A multi-disciplinary journal for clinicians and researchers with interest in the Aorta and its first-order branches, intended for cardiac surgeons, cardiologists, vascular surgeons, interventional radiologists, geneticists, molecular biologists, engineers, and industry scientists, among others.

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Please reference product Instructions for Use for more information regarding indications, warnings, precautions, contraindications and adverse events.

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Distinguished Lecture Given at the Opening of the 5th International Meeting on Aortic Disease, Liège, Belgium (September 15, 2016)

Frank A. Lederle, MD
Minneapolis Veterans Affairs (VA) Medical Center, Minneapolis, Minnesota, USA

Key Words
Aortic aneurysm • Writing and publishing • Clinical trials

It is my pleasure to give this opening talk for the fifth edition of the International Meeting on Aortic Disease – which, as I’ve said before, is my favorite meeting. As many of you know, it began in 2008 as a tribute to Liege’s eminent vascular surgeon and scientist Ray Limet, and has recurred every other year since. It remains about science rather than marketing, and has the right mix of talks, breaks, and social events to get to know colleagues worldwide. I was honored to be invited to give this talk, but also a little worried, especially seeing it billed as a “distinguished lecture”. This seemed to call for something like wisdom, a commodity that’s always in short supply (as you will soon see), so I intend to borrow liberally from others toward the end. Anyway, I will talk for a while and you can decide how distinguished you think it is.

I am especially honored to be addressing this audience because, unlike most of you, I was not trained in aortic diseases. I must have had a lecture on the topic in medical school, but I don’t remember it. Instead I trained as an internist and developed an interest in clinical research (again with no training!) after joining the faculty at the Minneapolis Veterans Affairs (VA) Medical Center. Our general internal medicine group was interested in research methodology and preventive medicine – smoking cessation, flu shots, prostate cancer screening, and the like.

I was looking for a research topic when the January 1986 American Cancer Society journal CA arrived in my mailbox listing the top 15 causes of death in the United States, and I was surprised to find aortic aneurysm among them. All the other “top 15” had societies and campaigns dedicated to their eradication, whereas this one seemed to be just sitting there waiting for someone to take an interest. About that same time I also came across Jack Collin’s November 1985 editorial on “Screening for Abdominal Aortic Aneurysms”[1], inspired by an abstract by Twomey from the year before. These revelations prompted me to do an aneurysm screening project in our clinic, which was published in 1988[2].

My next thought was to do a randomized trial of screening for abdominal aortic aneurysms, but when I thought about it more, it seemed to me that there was a serious problem. Sudden deaths without autopsy, which are quite common and usually not due to aneurysms, would be much more likely to be attributed to aneurysm rupture in the screened group (where many aneurysms would be diagnosed) than in the control group (where there would be fewer known aneurysms), which would have the effect of hiding any true reduction in rupture mortality from screening.

I tried to find ways to deal with this problem in a 1990 article in the Journal of Clinical Epidemiology...
[3], but none of them were feasible. The only reaction I ever got to that article that basically explained why a randomized trial of aneurysm screening could not be successful was years later from my friend Alan Scott, the principle investigator of the two British aneurysm screening trials that changed the world. His comment was “I’m glad I didn’t see it”.

Another problem for me doing a screening trial was that unlike in other countries at that time, the US already required consent from everyone first, resulting in much more work and cost and many cross-overs. The four trials that were actually conducted, all outside the US, just randomized a population list and invited half to screening, with the controls never knowing they were being studied.

Because a screening trial was impractical for me, a ‘repair of small aneurysms’ trial seemed like the next best thing. If repair of small aneurysms was beneficial, it would help make a strong case for screening. If it was not beneficial, the cost-effectiveness of screening would be greatly improved by avoiding repair of all those small aneurysms. Besides, a ‘repair of small aneurysms’ trial addressed a decision that was interesting enough in its own right. You have a common cause of death that lies in wait, easily detectable for many years, but with a treatment that is itself risky and must be applied selectively.

During the Wall Street Journal’s 2004 Pulitzer Prize-winning series on aortic aneurysm, one of the reporters asked my opinion of a surgeon’s comment that deciding whether to repair an aortic aneurysm was like deciding whether to repair a defective hose in an airplane engine before you took off – meaning that you would be crazy not to. I thought the analogy should take account of a few other things, that is: aneurysm repair itself offered a risk of ‘crashing’, and its result, a synthetic graft, was not quite ‘as good as new’. I suggested a revised analogy of whether to repair the airplane engine hose with your jacket sleeve after turning the engine off in mid-flight. The reporter decided to steer clear of airplane analogies, but you can’t help being fascinated by a clinical problem like this!

In 1990, a new colleague joined our group from the Boston VA, where her mentor was chief of the VA Cooperative Studies Program and she had a Cooperative study approved for planning. This provided me with encouragement (and a template) to submit a letter of intent for the Aneurysm Detection and Management (ADAM) study to VA Cooperative Studies that year. In 1992, as we were going before the evaluation committee, the Society for Vascular Surgery recommended elective repair of all abdominal aortic aneurysms 4.0 cm or larger, which raised the stakes and the study was approved and funded.

After that I had to take long phone calls from vascular surgeons telling me how unethical the study was for delaying surgery in the surveillance group. However, once we got going, a major VA medical center refused to participate because they considered repairing 4.0 cm aneurysms to be unethical, so at least we had equipoise of outrage!

As you know, the results of the two small aneurysm trials, ADAM and UK Small Aneurysm Trial (UKSAT), showed no benefit from repairing abdominal aortic aneurysms smaller than 5.5 cm in diameter. While no one has challenged the validity of these findings, it has been a disappointment to me that, to this day, many (and in my own country, perhaps most) of the abdominal aortic aneurysms repaired are smaller than 5.5 cm. Various justifications for this practice have been proposed, but the reasons are not valid and don’t stand up to scrutiny. It seems that people just want to repair small aneurysms, regardless of the data showing that it is not good for the patient. This has surprised me, because all the vascular surgeons I know are so profoundly dedicated to their patients’ welfare in every other way.

For me, after the ADAM trial, one large study led to others, including the Natural History of Large Aneurysms Study, published in 2002 [4] and the VA Open Versus Endovascular Repair (OVER) Trial, published in 2012 [5]. My current trial will sound less “vascular” by your reckoning – a comparison of major cardiovascular outcomes after treatment of hypertension with chlorothalidone or hydrochlorothiazide (2 similar diuretics) using a new low-cost centralized design [6]. This and similar designs used by ADAPTABLE, the NIH’s first National Patient-Centered Clinical Research Network trial on aspirin dosing, and TASTE, a recent Swedish Registry trial on thrombus aspiration, are worth your attention as they chart a path to a future of less expensive randomized trials, on which we will increasingly depend.

Anyway, for me this amounts to about 30 years in clinical research and leading large trials, mostly on abdominal aortic aneurysms, and I’d like to finish up by sharing a few things I’ve learned over that time,
especially in hope of benefitting the younger investigators.

First, ask a good question. The best questions can be stated clearly and are easily understood by non-experts. As one author put it, “Until you can explain your study to the janitor and see his eyes light up, you are not ready to start” [7]. I like to look for things that are widely believed or are enshrined in guidelines, but that I think are probably wrong. And I am not the only who thinks this way. The pathologist Paul Broca said “The least questioned assumptions are often the most questionable.”

Physicist Richard Feynman said “Learn from science that you must doubt the experts.” Playwrite George Bernard Shaw said “All great truths begin as blasphemies.” And Alvan Feinstein, one of the founders of clinical epidemiology, said “the agreement of experts has been a traditional source of all the errors that have been established throughout medical history” [8]. There are still plenty of widely accepted “facts” out there that are not true, and you probably each know of some – I encourage you to point your research in that direction.

As principal investigator of your own study, you are the one who must keep pushing it forward and who knows the big picture so well that you can ensure that any changes to your design don’t cause worse problems than they solve. While few people can actually stop you, many can slow you down. In particular, anytime that you assume that some part of your study is going well because someone else is looking after it, you may be headed for a surprise. I have found that if the principal investigator is not keeping an eye on it personally, it probably isn’t getting done. Sitting around the table (real or virtual), be sure you have done your homework, avoid groupthink, provide your own honest independent assessments, don’t overstate your conclusions, and if you have nothing to say, say nothing.

I’d also like to say a few words about writing. After all, that’s all there is in the end. Always keep the eventual journal article in mind while you plan your study, and keep the possible reviews and letters in mind while you write the journal article. Never write a sentence you can’t defend – it will likely turn up in quotes in one of those reviews or letters. And don’t forget to write the article! Most presented abstracts are never published as manuscripts, in most cases because they are never submitted as manuscripts [9]. I submit the meeting abstract after the paper is written – the paper is no harder that way but the abstract is much easier and more accurate, and actually agrees with the article! And don’t have someone else write your paper! There were surgeons in our hospital who would have their secretary write their articles! Do your own word processing – it’s much better than the old days of typewriters – you can throw ideas and content into the document throughout the whole design and study period, and edit it later.

Best-selling author John Grisham said “The best advice I ever got was to write at least one page a day. Until you write a page, nothing is going to happen.” In a study by Boice, those who set aside 15-30 minutes a day to write were more likely to obtain academic promotion than were binge writers [10]. You can start the writing session painlessly by going over what you’ve already written. As US Supreme Court Justice Louis Brandeis noted “There is no good writing, only good re-writing.”

After double-checking your data, stand by your results, even if they refute your bias and everyone else’s. As Isaac Asimov put it, “The most exciting phrase to hear in science, the one that heralds the most discoveries, is not “Eureka!”, but “That’s funny....” Don’t fall into the mistake John Kenneth Galbraith warned of when he said “Faced with the choice between changing one’s mind and proving that there is no need to do so, almost everyone gets busy on the proof.” The best way to stay unbiased is to stay unbuyed, so beware of financial relationships with industry. Here I repeat Upton Sinclair’s observation that “It is difficult to get a man to understand something when his salary depends upon his not understanding it.”

Some authors like to write long and rambling discussions, stating their favorite opinions on a variety of topics. This never helps get a manuscript accepted and can hurt, especially if the reviewer has different opinions or you overstate your findings. Let the data speak for themselves, and remember your findings don’t ‘prove’ anything, they agree with or don’t agree with some hypothesis, thereby contributing to the collective body of knowledge. Dean Hess wrote [11]: “The purpose of research is to discover and not to prove. It is easy to fall into the trap of designing the study to prove your bias rather than to discover the truth.”

Also important is what you do with the paper when you get it back from the journal. To quote myself from a 2006 talk: “While it is often necessary to write a strongly worded letter, it is rarely necessary to mail it”. The fault
is always with the author, as in “I may have failed to convey...”. Learn to handle rejection; we only count the victories on our résumés anyway. Winston Churchill said “Success is the ability to go from one failure to another with no loss of enthusiasm.” A rejection can also be the beginning of a dialog (and several editors have said so in print). I have had five flat-out rejections later accepted by the rejecting journal.

Another thing I have learned is that, once you pass the age of 50, nothing is more satisfying than mentoring junior investigators, and doing so strictly for their professional advantage, not your own. Of course, only in that way do you really benefit in the ways that count. Erik Eriksen, a successor to Piaget in sorting out what makes us mentally healthy throughout our lives, talked a lot about this. His 7th stage of life he termed: Generativity vs. Stagnation. Generativity is described as “primarily the concern in establishing and guiding the next generation” and he speaks of “the only happiness that is lasting: to increase, by whatever is yours to give, the goodwill and higher order in your sector of the world” [12]. Many of you already know from experience how satisfying mentoring can be.

Finally, I’ve learned that we should remember those who got us here. In the case of IMAD5, that can only mean our conference director, Natzi Sakalihasan. Ralph Waldo Emerson said that “An institution is the lengthened shadow of one man”, and if the institution is the International Meeting for Aortic Diseases, that man is Natzi Sakalihasan. To bring us all together for the fifth time to focus on science without benefit of society dues or intrusion by infomercials is an awesome achievement, and I thank him for it.

I’ve thrown a lot of quotes at you in this little talk, but I’d like to throw out a few more, the first because it’s my favorite election year story. When Adlai Stevenson was running for president against Dwight Eisenhower, a woman called out from the audience “Senator, you have the vote of every thinking person!” Stevenson replied “That’s not enough, madam, I need a majority!” He lost to Eisenhower twice.

