [1]. Our further experiments will address the question of whether HDL elevation may be a therapeutic option.

Methods: Experiment 1. AAs were generated in Ang II-induced ApoE deficient animals and following randomization to two groups animals received saline (sc) or rHDLs at 1(10 mg/kg) (sc) on alternate days for six weeks. MRI scans (4.7T) were obtained before and after treatment and the area (mm²) measured at the maximal area.

Experiment 2. Having generated AAs in Angli-induced ApoE deficient mice, following randomization, one group received Adnull (an Adenoviral construct containing no additional gene) and the other group received AdAI (an Adenoviral construct containing human ApoAI2). Mice were MRI scanned before and 4 weeks after injection to determine the effect of elevating HDLs in this manner. In addition, between group evaluation of maximal aortic area was evaluated using histological analysis.

Results: rHDL regresses Ang II induced aneurysm formation (Table 1). AAI increased the plasma concentration of human ApoA-I when compared to Adnull (1.872 ± 0.547 g/L vs 0.043 ± 0.001 g/L, n=5). Changes in size of aneurysm following AAI injection were inconclusive when measured using MRI; histological assessment is currently being completed.

Table 1.

<table>
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<th>Post-treatment</th>
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</table>

References

Long-term experience of surgery of TAAD type A in Ukraine

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Background: Present our approach and show results of surgical treatment of type A TAAD based of our experience.

Methods: 582 consecutive patients with type A TAAD were operated on from 1980 to 2014 in the our clinic (348 (62,6%) males). Their age ranged 20 – 78 years, mean 51,7 ± 9,2. Acute (subacute) dissection took place at 128 (22,5%) pts, chronic – in 20 (13,5%). The causes of aneurysms forming were: arterial hypertension, atherosclerosis – in 363 (62,4%); MS – 82 (14,1%); cystomedianecrosis – 67 (11,5%); BAV – 48 (8,2%); blunt aortic injury – in 8 (1,4%) cases, unknown – 11 (1,5%); lues – 3 (0,5%). In acute (subacute) stages of dissection we performed 453 (77,8%), others – 129 (22,2%) had chronic process. Main part of patients, 379 (65,1%) had type I, others 203 (34,1%) – type II according De Bakey classification. The preoperative status included acute aortic valve insufficiency – 258 (44,3%); haemopericardium (heart tamponade) – 104 (17,9%); acute renal insufficiency – 57 (9,8%); multiorgan failure – 17 (2,9%) patients. All operations were performed with bypass, mild hypothermia (26-30°C), 192 (32,4%) patients with arch injury – deep hypothermia (18-20°DI) and retrograde cerebral perfusion. We used: supracoronal grafting with valve resuspension – in 366 (62,9%) pts, Bentall-de Bono operation in 210 (36,1%); other – 6 operation in 2 (1,0%), 18 (3,1%) patients received I-3 CABG.

Results: Mean blood loss after operation composed 504 ± 73,7 ml. Hemorrhage became the reoperation reason in 17 (2,9%) pts. Temporary neurological complications were observed in 18 (3,0%) pts. There were no change in deep and mild hypothermia group. Permanent neurological complications composed 7 (1,2%), but they but they weren't observed completely since 2008. The postoperative 30 days mortality composed 12,7% on the all period and reduced up to 5,1% for the last 4 years; was slightly higher in acute dissection group, 13% and 11,6% in comparison.

Conclusion: Obtained surgical experience, improvement of heart and brain protection in surgical treatment of dissecting aneurysms type A permitted to achieve hospital mortality 5,1%.

ApoA-I/HDL as diagnostic, prognostic and therapeutic biomarkers of abdominal aortic aneurysm

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Objective: Abdominal aortic aneurysm (AAA) evolution is unpredictable, so we aimed to identify biomarkers that could help in the prognosis as well as in finding potential therapeutic targets to slow AAA progression.

Approach and Results: A differential quantitative proteomic analysis of plasma proteins was performed in AAA patients at different stage of evolution [small AAA (aortic size = 3–5cm) vs large AAA (aortic size>5 cm)] by using iTRAQ labelling, high-throughput nano-LC-MS/MS and a novel multi-layered statistical model. Among the proteins identified, ApoA-I was decreased in large compared to small AAA patients. These results were validated by ELISA in plasma samples from small (n=26) and large AAA (n=26) patients [150(12–168) vs 135(113–144) mg/dl, respectively, p < 0.001]. As expected, ApoA-I levels strongly correlated with HDL concentration (r = 0.9, p < 0.001). ApoA-I/HDL levels showed a negative correlation with aortic size (r = −0.4, p < 0.01) and thrombus volume (r = −0.3, p < 0.01), which remained significant after adjusting for traditional risk factors. In a prospective study, HDL became a strong indepen-
dent predictor for aneurysmal growth rate in multiple linear regression analysis (n = 122, p = 0.008) and was significantly negatively associated with need for surgical repair (Adjusted HR: 0.18, 95% CI: 0.04–0.74, p = 0.018). Moreover, in a nationwide Danish registry, mean HDL concentration in large AAA patients (n = 6,560) was almost half of what was noticed in patients with aortoiliac occlusive disease (n = 23,496) (0.89 (2.99) mmol/l vs 1.59 (5.74) mmol/l, p < 0.001). Finally, administration of an ApoA1 mimetic peptide decreased the mean aortic diameter of AAA in AngII-infused mice compared to those injected with saline (1.4 ± 0.1 vs 1.7 ± 0.2 mm at 28 days).

Conclusion: ApoA-I/HDL levels are negatively associated to AAA evolution. Therapies targeting HDL functionality could halt AAA formation.