The last quote I offer for no other reason than that I like it. It’s from Jack Handey, and goes: “Before you criticize someone, you should walk a mile in their shoes. That way, when you criticize them, you’re a mile away and you have their shoes.” Thank you for your attention, and please enjoy this wonderful meeting.

Conflict of Interest

The author declares no conflict of interest in regard to this publication.

References

8. Pierson DJ. The top 10 reasons why manuscripts are not accepted for publication. Respir Care 2004;49:1246-52. PMID: 15447812
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Lower Aorto-Iliac Bifurcation Position and Incident Cardiovascular Disease: A Multi-Ethnic Study of Atherosclerosis (MESA)

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Abstract

Background: With increasing age, a downward shift of the aorto-iliac bifurcation relative to the lumbar spine occurs. A lower bifurcation position is an independent marker for adverse vascular aging and is associated with increased burden of cardiovascular disease (CVD) risk factors; however, the associations between lower bifurcation position and CVD events remain unknown.

Methods: Abdominal computed tomography scans were used to measure the aorto-iliac bifurcation distance (AIBD, distance from the aorto-iliac bifurcation to the L5/S1 disc space). Cox proportional hazard analysis was used to determine the independent hazard of a lower bifurcation position (smaller AIBD) for incident coronary heart disease (CHD, defined as myocardial infarction, resuscitated cardiac arrest, or sudden cardiac death), CVD (CHD plus stroke or stroke death), and all-cause mortality (ACM).

Results: In the 1,711 study participants (51% male), the mean AIBD was 26 ± 15 mm. After a median follow-up of 10 years, 63 (3.7%) developed CHD, 100 (5.8%) developed CVD, and 129 (7.5%) were deceased. Compared to the 4th quartile of AIBD (highest bifurcation position), participants in the 1st quartile (lowest bifurcation position) had increased risk for CHD (hazard ratio (HR) = 1.5, 95% confidence interval (CI): 0.8-3.0, P = 0.2), CVD (HR = 1.8, 95% CI: 0.9-2.7, P = 0.1), and ACM (HR = 2.2, 95% CI: 1.3-3.6, P = 0.01). After adjustments for CVD risk factors, the HR for ACM was no longer significant.

Conclusion: Despite being an independent marker for adverse vascular changes in the aorta, a lower aorto-iliac bifurcation position was not independently associated with future CVD events. The opposing effects of atherosclerosis and stiffness in the aorta may, in part, explain our null findings.

Key words

Aorto-iliac bifurcation distance • Cardiovascular disease events • Atherosclerosis arterial stiffness

Introduction

The aorto-iliac bifurcation distance (AIBD) is the distance (mm) from the aorto-iliac bifurcation to the L5/S1 disc space and is used to determine the position of the bifurcation relative to the lumbar spine. Thus, a larger AIBD indicates a higher bifurcation position, while a smaller AIBD indicates a lower bifurcation position. In two separate cohorts (n = 748, n = 1,711), we found a lower bifurcation position with increasing age, independent of cardiovascular disease (CVD) risk factors [1, 2]. In the Multi-Ethnic Study of Atherosclerosis (MESA), we additionally found that atherosclerotic risk factors of male gender, smoking, and hypertension were associated with a lower bifurcation position [2].
In contrast, diabetes and elevated triglycerides, which are commonly associated with arterial stiffness, were associated with a higher bifurcation position. Associations of a lower bifurcation position with incident CVD events, however, remain unknown. Thus, we sought to determine the associations between a lower bifurcation position and future coronary heart disease (CHD), which was defined as myocardial infarction, resuscitated cardiac arrest, sudden cardiac death; CVD, which was defined as CHD plus stroke and stroke death; and all-cause mortality (ACM).

Materials and Methods

Study Design and Participants

A detailed description of the MESA study design has been published previously [3]. In brief, MESA is a multicenter, prospective cohort designed to investigate the epidemiology of atherosclerosis. Between July 2000 and August 2002, 6814 men and women (age 45-84 y), who were of Caucasian, Hispanic, African, and Chinese ethnicity and were free from clinically manifest CVD, were recruited for baseline visits at six US field centers: New York, New York; Baltimore, Maryland; Winston-Salem, North Carolina, St. Paul, Minnesota; Chicago, Illinois; and Los Angeles, California.

During follow-up visits between August 2002 and September 2005, 2,202 MESA participants who were representative of the study population were asked to participate in an ancillary study that focused on abdominal aortic calcium. Of these, 2,172 agreed to participate. Individuals were excluded if they were premenopausal or had a recent abdominal computed tomography (CT) scan. The AIBD was measured in 1,711 participants with identifiable bifurcations and L5-S1 disk spaces on CT (method below). Signed informed consent was obtained from all participants, and institutional review board approval was obtained from all participating institutions.

CVD Events

A detailed description of the adjudication process for CVD events has been previously published [3]. Briefly, participants or their next of kin (if participants were unavailable) were contacted at intervals of 9-12 months by telephone, and trained interviewers inquired about interim hospital admissions, cardiovascular outpatient diagnoses, and death. Medical records and death certificates were requested for verification. Two physicians blinded to participants’ risk factors reviewed the data, classified CVD events, and assigned incidence dates. If disagreements persisted after adjudication, a full mortality and morbidity review committee made the final classification. For the current study, CVD events included CHD (myocardial infarction, resuscitated cardiac arrest, or CHD death), CVD (CHD plus non-fatal or fatal stroke), and ACM.

AIBD

Procedures for AIBD measurement have previously been published [2]. Briefly, computer software (Osiris 4.19; University of Geneva, Geneva, Switzerland) was used to identify the coordinates in the x-, y-, and z-planes for the aortic bifurcation and the L5-S1 disk space. A straight distance between the aortic bifurcation and the L5-S1 disc space was measured as the difference of the z-plane coordinates (interclass correlation = 0.89; Figure 1).

Risk Factor Assessment

Participants completed standardized questionnaires at baseline to obtain information on demographics, medical history, and smoking history. A medication inventory was performed, and patients were classified by their use of antihypertensive or hypoglycemic medications. Systolic blood pressure (SBP) was measured three times in the seated position with a Dinamap model Pro 100 automated oscillometric sphygmomanometer (Critikon, Tampa, FL, USA). The mean of the final two measurements was used. Blood samples were obtained after a 12-h fast for the measurements of total cholesterol and high-density lipoprotein (HDL) cholesterol. Diabetes was defined as fasting plasma glucose > 126 mg/dL or use of hypoglycemic medications.

Statistical Analysis

Cohort characteristics were summarized by means (SD) and proportions. Analysis of variance was used to compare patient characteristics. Kaplan-Meier curves and log-rank tests were used to investigate differential survival among AIBD quartiles. Cox proportional hazard regression was used to examine the association of AIBD (continuous and quartiles) for incident CHD, CVD, and ACM. Model 1 was unadjusted, and model 2 was adjusted for age, gender, ethnicity, smoking, diabetes, SBP, hypertension medication use, and total and HDL cholesterol. All analyses were conducted using PASW Statistics 20 (IBM Corp. 2011 Armonk, IL, USA). P-values < 0.05 (two-sided) were considered significant.

Figure 1. Sagittal computed tomography image of the abdomen. Arrow 1 = aorto-iliac bifurcation. Arrow 2 = posterior L5-S1 disc space. Vertical line = aorto-iliac bifurcation distance (AIBD), which was calculated from coordinates (X, Y, and Z) of arrows 1 and 2.
Results

In the 1,711 participants (51% male), the mean age was 65 ± 10 y, and the mean AIBD was 26 ± 15 mm. Compared to the 4th AIBD quartile (highest bifurcation position), the 1st AIBD quartile (lowest bifurcation position) had more smokers and higher SBP (Table 1). In our cohort, 63 (3.7%) CHD events, 100 (5.8%) CVD events, and 129 (7.5%) total deaths occurred (Table 2). The log-rank survival tests among AIBD quartiles for CHD ($\chi^2 = 2.1, P = 0.05$), CVD ($\chi^2 = 3.8, P = 0.3$), and ACM ($\chi^2 = 15, P < 0.01$) are shown in Table 2. The Kaplan-Meier curves of AIBD quartiles for ACM are shown in Figure 1. The 1st AIBD quartile (lowest bifurcation position) had the poorest survival followed by the 2nd, 3rd, and 4th quartiles (highest bifurcation position), respectively.

Table 3 presents the Cox proportional hazard regression of AIBD (continuous and quartiles) for incident CVD events. In model 1 (unadjusted), the per-standard deviation increase in AIBD (higher bifurcation position) was significantly associated with reduced ACM (HR = 0.98, 95% CI: 0.97-0.99, $P < 0.01$) but not significantly associated with a decreased hazard for CHD (HR = 0.99, 95% CI: 0.97-1.0, $P = 0.2$) and CVD (HR = 0.99, 95% CI: 0.99-1.0, $P = 0.06$). Also in the unadjusted models, we found that decreasing AIBD quartiles (lower bifurcation position) were associated with stepwise increasing hazard for CHD, CVD, and ACM. Compared to the 4th quartile of AIBD (highest bifurcation position), individuals in the 1st quartile (lowest bifurcation position) were 2.2 times as likely to experience ACM, and this increase was the only significant finding ($P < 0.01$). After adjustments for traditional CVD risk factors of age, gender, ethnicity, smoking, diabetes, SBP, hypertension medication use, and total and HDL cholesterol, however, the associations of AIBD (continuous and quartiles) for ACM were no longer significant.

Discussion

In a multi-ethnic cohort of community-living older adults, we found that a smaller AIBD (lower

Table 1. Cohort characteristics by AIBD quartile.

<table>
<thead>
<tr>
<th>N=1,711</th>
<th>Cohort</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIBD, mm</td>
<td>26 (15)</td>
<td>7 (9)</td>
<td>21 (3)</td>
<td>31 (3)</td>
<td>45 (8)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Age, y</td>
<td>65 (10)</td>
<td>69 (9)</td>
<td>65 (10)</td>
<td>63 (9)</td>
<td>61 (9)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Male</td>
<td>867 (51%)</td>
<td>54% (50)</td>
<td>49% (50)</td>
<td>49% (50)</td>
<td>51% (50)</td>
<td>0.37</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>725 (42%)</td>
<td>43% (50)</td>
<td>42% (49)</td>
<td>40% (49)</td>
<td>45% (50)</td>
<td>0.48</td>
</tr>
<tr>
<td>Hispanic</td>
<td>427 (25%)</td>
<td>24% (43)</td>
<td>26% (44)</td>
<td>27% (44)</td>
<td>23% (42)</td>
<td>0.57</td>
</tr>
<tr>
<td>African</td>
<td>352 (21%)</td>
<td>22% (42)</td>
<td>18% (38)</td>
<td>21% (41)</td>
<td>21% (41)</td>
<td>0.45</td>
</tr>
<tr>
<td>Chinese</td>
<td>207 (12%)</td>
<td>11% (31)</td>
<td>14% (35)</td>
<td>12% (33)</td>
<td>11% (31)</td>
<td>0.29</td>
</tr>
<tr>
<td>Smoking</td>
<td>861 (50%)</td>
<td>58% (49)</td>
<td>49% (50)</td>
<td>45% (50)</td>
<td>50% (50)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Diabetes</td>
<td>215 (13%)</td>
<td>12% (32)</td>
<td>11% (31)</td>
<td>14% (35)</td>
<td>13% (34)</td>
<td>0.63</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>127 (21)</td>
<td>130 (22)</td>
<td>127 (22)</td>
<td>126 (22)</td>
<td>123 (19)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Hypertension medication</td>
<td>35%</td>
<td>39 (49)</td>
<td>35 (48)</td>
<td>34 (47)</td>
<td>32 (47)</td>
<td>0.22</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>196 (35)</td>
<td>193 (35)</td>
<td>196 (34)</td>
<td>195 (51)</td>
<td>199 (35)</td>
<td>0.09</td>
</tr>
<tr>
<td>HDL cholesterol, mg/dL</td>
<td>51 (15)</td>
<td>51 (16)</td>
<td>52 (15)</td>
<td>50 (15)</td>
<td>51 (15)</td>
<td>0.5</td>
</tr>
</tbody>
</table>

ACM = all-cause mortality; AIBD = aorto-iliac bifurcation distance; HDL = high-density lipoprotein; Q = quartile.

Data are means (SD), n (%). $P$ represents quartile comparisons.
bifurcation position) was significantly associated with increased hazard for incident ACM. We also found that this increased risk was explained by traditional CVD risk factors. No significant associations were observed between the AIBD and incident CHD and CVD; although, their trends were similar to that of ACM.

Prior studies have reported a lower aorto-iliac bifurcation position with older age (age-related bifurcation descent) [4, 5]. We were the first to report that in two separate cohorts, one clinical and the other community-based, CVD risk factors were independently associated with age-related bifurcation descent [1, 2]. Furthermore, in a multi-ethnic cohort, we reported that atherosclerotic risk factors of age, gender, hypertension, and smoking were independently associated with a lower bifurcation position. In contrast, risk factors that are commonly associated with arterial stiffness, such as diabetes and elevated triglycerides, were associated with a higher bifurcation position. We surmised that a lower bifurcation position may be an independent marker for vascular aging and hypothesized that a lower bifurcation position may also be an independent marker for incident CVD events.

Supportive of our hypothesis, we found that decreasing AIBD quartiles (lower bifurcation position) were associated with stepwise increasing risk for incident CHD, CVD, and ACM. These findings, however, were only significant in unadjusted models for ACM only, as the associations were attenuated after adjustments for common CVD risk factors. With older age, atherosclerotic changes in the aorta are associated with increasing aortic diameter

<table>
<thead>
<tr>
<th>N = 1,711</th>
<th>CHD</th>
<th>V</th>
<th>ACM</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD, 63 (3.7%)</td>
<td>2.1</td>
<td>0.5</td>
<td>1.1 (0.5-2.1)</td>
</tr>
<tr>
<td>CVD, 100 (5.8%)</td>
<td>3.8</td>
<td>0.3</td>
<td>1.2 (0.7-2.1)</td>
</tr>
<tr>
<td>ACM, 129 (7.5%)</td>
<td>15</td>
<td>&lt;0.01</td>
<td>2.2 (1.3-3.6)</td>
</tr>
</tbody>
</table>

ACM = all-cause mortality; AIBD = aorto-iliac bifurcation distance; CHD = coronary heart disease (defined as myocardial infarction, resuscitated cardiac arrest, and sudden cardiac death); CVD = cardiovascular disease (defined as CHD plus stroke and stroke death).

<table>
<thead>
<tr>
<th>N = 1,711</th>
<th>CHD</th>
<th>V</th>
<th>ACM</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIBD, mm, per SD</td>
<td>0.99 (0.97-1.0)</td>
<td>0.2</td>
<td>0.99 (0.98-1.0)</td>
</tr>
<tr>
<td>Q4 (≥36 mm)</td>
<td>1 [Ref]</td>
<td>1 [Ref]</td>
<td>1 [Ref]</td>
</tr>
<tr>
<td>Q3 (26-36 mm)</td>
<td>1.0 (0.5-2.1)</td>
<td>1.0</td>
<td>1.1 (0.6-2.0)</td>
</tr>
<tr>
<td>Q2 (17-26 mm)</td>
<td>1.1 (0.5-2.4)</td>
<td>0.8</td>
<td>1.2 (0.7-2.1)</td>
</tr>
<tr>
<td>Q1 (≤17 mm)</td>
<td>1.5 (0.8-3.0)</td>
<td>0.2</td>
<td>1.6 (0.9-2.7)</td>
</tr>
</tbody>
</table>

ACM = all-cause mortality; AIBD = aorto-iliac bifurcation distance; CHD = coronary heart disease (defined as myocardial infarction, resuscitated cardiac arrest, and sudden cardiac death); CI = confidence interval; CVD = cardiovascular disease (defined as CHD plus stroke and stroke death); HR = hazard ratio; Q = quartile.

*Model adjusted for age, gender, ethnicity, smoking, diabetes, systolic blood pressure, hypertension medications, and total and high-density lipoprotein cholesterol.
trasonography, the primary screening modality for aortic disease, is a proven and more cost-effective method without radiation exposure. Importantly, our results have strong research implications for anatomical changes in vascular beds, and if coupled with advancements in diagnostic imaging, these findings may aid future clinical use.

In conclusion, in a multi-ethnic cohort of community-living, healthy older adults, a lower bifurcation position was not independently associated with CVD events. The opposing effects of atherosclerosis and stiffness in the aorta may, in part, explain our null findings.

Acknowledgements

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Conflict of Interest

The authors have no conflict of interest relevant to this publication.

References


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Case Report

AORTA, October 2016, Volume 4, Issue 5:162-166
DOI: http://dx.doi.org/10.12945/j.aorta.2016.15.034

Treatment of Dacron Grafting Dilatation with Endovascular Stent Grafting

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Abstract

Dacron grafts are frequently used during surgical revascularization procedures. Complications including graft thrombosis and infection are well known; however, aneurysm formation is extremely rare. In this report, we describe dilatation of a Dacron graft detected four years after aortobifemoral bypass procedure in a 50-year-old male patient who was treated with endovascular stent grafting.

Key Words
Peripheral arterial disease • Bypass • Dacron graft • Dilatation • Endovascular stent graft

Introduction

Surgical revascularization procedures are effective therapies for patients with peripheral arterial diseases. Dacron grafts are frequently used during these procedures. Infection, graft thrombosis, and pseudoaneurysm are well known complications. Although reported in the literature, rupture or aneurysm formation is a very rare complication with knitted Dacron grafts [1, 2]. The latter may be completely asymptomatic and be diagnosed with radiologic techniques or present as a pulsatile mass and its consequences [3].

In this report, we present a patient with dilatation of the Dacron graft following aortobifemoral bypass surgery together with a management strategy for the disorder.

Case Presentation

A 50-year-old male patient presented to our institution with left leg pain and a pulsatile mass in left femoral region. He had undergone an aortobifemoral bypass procedure with an 18 × 9-mm, 45-cm knitted polyester vascular graft (FlowNit Bioseal, Knitted Polyester Vascular Graft, L: 45 cm, D: 18 × 9 mm; collagen-coated, JOTEC Vascular Prosthesis, JOTEC GmbH, Hechingen, Germany) for the treatment of aortoiliac occlusive disease in 2011. He was an active smoker but did not have other comorbidities. He had been asymptomatic until he presented to the clinic with claudication of the right leg in 2013. Control computed tomography (CT) angiography revealed aneurysm formation and thrombosis of the right leg. Control magnetic resonance angiography (MRA) at the time of presentation showed severe dilatation of the graft. The patient was referred to our institution for a second opinion.

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common femoral artery (Figure 1A1, 1A2, 1A3). Prior to operation planning, the patient had undergone conventional angiography in 2014, which indicated complete thrombosis of the right limb of the graft (Figure 1B). Angiography performed in 2013 and 2014 also showed dilatation of the Dacron graft (Figure 1A1, 1B). He underwent crossover bypass with a saphenous vein from the left limb of the graft to the right profunda femoral and superficial femoral arteries. A control CT angiography showed patent bypass grafts together with increased diameter of the Dacron graft with a body size of 28.5 mm and 13.3-mm leg size (Figure 1C1, 1C2). He presented with an enlarging pulsatile mass at the left femoral region 6 months postoperatively. CT revealed further dilatation of the Dacron graft (29.4-mm body size, 14-mm leg size) and a 50-mm diameter left femoral aneurysm (Figure 1D). All the radiographic measurements were performed by the radiologists with ExtremePACS viewer software (Hacettepe Teknokent A.S., Ankara, Turkey). We planned surgical correction of the left femoral aneurysm and endovascular security for the dilated Dacron graft after obtaining the patient’s consent.

The operation was performed with sedation and local infiltration anesthesia with a 50% mixture of prilocaine hydrochloride and bupivacaine hydrochloride. A standard longitudinal femoral incision was performed, and the dilated leg of the aneurysm, common, profunda, and superficial femoral arteries were dissected. There was no sign of infection or any other cause to explain the progressive dilatation of the Dacron material. A Linderquist extrastiff guide wire 0.035 (Cook Medical Inc., Bloomington, IN, USA) was positioned at the ascending aorta through a 5 French (F) sheath inserted in to the left leg of the graft through the aneurysm. A 5 F sheath was inserted percutaneously through the right brachial artery. A 5 F pigtail catheter was directed for angiographic monitoring of the stent graft position though this 5 F sheath. After intravenous administration of 5,000 units of heparin, we inserted the main body (size: 23 × 14 × 105 mm, Medtronic Endurant Stent Graft System, Santa Roja, CA, USA) and leg extension (size: 16 × 16 × 120 mm, Medtronic Endurant Stent Graft System) through the left leg of the aortobifemoral Dacron graft and positioned and expanded at the infrarenal aorta covering the dilated Dacron graft until the crossover femoral bypass. The aneurysm at the femoral region containing the dilated Dacron graft segment was then resected, and arterial continuity was provided with a ringed 8-mm expanded polytetrafluoroethylene graft (FUSION Vascular Graft, Maquet Cardiovascular, Wayne, NJ, USA) that was interposed between the left limb of the bypass graft and left common femoral artery.

The postoperative course was uneventful, and the patient was discharged symptom free from the hospital on the fifth postoperative day. He has been doing well for 2 years and receives acetylsalicylic acid, atorvastatin, pentoxyphylline, and clopidogrel. The patient was investigated for systemic connective disorders and found to be negative. Control CT confirmed successful surgical and endovascular treatment (Figure 2).

Discussion

Dacron grafts are frequently used during the treatment of aortic and peripheral arterial pathologies. Different types of Dacron grafts such as knitted, woven, flat, and swollen are available in the market. While woven grafts are generally used for thoracic and abdominal aortic aneurysm repairs and aortic replacement, knitted grafts are used for arterial bypass procedures of the aorta, iliac, common femoral, and superficial femoral arteries. Graft patency rates are quite promising in selected patients and revascularization locations; however, the procedures are not event free [4]. Complications include infection, graft thrombosis, pseudoaneurysm, aneurysm or dilatation, and rupture [5].

The intrinsic Dacron graft failure rate ranges from 0.5-3% [6]. The most common complications are infection and graft thrombosis; Dacron graft aneurysms are very rare disorders. This complication is reported to occur in 1-3% of patients with graft replacement and are usually seen 4-6 years after surgery [5]. The first report on this disorder mentioned aneurysmal dilatation of Dacron graft 5.5 years after surgical treatment [7]. Etiology of anastomotic complications are variable and include infections, surgical procedure problems, collagen tissue disorders, and atherosclerotic diseases. In contrast, a nonanastomotic aneu-
Figure 1. Preoperative computed tomography (CT) angiography showing Dacron graft dilation (29.4-mm body size, 14-mm leg size) and a 50-mm diameter left femoral aneurysm together with crossover femoral bypass with saphenous vein grafts. Panel A1: Control CT in 2013 revealed dilatation of the Dacron graft. Panel A2: Both legs of the Dacron were patent, but the right common femoral artery was thrombosed. Panel A3: CT shows a thrombosed right femoral artery and dilated left femoral artery. Panel B: Prior to operation planning, the patient underwent conventional angiography in 2014, which indicated complete thrombosis of the right limb of the graft and further dilatation of the Dacron graft (body size 27.2 mm). Panels C1-C2: A control CT angiography in 2014 showed an increase in diameter of the Dacron graft with a body size of 28.5 mm and 13.3-mm leg size. Panel D: When the patient presented with an enlarging pulsatile mass at the left femoral region 6 months after the operation, the CT angiography revealed further dilatation of the Dacron graft (axial view, 29.4-mm body size).
Most cases may present with generalized dilation. However, the literature includes very rare disorders like multiple saccular aneurysms [14]. CT is a useful and reliable imaging method and commonly used for diagnosing graft dilatation [3].

Therapy modalities include surgical and endovascular treatments, with the latter typically preferred to open surgery. It reduces mortality, morbidity, and hospital stay length and avoids open surgery complications [2]. In the present case, we detected Dacron graft dilatation together with a femoral aneurysm comprising both the native artery and the leg of the graft. Preventing further Dacron graft dilatation was achieved with endovascular therapy, which was also a more comfortable and safe therapy option for compared with conservative surgical graft removal and replacement.

**Conclusion**

In conclusion, the risk of aneurysm and rupture is very rare but known complications with Dacron grafts used for arterial reconstructions. Treatment should be considered for dilated portions of the Dacron prosthesis. Endovascular stent graft repair seems an easier and more comfortable therapy option in patients with Dacron graft aneurysms.

**Acknowledgment**

The export director and international product specialist of the JOTEC company were informed about the issue, and the international sales director replied that the Turkish distribution partner would contact us, but this has not yet happened.

**Conflict of Interest**

The authors have no conflict of interest relevant to this publication.
References


Frozen Elephant Trunk and Antegrade Visceral Debranching in the Surgical Treatment of Type B Aortic Dissection: An Alternative Method

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Abstract

Intervention is inevitable in complicated Type B aortic dissections. Classical surgical procedures and endovascular interventions are far from ideal treatments due to their high risk of periprocedural complications and mortality. There is often a need for alternative method in cases of difficult anatomy. We present the combined use of frozen elephant trunk and antegrade visceral debranching methods in the treatment of a 54-year-old male patient with complicated Type B aortic dissection.

Key Words

Aortic dissection • Intervention • Surgery

Introduction

The classical surgery for Type B aortic dissection, which is performed by opening the thoracic and abdominal cavities and replacing the aorta and its branches, carries high morbidity and mortality and requires experience. Reports indicating mortality rates higher than 20%, even from the most experienced centers, clearly demonstrate the need for alternative methods [1].

Although commonly used endovascular interventions have successful early- and intermediate-term results in cases of anatomical convenience, there are considerably high rates of retrograde dissection and endoleaks. While problems related to the intervention site, such as bilateral iliac artery stenosis or dissection, may prevent access to the lesion, solutions such as fenestrated and custom-made grafts may fail in cases with visceral organs supplied from a false lumen [2].

Our center implemented the novel procedure of combined use of the frozen elephant trunk (FET) procedure with antegrade visceral debranching as an alternative surgical technique for the treatment of complicated Type B aortic dissection. The indications, advantages, and limitations of this technique are presented in the context of the treatment of a case admitted to our clinic.

Case Presentation

A 54-year-old male patient having no systemic disease except hypertension was admitted to the emergency service of our hospital with a 1-week history of back and abdominal pain. Contrast-enhanced computed tomography (CT) angiography revealed a dissection flap starting 5 mm distal to subclavian artery,
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involving the celiac and right renal arteries and extending to both common iliac arteries (Figure 1). The diameter of the descending aorta was 68 mm at the level of the subclavian artery, 47 mm at the level of aortic truncus, and 32 mm at the level of diaphragm. The patient was referred to our department and hospitalized for advanced investigation and treatment. When his pain and signs of malperfusion worsened, he was taken to emergency surgery.

Surgical Technique

Surgery began after a central venous catheter was introduced through the right jugular vein, arterial pressure monitoring was started by placing a left radial line, cerebral pulse oximetry monitoring was accomplished, and a catheter was placed for cerebrospinal fluid pressure measurements. The right axillary artery was exposed. Following median sternotomy, the abdomen was opened by a midline incision, and the celiac trunk and right renal arteries were exposed and secured with surgical tape. Cardiopulmonary perfusion was started after systemic heparinization, right axillary arterial and two-stage unicaval venous cannulation. The patient was cooled. A Dacron Y-tube graft (24 × 12) was passed through the transverse sinus. Perfusion pressure was reduced, and the proximal end of the Dacron tube graft was anastomosed end to side to the ascending aorta anterior to the transverse sinus under side clamping. When the trans-esophageal temperature reached 25°C, an aortic cross clamp was placed, and the heart was arrested by antegrade tepid blood cardioplegia. After cardiac arrest, the cross clamp was moved to the brachiocephalic artery, and antegrade selective cerebral perfusion (flowrate: 10-15 mL/kg/min) was established. Aortotomy was performed distal to the left subclavian artery, and it was observed that the dissection flap was 10-15 mm distal to the left subclavian artery. Single 4/0 pledgeted Prolene sutures were placed into the aorta distal to the subclavian artery. A 24 × 150 mm E-Vita Open Plus (JOTEC® GmbH, Germany) graft was introduced through the subclavian artery to the level of seventh vertebra and deployed according to the recommendations of the graft manufacturer. The proximal end of the graft was sutured to the aorta distal to the subclavian artery using preplaced Prolene sutures. After primary closure of the aortotomy, air was evacuated, the clamp was removed, and selective antegrade cerebral perfusion (58 minutes) was discontinued.

The implanted Dacron tube graft was passed through the aortic hiatus to the abdominal cavity. The proximal ends of celiac and right renal arteries were ligated, and distal ends were anastomosed end-to-end with the legs of the Dacron graft. The surgery was completed in a total perfusion time of 140 minutes. The patient's intensive care stay was prolonged due to respiratory complications, and he was transferred to the ward on postoperative day 6. He was discharged uneventfully on postoperative day 15.

In follow-up performed at 1, 6, and 16 months, the diameter of the descending aorta was measured as 58, 56, and 55 mm, respectively, in control contrast-enhanced CT, and it was observed that descending aorta was completely thrombosed at the level of the graft and bypass grafts were patent. There were no clinical signs of malperfusion (Figure 2).

Discussion

Early intervention in cases with acute Type B dissection is not recommended because classical surgery
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construction are segmentation of the dissection flap, interventions using noncovered stents, or extra-anatomic bypass [8, 9]. Although the early results of noncovered stents are encouraging, long-term outcomes and problems related to their use are not yet known.

We thought that restoration of blood flow of malperfused organs via the dissected iliac artery was not convenient in the present case, and access by the femoral route was not safe due to bilateral iliac artery dissection. Extra-anatomic bypass solutions performed to the malperfused organ supplied from a dissected artery may be problematic because of structural problems and turbulence due to the retrograde flow. Although high patency rates are reported in the literature, potential problems related to retrograde flow are not known [10].

To the best of our knowledge, this case is the first isolated Type III aortic dissection case in the literature in which antegrade perfusion of the malperfused organs was provided from the ascending aorta (preserved from dissection) and the intimal rupture was closed with an open FET procedure instead of using the unsafe femoral route.

Our surgical method carries the potential to answer many problems. It provides direct visualization of the primary tear in the aorta. It permits closure of the rupture with a graft, completely eliminating Type Ia endoleaks and the risk of retrograde dissection by suturing the proximal end of the graft to the aorta. It provides convenience for a probable second surgery by the graft placed to the descending aorta. It achieves simultaneous perfusion of all visceral organs by antegrade (according to the direction of the flow) debranching. Thus, we believe there are multiple advantages of this method. The need for cardiopulmonary bypass and selective antegrade cerebral perfusion for the application of the procedure are the greatest disadvantages.

In conclusion, the FET method is an alternative in the treatment of cases with complicated Type III aortic dissection in which the femoral route cannot be used. This method, while preventing the proximal spread of dissection, removes the risk of Type 1a endoleaks. By stabilizing the dissection flap in the descending aorta, the graft preserves perfusion of the organs supplied from the true lumen. After the procedure, the

Figure 2. Postoperative three-dimensional computed tomography angiography image.

carries high morbidity, and endovascular interventions carry risk of retrograde dissection and have unknown long-term results. Surgical or endovascular interventions are indicated in complicated cases (i.e., in cases with rupture, treatment-resistant hypertension, uncontrolled pain and malperfusion syndrome) [3, 4]. There is an increasing trend for endovascular interventions in recent years as they promise more successful results than medical and classical surgical treatment in cases with life-threatening ruptures [5]. Besides problems related to the intervention site like bilateral iliac artery stenosis or dissection, which may make the intervention impossible, the routine use of this intervention is restricted due to the risk of retrograde thoracic aortic dissection during and after the procedure and Type Ia endoleaks [6].

Another vulnerable point in endovascular interventions is the presence of a dissection flap involving visceral artery branches in patients with malperfusion. Perfusion defects are among the most important factors increasing mortality in these patients [1, 7]. In the presence of dynamic obstruction, organ perfusion and symptoms can be improved after an endovascular procedure, but the treatment options for patients with continued malperfusion or static ob-
visceral organs with malperfusion can be supplied in the normal flow direction using the vessel preserved from dissection (antegrade) in the same session. The greatest limitation is the need for cerebral perfusion and cardiopulmonary bypass during the procedure. We suggest that this method can be an alternative in selected cases.

References


EDITOR’S QUESTIONS:

1. Did this patient manifest clinical malperfusion or just radiographic?

   The patient was complaining of abdominal pain, presumably due to ischemia triggered by dynamic and static blood flow obstruction.

2. Tell us why you use the transverse sinus, rather than an anterior trajectory from the ascending aorta.

   The Dacron graft was passed through the transverse sinus to avoid kinking during its course in the mediastinum.

3. Your technique may have benefits even if there is good femoral access (e.g., fixing the FET fully, preventing retrograde dissection). Should your technique be preferred even if there is good femoral access?

   In complicated type B acute aortic dissections, there is a risk of retrograde ascending dissection during or after the TEVAR procedure if the ascending aorta or aortic arch diameters are larger than 4 centimeters [1]. Therefore, we propose that our technique should be preferred in patients with a retrograde dissection risk even if there is good femoral access.

   1. Williams JB, Andersen ND, Bhattacharyya SD,

4. Describe the aortic anatomy we see around the diaphragm in the post-operative 3D reconstruction?

Both true and thrombosed false lumens were seen; however, expansion of true lumen was not yet sufficient. Considering that there are no re-entries down to the level of the celiac trunk, we can say that the procedure was successful.

5. For the “tacking” sutures that you place beyond the subclavian and use to perfuse the graft, can you place these around the full circumference of the descending aorta? How?

Those Prolene sutures were placed around the full circumference of the descending aorta. However, the first four were placed to secure the posterior wall prior to introduction of the frozen elephant trunk graft because the posterior wall had limited accessibility due to incomplete transection of the descending aorta. The remaining sutures were placed later on, and the FET graft was fixed.
Iatrogenic Supravalvular Aortic Stenosis

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Abstract

We describe a case of hemolytic anemia and proximal anastomotic site stenosis following emergency repair of a Type A aortic dissection. This rare complication led to a reoperation to correct the iatrogenic aortic stenosis and cure the consequent hemolysis. A “sandwich” technique (with two Teflon strips on the outside and inside of the aortic wall) was used in the initial repair to reinforce the suture line and prevent bleeding from the aortic anastomoses. At the time of reoperation, the inner Teflon strip at the proximal aortic anastomosis was found to have inverted into the aortic lumen, as suggested by the preoperative magnetic resonance imaging. Surgical treatment consisted of resecting the portion of inner Teflon that had turned in and tacking the remaining part back onto the aortic wall. The observed hemolysis was likely due to the turbulent flow associated with the supra-aortic stenosis and the collision of red cells with the internal Teflon strip. The patient made an uncomplicated recovery with no further hemolysis and was discharged on postoperative day 8.

Key Words:

Aortic dissection • Hemolysis • Teflon strip • Sandwich technique

Introduction

Type A aortic dissection represents a true surgical emergency. As a consequence of the progress in aortic surgery developed in the last two decades, including surgical, brain protection, and perfusion techniques [1, 2], morbidity and mortality related to this condition have improved but remain substantial [3]. We report a case of successful treatment of hemolytic anemia and severe stenosis of the proximal aortic anastomosis resulting from the surgical repair of acute Type A aortic dissection.
Hemolysis was suspected and eventually confirmed on blood film, which showed occasional schistocytes with helmet cells, slight rouleaux formation, and mild uniform thrombocytosis. Hemolysis markers were raised (lactate dehydrogenase 2,018 U/L; bilirubin 23 μmol/L). Echocardiography showed no valve lesion, while the ascending aorta was not well visualized. Computed tomography (CT) was nondiagnostic. Magnetic resonance imaging (MRI) consisting of steady-state free precession cine images were acquired on a Siemens Avanto 1.5T MRI system using a 32-channel surface coil. They revealed a high velocity central jet at the level of the proximal graft anastomosis with the residual orifice measuring approximately 8 mm in diameter and a significant degree of turbulence across the stenosis, with a peak gradient to 67 mmHg (Figures 1 and 2).

The only conceivable explanation was that the proximal edge of the internal strip of Teflon had been lifted into the center of the aortic lumen by the blood flow. During revision surgery, the graft was opened immediately distal to the anastomosis, and redundant Teflon was partly trimmed and partly tacked back onto the aortic wall with 4-0 Prolene sutures (Figures 3 and 4). The patient made an uncomplicated recovery with no further hemolysis and was discharged on postoperative day 8. She remained well at follow-up 10 weeks later, and blood tests showed normal hemoglobin (116 g/dL).

Discussion

Hemolytic anemia and stenosis of the anastomotic site are extremely rare complications, and there are few reports describing this unfortunate event [4-8]. The main cause appears to be the inverted and stiffened internal felt strip. The use of an internal felt strip as part of the sandwich technique for the treatment of Type A aortic dissection is not unusual. The aim of this approach is to reinforce the fragile, dissected aortic wall and prevent or minimize bleeding from the anastomotic site.

The risk of complications such as clot formation, hemolysis, and stenosis of the anastomotic site should be therefore carefully considered and bala...
Acknowledgement

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Conflict of Interest

The authors have no conflict of interest relevant to this publication.

References


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Combined Transapical Transcatheter Aortic Valve Replacement and Thoracic Endovascular Aortic Repair for Severe Aortic Stenosis and Arch Aneurysm

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Abstract

An 83-year-old male with multiple comorbidities presented with critical aortic stenosis and a saccular aortic arch aneurysm. Through a mini thoracotomy, a balloon expandable transcatheter aortic valve was delivered transapically. A thoracic stent graft was then delivered through the prosthetic valve and deployed in the arch, while a covered stent was deployed in the left common carotid artery. Three-year postoperative computed tomography showed a thrombosed arch aneurysm with decreased size. This case demonstrates the feasibility of using combined transapical transcatheter technologies to treat multicomponent disease in a high-risk patient during a single operation.

Key Words
Aortic valve • Aortic arch aneurysm • Thoracic endovascular aortic repair.

Introduction

Transcatheter approaches for managing complex aortic and aortic valve disease have been rapidly adopted, especially for high-risk patients. Increasing understanding of valve disease and technological advancements continue to improve outcomes [1, 2]. A significant proportion of patients with aortic stenosis (AS) also have thoracic aortic aneurysm that warrants intervention. In high-risk patients, treating both lesions simultaneously may compound the risk for surgical repair. In this case report, combined transapical transcatheter aortic valve replacement (TAVR) and thoracic endovascular aortic repair (TEVAR) were performed successfully to treat critical AS and aortic arch aneurysm during a single operation.

Case Presentation

An 83-year-old male presented with dyspnea on exertion in concert with New York Heart Association Class III symptoms secondary to known severe AS. The patient's past medical history included hypertension, hyperlipidemia, chronic obstructive pulmonary disease, insulin-dependent diabetes, cerebrovascular accident, and lung cancer postradiation. He also had a history of coronary artery disease and ascending aortic aneurysm. The patient underwent triple coronary artery bypass grafting in 1979 and again in 1996
for this condition, including ascending aortic replacement with an interposition polyester graft.

A preoperative echocardiogram showed a left ventricular ejection fraction of 53% with moderate aortic valve regurgitation and severe AS. Mean and peak gradients were 40 and 67 mm Hg, respectively, with an area of 0.74 cm². Preoperative computed tomography angiography (CTA) revealed an aortic arch saccular aneurysm that measured 4.2 cm in diameter and abutted the left subclavian artery (Figure 1). Iliac arteries were severely tortuous with calcified atherosclerotic changes. Cardiac catheterization showed patent coronary artery bypass grafts. The patient was deemed very high risk for both open cardiac surgery and transfemoral approaches. Thus, we recommended transapical endovascular repair with arch TEVAR and TAVR.

One day before the endovascular repairs, the patient underwent left common carotid artery-to-left subclavian artery bypass with an 8-mm ringed polytetrafluoroethylene interposition graft. Via a mini thoracotomy, concentric purse-string sutures were placed in the left ventricular apex, followed by wire access across the aortic valve. Access into the ascending aorta was obtained through the left common carotid artery. Percutaneous femoral access was used for angiography. Balloon valvuloplasty was performed, and then an Edwards Sapien 26-mm prosthetic valve was deployed during rapid ventricular pacing. Using the same wire through the transapical sheath, a 32 mm × 120 mm Zenith TX2 stent graft (Cook Inc., Bloomington, IN, USA) was delivered through the prosthetic valve across the aortic arch with the back end of the device aligned with the innominate artery. Because an adequate landing zone required partial coverage of the left common carotid artery, a 10 mm × 5 cm Viabahn endovascular stent graft (Gore, Flagstaff, AZ, USA) was inserted into the left common carotid artery. The arch stent graft was then deployed during rapid ventricular pacing followed by the left common carotid stent graft. Both stent grafts were expanded via the balloons to optimize conformability. The postoperative echocardiogram confirmed a well-seated prosthetic valve with 1+ posterior paravalvular leak. CTA demonstrated an excellent aortic repair with patent arch branch vessels and no endoleak. One month

![Figure 1. Pre- and postoperative computed tomography (CT) images with volume-rendered reconstruction CT and a transverse view of the aneurysm. Panel A. Preoperative CT showing an aortic arch aneurysm that abuts the left subclavian artery. Panel B. Postoperative CT image showing excellent aneurysm repair and aortic valve implantation. Panel C. CT image taken 3 years postprocedure shows a thrombosed arch aneurysm with decreased size.](image-url)
postoperatively, the echocardiogram and CTA findings remained unchanged (Figure 1). The patient was still alive and asymptomatic 3 years postoperatively. The CTA at follow-up exhibited a thrombosed arch aneurysm that measured 3.9 cm in diameter (Figure 1).

Discussion

This case demonstrates the feasibility of combining two different transcatheter technologies to treat multicomponent disease in a high-risk patient via the transapical route in a single operation. Aortic valve disease is commonly associated with thoracic aortic aneurysm. As a result, as we continue to offer TAVR to more high-risk patients, it is likely that we will see more patients with combined valve and aortic disease [3, 4]. The transapical approach has evolved in recent years and is associated with minimal mortality when performed by experienced surgical teams [5]. With the use of three different commercially available devices, we were able to design a treatment strategy to fit the patient’s anatomy [6]. As we expand endovascular therapies to the proximal aorta, we will require disease-specific devices, such as those with branches for the arch vessels [7]. Further development of transcatheter technology will likely include the combination of TAVR and TEVAR as a treatment option in patients with even more proximal thoracic aortic disease that encroach on or involve the aortic root [8].

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Conflict of Interest

The authors have no conflict of interest relevant to this publication.

References


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David-V Procedure in a Patient with Aortic Dilation and Competent Quadricuspid Aortic Valve: Are Genetics to Blame?

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Abstract

Quadricuspid aortic valves (QAVs) are extremely rare. In this case study, we report a David-V valve-sparing aortic root replacement with reimplantation of a native QAV in a patient with aortic dilation, normal valve function, and a family history of aortic dissection. Microscopic pathological examination of the excised section of the aorta revealed scattered small foci of cystic medical degeneration throughout. A genetic predisposition for aortic dilation may be present in patients with QAV, even in the setting of a competent valve. Regular screening for aortic dilation in patients with known QAV should therefore be considered.

Key Words

Quadricuspid aortic valve • Aortic dilation • Genetics

Introduction

First described by Babington in 1847 [1], quadricuspid aortic valve (QAV) is a rare congenital anomaly with an estimated prevalence of 0.003-0.04% in the general population [2, 3]. QAV associated with aortic regurgitation or stenosis commonly requires replacement or repair in the fifth or sixth decade of life [4]. Ascending aortic aneurysm has historically been reported only rarely in cases of QAV, but two recent series published from the Cleveland Clinic and Mayo Clinic identified aortic dilation in 30-40% of patients with QAV [5, 6]. However, whether aortic dilation associated with QAV is genetically or hemodynamically mediated remains controversial [7]. We report a David-V valve-sparing aortic root replacement with reimplantation of a native QAV in a patient with aortic dilation and normal valve function. The patient’s presentation, operative findings, and pathological analysis suggest that a genetic predisposition for aortic dilation may be present in some patients with QAV.

Case Presentation

A 47-year-old white male with a family history of aortic dissection presented with new onset chest pain and dyspnea exacerbated by exertion. The patient reported exercising regularly with no dyspnea at rest. The patient’s brother had previously died from an aortic dissection.

Computed tomography of the chest revealed an aneurysm in the ascending aorta with a dilated aortic root diameter of 4.5 cm maximally. Dilation of the proximal and mid-ascending aorta was observed and measured 4.0 cm in diameter maximally for a length of 7.0 cm. Transthoracic echocardiography (TTE) confirmed the aneurysm. No aortic regurgitation or aortic stenosis was visualized by TTE, and the left ventricular...
ejection fraction was 55-65%. Given the patient’s strong family history, prophylactic surgical aortic root and ascending aortic replacement was planned.

A David-V valve-sparing aortic root replacement was performed via median sternotomy on cardiopulmonary bypass. Preoperative echocardiography demonstrated a tricuspid aortic valve, but the patient was found to have QAV in the operating room. A small 1-cm cusp at the left non-commissure area with two separate commissural posts was visualized (Type B QAV; Figure 1) [2]. Upon further inspection, the valve was functioning well. Therefore, the native QAV was reimplanted with the two commissural posts suspended together at the left non-commissure area (Figure 2).

A 30-mm aortic graft with a prefabricated sinus segment was trimmed to size, and subannular sutures were placed through the bottom of the Valsalva portion of the graft. Sizing of the graft was estimated from the commissural height at the left non-commissure. The commissure posts were resuspended at the neosinotubular junction. The valve remained competent and was then suspended and sewn into the Valsalva portion of the graft. The left and right coronary buttons were sewn into the graft, which was then sewn into the distal ascending aorta. The patient was weaned from cardiopulmonary bypass without difficulty. Trivial aortic insufficiency was detected at the time of closure (Figure 3). The patient tolerated the procedure well and was discharged from the hospital on the third postoperative day.

Microscopic pathological examination of the excised section of aorta revealed focal laminar necrosis with scattered foci of cystic medial degeneration throughout. No significant inflammation was present.

Discussion

Two recently published case series that described patients with surgically treated QAV and patients with QAV identified from an echocardiographic database reported a high prevalence of aortic root and ascending aortic dilation in patients with QAV, suggesting the two abnormalities may share a pathophysiologic link [5, 6]. Whether the aortic dilation...
observed in patients with QAV is the result of a genetically mediated aortopathy, altered hemodynamic factors associated with the abnormal valve, or both is unknown [7]. Given our patient’s family history of dissection, the lack of aortic valve dysfunction, and the cystic medial necrosis identified by pathology analysis, we postulate that an unidentified genetic etiology that links QAV with aortic dilation may be present in some patients, including the one described herein, although no other signs of connective tissue disorder were noted in the medical history or physical exam and definitive genetic testing was not performed [8]. Although the patient’s brother’s aortic valve morphology was unknown and focal laminar necrosis, which is associated with acquired degeneration of the aortic wall, was identified by pathology in addition to cystic medial necrosis, our patient’s case nevertheless offers some limited insight into the etiology of aortic dilation associated with QAV. Because a genetic predisposition for aortic dilation may be present in patients with QAV, regular screening for aortic dilation in this population should be considered.

Conflict of Interest

The authors have no conflict of interest relevant to this publication.

References


The following pages summarize and review this issue’s articles for an audience without a background in medicine or research.

Frank A. Lederle: Distinguished Lecture given at the opening of the 5th International Meeting on Aortic Disease, Liège, Belgium (September 15, 2016)

In his lecture, Frank Lederle begins by telling the story how he became a researcher in aortic aneurysm disease (diseases of the aorta, the body’s main vessel) even though he is not a surgeon. His interest was sparked by the fact that aortic aneurysm disease was one of the top 15 causes of death in the USA. He started his research with an aneurysm screening project and later lead investigations on surgery on patients with small aneurysms. They showed that the benefit of surgery in patients with aneurysms of the aorta in their abdomen does not outweigh its risks in patients with aneurysms of diameters of below 5.5cm.

He continues by sharing what he learned on conducting successful research in his career as a scientist. His first advice is to choose a relevant, but easily explained question. A good choice is to question unproven facts that are nevertheless accepted in the research community. He furthermore recommends to keep a close eye on the study to make sure everything goes according to plan. Once the study is done, actually writing the article and submitting it to a journal is important. Whatever is written should be defensible by data, and as an investigator, one should stand to his results even if they do not agree with one’s opinion. He especially warns of close financial relationships with the industry to avoid being financially forced to support a certain theory. The purpose of research should be in discovery, not proving a preexisting theory. Finally, the speaker underlines the importance of mentoring young investigators and to remember one’s own mentors.

Nketi I. Forbang et al.: “Lower Aorto-iliac Bifurcation Position and Incident Cardiovascular Disease: The Multi Ethnic Study of Artherosclerosis (MESA)”

The aorta, the body’s main artery, descends from the heart downwards through the abdomen where it splits in two vessels supplying the legs with blood. This furcation is called “aorto-iliac bifurcation”. With age, it moves downward relative to the spinal column. The distance from a given location in the spine to the furcation (AIBD) increases thus with age. The AIBD has been associated with risk factors for cardiovascular disease. In their study, Forbang et al. investigated a possible association of AIBD and actual cardiovascular events such as heart attack or stroke and overall death. The investigators measured the AIBD in 1511 participants and observed if the abovementioned events occurred during the following years. They came to the conclusion that the AIBD is associated with risk factors for cardiovascular disease, but is not itself a risk factor for cardiovascular events or death of any cause.

Case Reports

Murat Ugurlucan et al.: “Treatment of Dacron Graft Dilatation with Endovascular Stent Grafting”
Dacron grafts are used in a variety of procedures as a prosthesis to replace or stabilize a vessel. Complications such as infection or thrombosis are well known. Graft dilatation however is rare. Murat Ugurlucan et al. present a case of a patient who had a significant dilatation of the graft four years after it was used for a bypass creating a bridge from the aorta to both arteries in the groins. The dilatation occurred in the abdominal part of the prosthesis. Furthermore, the femoral artery in his left groin was dilated. To cover the dilated graft, another tubed stent graft prosthesis was inserted through the vessel in the left leg and positioned in the dilated prosthesis. The dilated vessel in the left groin was surgically removed and replaced by a second prosthesis. The patient recovered without complications. Dilation of Dacron prostheses is very rare and usually caused by graft failure. Minimally invasive treatment strategies are often an appropriate solution.

Altung Tuncer et al.: “Frozen Elephant Trunk and Antegrad Visceral Debranching in the Surgical Treatment of Type B Aortic Dissection: an Alternative Method”

In aortic dissection, the patient develops a disruption of the layers of the vessel wall of the aorta, the body’s main vessel. In Type B dissection, the disruption involves the descending part of the aorta that runs downwards from the chest through the abdomen. In a best-case scenario, no intervention is necessary. If complications such as rupture or impaired blood flow to the spinal cord or inner organs arise, surgery or a minimally invasive (interventional) procedure in which a stent graft prosthesis is inserted in the aorta might be necessary. Altung Tuncer et al. report a case of a patient with complicated type B dissection whom they treated with a combined surgical and interventional approach. The aorta was partly replaced with a tubed graft prosthesis and partly stabilized from the inside with a stent graft prosthesis. Furthermore, a “debranching” was performed, in which two arteries that provide blood flow to abdominal organs were connected to the healthy aorta with another tubed prosthesis to provide them with blood flow. The patient’s recovery was prolonged but he was discharged home in good condition. This case report describes a surgical technique that avoids some potential complications of the common treatment methods, and allows both repair of parts of the dissected aorta as well as a separate connection of abdominal vessels to the healthy aorta. However, the presented technique consists of a major open surgical procedure and therefore carries significant risks as well.

Paolo Bosco et al.: “Iatrogenic Supravalvular Aortic Stenosis”

Bosco et al. report a rare case of a patient who had undergone surgical repair for acute type A aortic dissection, a life-threatening disease in which the patient develops a disruption of the layers of the vessel wall of the aorta, the body’s main vessel. To reinforce the aortic wall during surgery, a felt strip was used. After surgery, this felt strip inverted and caused a narrowing of the vessel. The narrowing led to turbulences in blood flow which damaged the patient’s red blood cells. The patient had to undergo reoperation to repair the narrowing and recovered without further complications.

Yuanjia Zhu et al.: “Combined Transapical Transcatheter Aortic Valve Replacement and Thoracic Endovascular Aortic Repair for Severe Aortic Stenosis and Arch Aneurysm”

Zhu et al. report a case of a patient who had a severe calcification and narrowing of his aortic valve, which constitutes the gate between the heart and the aorta, the body’s main vessel. Furthermore, his aorta had a dilation (aneurysm) in its transverse part before descending to the abdomen. Because the patient was too sick for open surgery, a minimally invasive approach was chosen. In a first step, the vessel providing blood flow to the left arm was bypassed. On the subsequent day, the main procedure was performed. A small incision was made in his chest above the tip of the heart. A folded aortic valve prosthesis was inserted through the tip of the heart and expanded in the position of the aortic valve. Through the same incision, a tubed graft prosthesis was inserted in the aorta to cover the aneurysm. The vessel supplying the brain that leads along the left side of the throat was stabilized with a stent graft prosthesis as well. The patient recovered without major complications. Imaging studies after surgery showed a stable aorta and adequate valve function. This case shows that combined minimally invasive valve and endovascular procedures can be an alternative to surgery in high
risk patients with aortic valve disease and disease of the initial part of the aorta.

Katherine Hebeler et al.: “David-V Procedure in a Patient with Aortic Dilation and Competent Quadricuspid Aortic Valve: Are Genetics to Blame?”

A quadricuspid aortic valve is a rare anomaly of the aortic valve, which is the gate between the heart and the aorta, the body’s main vessel. Usually, the aortic valve has three valvular cusps. The quadricuspid variant has four valvular cusps and has been associated with aortic dilatation (aneurysm). However, it is still a matter of debate if the dilatation is caused by genetics or by blood flow abnormalities. Hebeler et al. describe a case of a patient with a quadricuspid aortic valve and a family history of aortic disease who had a dilatation of his aorta while the valve itself was functioning well. The dilated aorta was replaced in a procedure called “David V” in which the native aortic valve is sutured into a graft prosthesis that replaces the aorta. The diseased aortic wall was examined and showed signs of a specific type of aortic wall degeneration. The authors therefore suspect that patients with a quadricuspid aortic valve might have a genetic predisposition for aortic aneurysm even if the valve is functioning well. They therefore recommend regular screening for aortic dilatation in this patient group.
List of Upcoming Meetings

November 2016

1. EACTS Academy: Aortic Valve Surgery
   November 24-25, 2016
   Nancy, France
   Meeting information available at:
   www.eacts.org/academy/courses/aortic-valve-surgery

December 2016

1. International Conference for Innovations in Cardiovascular Systems
   December 4-6, 2016
   Tel Aviv, Israel
   Meeting information available at:
   2016.icimeeting.com

2. 13th European Cardiology Congress
   December 5-6, 2016
   Madrid, Spain
   Meeting information available at:
   cardiology.conferenceseries.com/europe

January 2017

1. 35th Annual International Symposium: Clinical Update in Anesthesiology, Surgery and Perioperative Medicine
   January 15-20, 2017
   Cancun, Mexico
   Meeting information available at:
   www.clinicalupdateinanesthesiology.org

2. Controversies and Updates in Vascular Surgery
   January 19-21, 2017
   Paris, France
   Meeting information available at:
   cacvs.org

3. 53rd Annual Meeting of the Society of Thoracic Surgeons and STS/AATS Tech-Con 2017
   January 21-25, 2017
   Houston, Texas
   Meeting information available at:
   www.sts.org/education-meetings/sts-annual-meeting

4. STS/CTSNet Career Fair at the 53rd Annual Meeting
   January 22-24, 2017
   Houston, Texas
   Meeting information available at:
   www.ctsnet.org/events/2017-sts-and-ctsnet-career-fair
5th International Meeting on Aortic Diseases: New Insights into an Old Problem

Natzi Sakalihasan, MD, PhD (course director)

During the last two decades, the field of aortic aneurysms as well as aortic dissections, bicuspid aortic valve (BAV) have progressed greatly, but significantly challenges are still ahead of us considering that aortic aneurysms and dissections are becoming more prevalent in industrialized countries. Studies involving genetic, genomic, biochemical and molecular biological approaches as well as imaging and surgical techniques discussed during this 5th International Meeting on Aortic Diseases (IMAD) will get us closer to the goal of better understanding of pathophysiology of aortic aneurysms, dissections and BAV. Moreover, once again, as in the past editions, it is a great pleasure to share reflections with all worldwide scientists and clinicians interested in aortic diseases thanks to AORTA.

EXTRA-AORTIC CARDIOVASCULAR FEATURES IN MARFAN SYNDROME - RELEVANCE AND MANAGEMENT

Julie De Backer
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Marfan syndrome (MFS), caused by mutations in the fibrillin 1 gene has been the leading disease model for the study of genetic aortic aneurysms and dissections. Aortic root aneurysm formation at the level of the sinus of Valsalva occurs in the vast majority of patients and aortic dissection is still one of the leading causes of death in patients with MFS. With better medical and surgical management, MFS patients grow older nowadays and other cardiovascular features are now emerging and gaining more attention. Mitral valve prolapse (MVP) has been recognized as a key feature in MFS and still plays a role in the diagnostic setting. Being a benign disease in the majority of non-MFS cases, the outcome of MVP in MFS is quite different and needs careful follow-up. Timely and appropriate surgical intervention needs to be carefully considered. Heart failure in MFS has been recognized as a major cause of mortality in surgical series for several decades now, but the understanding of the pathogenesis of myocardial dysfunction is still not entirely elucidated. Related to myocardial dysfunction to some extent, arrhythmias are more frequently documented in MFS patients and sudden arrhythmic death occurs more common than in the general population. Managing these extra-aortic features in MFS requires adequate knowledge and a specific approach in some cases. These issues will be discussed in this presentation.

References:

COMBINING MENDELIAN GENETICS AND GENETIC EPIDEMIOLOGY FOR AAA

Juliette Albuisson
Paris, France

The pace of new genes discovery in the field of Mendelian disorders has been dramatically accelerated by the availability of the human genome sequence in the 2000s, and the next-generation sequencing technologies in the 2010s. However, a majority of the elucidated conditions so far correspond to relatively simplified situations, where the prevalence and the penetrance of the condition are high and the genetic heterogeneity is low. Nowadays, geneticists meet more and more situations where gene identification in unknown disorders can be tricky. Heritable conditions that are very rare, heterogenous or with imperfect Mendelian transmission can only be elucidated using large cohorts of patients, with a very well-characterized phenotype. Generally, using exome sequencing alone is not efficient enough to...
elucidate these types of conditions. On the other hand, common conditions like cardiovascular disorders have been long studied using whole genome association studies and genotyping, or sequencing tools. The efficiency of these approaches to identify strong genetic effects is globally low, and odds-ratios do not generally reach 2. The concept of hidden heritability raised from these observations, pointing to the implication of other types of variants like rare or very rare variants, in common disorders. The power of recently developed strategies comes from combining exome or genome sequencing with recently developed genetic association analysis tools, allowing for the identification of rare variants with stronger effects. These latter have been specifically developed in the context of rare, heterogeneous, or polygenic disorders. We employed exome sequencing in the identification of genetic components of abdominal aortic aneurysm. This common cardiovascular disorder has a strong hereditary component and rare situations of fully penetrant, dominant inheritance. Exome sequencing was performed in a large family showing dominant inheritance, identifying only one strong candidate gene. Rare and very rare variants association analysis of the identified candidate gene was performed in a large cohort of 2500 sporadic and 500 familial AAA cases, using a recently developed association tool called SKAT-O. This combined approach allowed to characterize genetic effect of rare and very rare variants at the level of a single gene, with deleterious and protecting effect depending on the identified variants. Functional analysis of the variants and the role of the candidate gene is ongoing in cellular models.

WHOLE BLOOD DNA METHYLATION ANALYSIS IN AAA; AN EPIGENOME-WIDE ASSOCIATION STUDY
Gregory T. Jones
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Abdominal aortic aneurysm (AAA) is a complex disease, with several well-established genetic and environmental risk factors having been identified, nevertheless, much remains to be understood regarding its aetiology. It is becoming increasingly clear that there are interactions between genetic and environmental risk factors. Such interactions can be detected by alterations in epigenetic markers, such as the methylation of DNA CpG sites. An epigenome-wide approach was therefore applied to an AAA case control cohort in order to identify novel disease biomarkers.

Study Design and Methods: Whole blood methylation status of over 450,000 CpG sites was assessed in each of 961 males (488 cases and 473 AAA-free controls; mean age 72 years) using the Illumina Human Methylation450 bead chip array. Normalised methylation values were corrected for participant age and prior history of occlusive vascular disease. Results were filtered for CpGs known to be strongly associated with white blood cell composition.

Results: In total 50 gene loci (most with multiple CpG sites) were significantly (adjusted P<5x10-8) differentially methylated in AAA. Importantly, 18 (36%) of these loci matched those previously reported as being significantly associated with smoking. These included the strongest smoking associations reproducibly reported in the AHRQ, F2RL3, ALPL and IER3 genes. Approximately half of the CpG sites were also strongly associated with white blood cell composition. A pathway-based analysis implicated biological mechanisms such as interleukin signaling, vascular inflammation, T & B cell activation and blood coagulation. Protein expression of some of the genes associated with differentially expressed CpG sites was examined in aortic tissue. One such gene, YWHAQ, encodes for the 14-3-3 theta protein that was found to be significantly overexpressed within AAA-associ-
Results: Over the 12 year period, 103 incident acute AAA events occurred in the study population of 92,728 (male 72.8%, 59-2% 30-day case-fatality). Incidence/100,000/year was 55 in men aged 65-74 years, but increased to 112 at 75-85 and 298 at ≥85, with 66.0% of all events occurring at age ≥75yrs. Incidence at 65-74 was highest in male smokers (274), with 96.4% of events in men aged<75 years occurring in ever-smokers. Mean age (SD) (yrs) at event was lowest in current smokers (72.2 (7.2)), compared to ex-smokers (81.2 (7.0)) and never-smokers (83.7 (7.9)) (p<0.0001). Hypertension was the predominant risk factor in women (diagnosed in 92.9%) with 54.8% of all events in women occurring in hypertensives aged 75 and over. Extrapolating rates to the UK population, using trial evidence of screening efficacy, the current UK screening programme would prevent 5.6% of aneurysm-related deaths (315,200 scans/year: 1426/death prevented, 121/year-of-life saved). Screening only male smokers aged 65 and then all men at age 75 would prevent 21.1% of deaths (247,900 scans/year; 297/death prevented, 34/year-of-life saved).

Conclusions: Two-thirds of acute AAA events occurred at age ≥75yrs and over 25% of events occurred in women. Screening non-smokers at age 65 is likely to have very little impact on AAA event rates. Risk-factor targeted screening may prevent more deaths than current strategies.

**MORPHOLOGY OF RUPTURED Versus UNRUPTURED ABDOMINAL AORTIC ANEURYSMS**

Janet T. Powell on behalf of the IMPROVE trial and other collaborators at St. George's (lead Alan Karthikesalingam) and Perth (lead Barry Doyle).

Currently the best metric to assess the risk of aortic aneurysm rupture is the maximum aortic diameter. Recently aneurysm volume also has been investigated. However, other morphological characteristics, readily obtainable from 3D CT reconstructions, have largely been ignored as potential prognostic indicators.

The core laboratory for admission CT scans for IMPROVE trial patients provided an opportunity to compare the morphology of ruptured and unruptured aneurysms. These have been separated into abdominal aortic and common iliac aneurysms. Proximal aneurysm neck length, diameter and angle, maximum aortic diameter, iliac bifurcation angle and iliac artery diameter were measured according to protocol, with quality control for intra- and inter-observer variability of measurements.

For abdominal aortic aneurysms we have compared 294 confirmed cases of rupture with 907 elective cases according to a pre-specified analysis plan, adjusting for sex. For common iliac aneurysms the cases are fewer (and all male) and we have compared 9 cases of iliac rupture with 10 elective cases and these data will be presented. For both types of aneurysm, the angle of the iliac bifurcation appears to be the most influential measurement after maximum aneurysm diameter which distinguishes ruptured from intact aneurysms.

**AAA RUPTURE IN STOCKHOLM**

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This population based investigation includes all patients admitted to any of the seven emergency departments within Stockholm County diagnosed with rAAA 2009-2013. A total of 283 patients were identified, 30 % (n = 85) had a previously detected AAA. Men were in majority (76% vs 24%), and four years younger than women. A majority of patients admitted to an emergency department were treated (212/283, 75%), a similar proportion of women and men. Treated patients were younger (77 vs 84 years, p<0.001). One third were treated with EVAR was 27%, they were older than OR treated (79 vs 76 years, p=0.043). Patients with a previous diagnosis of AAA, before rupture occurred, had a higher mortality, partly due to a lower intervention rate (59 % versus 82 %, P < .001). Reasons for non-treatment when diagnosed with AAA were; denied elective surgery (36 %), patient choice (18 %), size-related (13 %) and surveillance deficiency (31 %). The majority of patients missed in surveillance were treated at rupture (85 %). Overall; 47% of patients admitted with rAAA survived 30 days, and 62% of treated patients survived 30 days, similar mortality for women and men. Our results and other contemporary series show a shift towards a higher rate of patients with rAAA being treated, increasing use of EVAR and continuously improving outcomes, similarly for women and men. Improved patient-specific protocols to reduce the surveillance gaps and new methods of determining rupture risk in each individual case of AAA could be two possible future strategies to reduce the incidence of rupture, in the previously diagnosed group. Data for patients treated 2014-2015 will also be included in the presentation.

References:

**AUSTRALIAN TRIALS TO IDENTIFY TREATMENTS TO SLOW AAA GROWTH**

Jonathan Golledge

James Cook University and The Townsville Hospital, Townsville, Australia

Background: Currently there is no treatment for small abdominal aortic aneurysms (AAAs). Fenofibrate has been shown to limit AAA development in two studies in mouse models associated with reduction in aortic concentration of the matrix protein osteopontin and reduced aortic inflammation. Fenofibrate has also been shown to have a number of other effects which may favourably modify AAA pathology including raising high density lipoprotein and reducing matrix metalloproteinase.

Methods: Fenofibrate in the management of AAA (FAME-2) is a multi-centre, prospective, randomised, placebo-controlled trial to assess the effect of 24 weeks oral therapy of 145mg of fenofibrate on pathological markers of AAA. The primary endpoints are circulating biomarkers of AAA, including osteopontin. Secondary outcomes include maximum diameter assessed on ultrasound. FAME-2 is a collaboration conducted from three vascular centres in Australia.

Discussion: Currently, no medication has been demonstrated to limit abdominal aortic aneurysm progression. FAME-2 is a pilot study to examine whether promising results in a rodent model can be confirmed in patients.

References:
AAA MEASUREMENT AND ENLARGEMENT
Frank A. Lederle

Background: No effective treatment is currently available to prevent progression of small and medium-sized abdominal aortic aneurysms (AAAs). Identification of drugs with sufficient promise to justify large expensive randomized trials remains challenging. One potentially useful strategy is to look for associations between commonly used drugs and AAA enlargement in appropriately adjusted observational studies.

Methods: Potential AAA measurements were identified from abdominal imaging reports in the electronic data files of three medical centres from 1995 to 2010. AAA measurements were extracted manually and patients with an aneurysm of 3 cm or larger, who had at least two measurements over an interval of at least 6 months, were identified. Other data were obtained from the electronic data files (demographics, co-morbidities, smoking status, drug use) to conduct a propensity analysis of the associations of drugs and other factors with AAA enlargement.

Results: From 52,962 abdominal imaging studies, 5,362 patients with an AAA of 3 cm or more were identified, of whom 2,428 had at least two measurements over at least 6 months. Mean AAA follow-up was 3.4 years and the mean AAA enlargement rate was 2.0 mm per year. Propensity analysis demonstrated no significant association of AAA enlargement with statins, beta-blockers, angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers. Diabetes was associated with a reduction in AAA enlargement of 1.2 mm per year (P = 0.008), and chronic obstructive pulmonary disease was associated with increased enlargement (0.5 mm per year; P = 0.050). Moderate AAA measurement variation and substantial terminal digit preference were also observed, but the digit preference became less pronounced after 2000.

Conclusion: This study confirms the negative association of diabetes with AAA progression. There was no evidence that commonly used cardiovascular drugs affect AAA enlargement.

CIRCULATING MiRNA ASSOCIATED WITH INSTABLE ABDOMINAL AORTIC ANEURYSM PET POSITIVE
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Background: Prediction of abdominal aortic aneurysm (AAA) rupture is a challenging issue. Small non-coding RNAs (miRNAs) are potent regulators of gene expression and are considered as valuable circulating biomarkers. Recently, 18F-FDG uptake detected by PET in AAA was correlated with cellular and molecular alterations presaging wall instability and its potential rupture. Our study aims at identifying circulating miRNAs correlated with a positive PET that could help discriminating patients at higher risk of rupture.

Methods: The levels of 372 miRNAs were evaluated by PCR array in plasma from 35 AAA patients displaying no FDG uptake (A0) and 22 patients with a positive PET (A+). The level of modulated miRNAs was validated by qPCR and was also measured in aneurysmal tissues.

Results: Six miRNAs were found significantly modulated in A+ vs A0 patients. They were significantly correlated between them and with PET-positivity but only two of them were also correlated with the AAA diameter. These miRNAs displayed significant discriminating power (ROC curve) between the A+ and A0 groups. Three down-regulated circulating miRNAs, miR-99b-5p, miR-125b-5p and miR-204-5p, were also significantly reduced in the aneurysmal tissue at the FDG-uptake site compared to a negative zone in the same aneurysm and as compared to A0 aneurysms. They were further significantly inversely correlated with the expression, at the positive uptake site, of some of their potential gene targets, most notably MMP13.

Conclusions: Six miRNAs were identified as potential new circulating biomarkers of PET+ AAA at high risk of rupture, three of them being similarly modulated in the metabolically active aneurysmal wall and might be directly involved in AAA instability.

FOCAL ADHESION KINASE IS A NOVEL TARGET FOR PHARMACOTHERAPY OF ABDOMINAL AORTIC ANEURYSM
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Abdominal aortic aneurysm (AAA) is characterized by chronic inflammatory cell infiltration and progressive destruction of the extracellular matrix by proteolytic enzymes. However, the molecular mechanisms that regulate chronic inflammation in AAA remain largely unknown. Focal adhesion kinase (FAK) is a cytoplasmic tyrosine kinase that plays critical roles in integrin-mediated signal transduction. We previously demonstrated in vitro that FAK is involved in inflammatory responses to mechanical strain in vascular smooth muscle cells. These findings led to the hypothesis that FAK might promote AAA progression by maintaining and enhancing inflammatory responses. In this study, we found that FAK was highly activated in human AAA wall specimens compared with non-AAA walls. Activated FAK was mostly localized to macrophages within AAA tissues. FAK inhibitor, PF573228, significantly reduced secretion of monocyte chemoattractant protein-1 and matrix metalloproteinase-9 from cultured macrophages after stimulation with tumor necrosis factor-alpha. Furthermore, we created the mouse model of AAA by periaortic application of calcium chloride. Treatment of mice with PF573228 over the entire experimental period (from weeks 0 to 6 after calcium application) significantly reduced inflammatory cell infiltration and disruption of the elastic lamellae, and prevented the development of AAA. Importantly, delayed treatment with PF573228 (only from weeks 3 to 6) blocked increases in cellular infiltration and elastin disruption in aortic walls, and significantly inhibited further progression of AAA. Our findings uncover a critical role of FAK in the development and progression of AAA, indicating that FAK represents a novel therapeutic target for the treatment of AAA.

TELMISARTAN IN THE MANAGEMENT OF ABDOMINAL AORTIC ANEURYSM (TEDY): THE STUDY PROTOCOL FOR A RANDOMIZED CONTROLLED TRIAL
Jonathan Golledge
James Cook University and The Townsville Hospital, Townsville, Australia

Background: Experimental studies suggest that angiotensin II plays a central role in the pathogenesis of abdominal aortic aneurysm. This trial aims to evaluate the efficacy of the angiotensin receptor blocker telmisartan in limiting the progression of abdominal aortic aneurysm. Telmisartan is amulticentre, parallel-design, randomised, double-blind, placebo-controlled trial with an intention-to-treat analysis. We aim to randomly assign 300 participants with small abdominal aortic aneurysm to either 40 mg of telmisartan or identical...
placebo and follow patients over 2 years. The primary endpoint will be abdominal aortic aneurysm growth as measured by 1) maximum infra-renal aortic volume on computed tomographic angiography, 2) maximum orthogonal diameter on computed tomographic angiography, and 3) maximum diameter on ultrasound. Secondary endpoints include change in resting brachial blood pressure, abdominal aortic aneurysm mural macrophage density, and health-related quality of life. TEDY is an international collaboration conducted from major vascular centres in Australia, the United States and the Netherlands.

Discussion: Currently, no medication has been convincingly demonstrated to limit abdominal aortic aneurysm progression. TEDY will examine the potential of a promising treatment strategy for patients with small abdominal aortic aneurysms.

References:

THE EFFECT OF METFORMIN ON AAA
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Diabetes mellitus is negatively associated with the prevalence and progression of abdominal aortic aneurysm (AAA) disease. We investigated the possibility that the oral hypoglycemic agent metformin (Glucophage) may influence the progression of AAA disease.

Methods: Preoperative AAA patients also noted to have diabetes were identified from an institutional database. Following assessment of individual cardiovascular and demographic risk factors and prescription drug regimens, odds ratios for categorical influences on annual AAA enlargement were calculated through nominal logistic regression. Experimental AAAs were created in normoglycemic mice to validate the database-derived observations as well to identify potential mechanisms of metformin-induced aneurysm suppression.

Results: Fifty eight patients met criteria for study inclusion. Of 11 distinct classes of medications considered, only metformin use was negatively associated with AAA enlargement. This association remained significant after controlling for gender, age, cigarette smoking status and obesity. The median enlargement AAA enlargement rate in patients not taking oral diabetic medication was 1.5 mm/y; by nominal logistic regression, metformin, hyperlipidemia and age > 70 years were associated with below-median enlargement, whereas sulphonylurea therapy, initial aortic diameter ≥ 40 mm, and statin use were associated with above-median enlargement. In experimental modeling, metformin dramatically suppressed the formation of AAA, with medial elastin and smooth muscle preservation and reduced aortic mural macrophage, CD8 T cell, and neovessel density.

Conclusions: Epidemiologic evidence of AAA suppression in diabetes may be attributable to concurrent therapy with the oral hypoglycemic agent metformin.

References:

WHAT DO WE KNOW ABOUT AAA AND DIABETES AND DOES IT MATTER
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Diabetes is generally considered to increase the risk of most manifestations of cardiovascular disease, particularly coronary heart disease and peripheral arterial disease. In contrast with occlusive arterial disease, there is a negative association between diabetes and abdominal aortic aneurysm (AAA). Several large cross-sectional studies have shown that the prevalence of AAA is 30% lower in the presence of diabetes. Cohort studies have shown that the incidence of new AAA is reduced by 60% and the expansion of existing AAAs is about 50% lower in diabetes. The underlying mechanisms for the negative association are still unclear. Whilst animal model studies and clinical observations suggest the importance of hyperglycaemia, there is also evidence that drugs used to treat diabetes, such as metformin, may play a role. One of the consequences of chronic hyperglycaemia is the increased formation of Advanced Glycation Endproducts (AGEs) due to non-enzymatic reactions between sugar metabolites and both proteins and lipids. The deposition of AGEs may result in complex changes in extra-cellular matrix, including fibrosis and resistance to proteolysis, which are compatible with reduction in AAA formation. On the other hand, binding of AGEs to a cell surface receptor (RAGE) can increase oxidative stress and inflammation – both associated with increased AAA formation. The association between AGE formation and AAAs can be assessed indirectly via biomarkers of the glycation pathway. The relationship between four of these biomarkers (glyoxal, methylglyoxal, carbamymethyllysine, and the soluble RAGE) and both aortic diameter and AAA presence in a cohort of ~900 men screened for AAA will be reported.

IMAGING ALTERNATIVES IN ORDER TO PREVENT RUPTURE (VOLUME VS DIAMETER)
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Background: The diagnosis and management of abdominal aortic aneurysms (AAA) currently relies on the aortic maximal diameter, which, however, is the subject of increasing discussion. Specifically, the threshold diameter criterion lacks a sound patient-individual assessment, is already about 20 years old, and may no longer adequately reflect current treatment options. Most important, AAA rupture is a complex event and a better understanding requires a multi-disciplinary approach [1].

Methods: All AAA patients at Karolinska University Hospital, Stockholm, Sweden who had undergone two computed tomography angiographies (CTA) with roughly one year’s interval (8-17 months) were retrospectively identified. Forty-one patients (9 female, 32 male) were included and digital three-dimensional reproductions of the aneurysms were segmented and analyzed from the 82 CTAs (A4clinics Research Edition, VASCOPS GmbH,
Austria). Specifically, AAA diameter, AAA volume were measured from 3D reconstructions, while Peak Wall Rupture Index (PWRI) was calculated based on a Finite Element Analysis (FEA) [2].

**Results:** Diameter growth rate did not correlate with baseline diameter ($r=0.15$, $p=0.34$) or with increasing PWRI ($r=0.17$, $p=0.30$). Volume growth rate correlated with baseline volume ($r=0.56$, $p=0.0001$) and volume growth rate higher than or equal to the sample median could be predicted with 90% sensitivity and 85% specificity, see Figure 1. Volume growth rate correlated with increasing PWRI ($r=0.75$, $p=0.0001$) and further results are reported elsewhere [3].

**Conclusion:** Our study clearly demonstrated that aneurysm volume, compared to its maximum diameter, better predicts aneurysm growth rate and correlates stronger with increasing biomechanical rupture risk. Our results support the notion of monitoring all three dimensions of an AAA.

![Figure 1](image)

**Figure 1** Baseline diameter versus baseline volume as growth predictor

Receiver Operator Characteristic (ROC) curves for baseline diameter (left) and baseline volume (right) to predict Abdominal Aortic Aneurysms diameter growth. Data is based on following-up 41 patients over approximately one year and demonstrates that aneurysm diameter growth can be reasonably predicted by baseline volume but not by baseline diameter. Dashed line in the left image represents flipping a coin, i.e. represents the ROC curve of no predictive information at all.

**References:**

**IS THE RISK DIFFERENT FOR FEMALE OR MALE FDRS TO AAA PATIENTS?**

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Although family history is well known as a risk factor for development of AAA, the problem is not systematically addressed in clinical practice. The prevalence of AAA is higher in persons with a family history than in smokers. Guidelines suggest selective screening of First Degree Relatives (FDRs) (regardless of sex) in the US at one time, and the ESVS guidelines at age 50-55 years, although the level of evidence is low. Male relatives, but not female, will however be invited within the population-based screening programs for elderly men in Sweden and the UK. Previous studies have reported contradictory findings regarding prevalence of AAA in FDRs, but most reports show an increased prevalence, approximately 10%. The prevalence in female FDRs is always lower, but this mainly reflects the lower prevalence overall in women in the population as compared to men (0.5-1% vs 1.5-4%). The risk for a male FDR (brothers) to develop an AAA is 20% compared to 6% in a female FDR, as reported from the Liege AAA Family study. In the Swedish Sibling study; 17% vs 6% prevalence in brothers and sisters was found; however this should be compared with the prevalence in the population, which gives a 12 times increased prevalence in female FDRs compared to women in the population, and 8-9 times in male. The age at which screening of FDRs could be adequate, has recently been investigated in our Swedish Sibling cohort. Our results, and others support a selective screening program for all FDRs (male and female at 50 and 55 years) supporting the ESVS guidelines. The population based screening at 65 could be too late for all FDRs, a finding supported by several reports on the increased diameter at diagnosis, growth rate and rupture risk in patients with AAA and a family history compared to non-familial AAA. The risk for the FDR to develop disease if the proband is a male or female has also been investigated, and quite contradictory findings from an increased risk to a similar risk are found (Darling, Mejnert, Larsson, Blanchard).

In conclusion, the risk for all FDRs to develop AAA is high compared to the population, even when smokers are analyzed separately. One should possibly compare the AAA prevalence in female FDRs with that of women in the population, rather than with male FDRs when developing selective screening programs. The male FDRs also have an increased chance of detection due to the ongoing population based screening programs.

**References:**

1. Abdominal Aortic Diameter Is Increased in Males with a Family History of Abdominal Aortic Aneurysms: Results from the Danish VIVA-trial, T.M.M. Joergensen a,*, K. Houlin a, A. Green b, J.S. Lindholt, Eur J Vasc Endovasc Surg (2014) 48, 669e675
LESSONS LEARNED FROM THE IMPROVE TRIAL
Janet T. Powell for the IMPROVE trial investigators

The Immediate Management of the Patient with Rupture: Open Versus Endovascular repair (IMPROVE) trial randomised 613 patients with an in hospital diagnosis of ruptured abdominal aortic aneurysm to either a strategy of endovascular first (with open repair as the default) versus open repair between 2009 and 2013.

The trial reported its primary outcome, 30-day mortality, early in 2014 [1] and 1-year outcomes in Spring 2015 [2] and now is poised to complete analysis of the final 3 year follow up. There was no difference in either 30-day or 1-year mortality between the randomised groups, although subgroup analyses at both timepoints were consistent with women having a survival advantage from an endovascular strategy. The 1-year results also reported quality of life, costs and cost-effectiveness, which were all better in the endovascular first strategy group [2].

Since this is perhaps the largest prospective series of patients with ruptured abdominal aortic aneurysm, we have been able to learn about other important aspects too, including the impact of pre-operative blood pressure, type of anaesthesia, aortic morphology and abdominal compartment syndrome [3,4]. We also have collaborated with 2 smaller European trials to publish individual patient data meta-analyses, which strengthen all the main observations of the IMPROVE trial [5].

References:

DIAGNOSTIC ALGORITHM FOR ACUTE AORTIC DISSECTION – IMAGING AND BIOMARKERS
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Diagnosis of acute aortic dissection still remains a challenge. Effective use of available diagnostic technologies including imaging and biomarkers is critical for immediate decision making. Recent developments in biomarkers such as D-dimer have established a potential role for biomarker-assisted diagnosis. Coupled with rapid imaging such as a triple rule-out CT would provide for a diagnostic algorithm of acute aortic dissection. Protocol-based diagnostic algorithms are helpful in the emergency setting and integration with available pathways such as for STEMI will be a topic that needs to be addressed.

INDIVIDUALIZED RISK ASSESSMENT IN TYPE B AORTIC DISSECTION
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Thoracic endovascular aortic repair is considered to be the first-line treatment for patients with complicated type B aortic dissection. Decision making is often based on physician experience and subjective clinical judgment and therefore the management of type B aortic dissection is complex. The long-term benefits of endovascular repair to prevent aortic-related mortality has been demonstrated in randomised controlled trials however recently attention has been turned to whether endovascular repair should be performed in uncomplicated cases. Pre-emptive surgery may not be the solution for all patients because of the occurrence of adverse events such death, stroke and paraplegia. A number of groups have undertaken studies to investigate morphological and false lumen characteristics that may be able to identify patients with uncomplicated type B aortic dissection at high risk of complications that would benefit from early endovascular intervention. Characteristics investigated include aortic diameter, the position, size and number of entry tears and false lumen thrombus volume. Functional imaging methods such as magnetic resonance and echocardiography are able to provide clinically relevant structural, hemodynamic and biomechanical information, which could be used for risk stratification of individual patients. A patient-specific approach designed to intervene only in patients that are at high risk of developing complications should improve the long-term outcome of these patients.

CAN WE PREDICT AORTIC SIZE PRIOR TO DISSECTION? YES!
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Objectives: Multiple studies have quantified the relationship between aortic size and risk of dissection. However, these studies estimated the risk of dissection without accounting for any increase in aortic size from the dissection process itself. This study aims to compare aortic size before and after dissection and to evaluate the change in size consequent to the dissection itself.

Methods: Fifty-five consecutive patients (29 Type-A; 26 Type-B) with aortic dissection (AoD) and incidental imaging studies prior to dissection were identified and compared to a control group of aeurysm patients (n=205). Average time between measurement at and prior to dissection was 1.7±1.9years (1.9±2.0years mean inter-image time in control group). A multivariate regression model controlling for growth rate, age and gender was created to estimate the effect of dissection itself on aortic size.

Results: Mean aortic sizes at prior to dissection were 54.2±7.0mm and 45.1±5.7mm for the ascending (AA), and 47.1±13.8mm and 39.5±13.1mm for the descending aorta (DA), respectively. Multivariable analysis revealed a significant impact by the dissection itself (p<.001) and estimated an increase in size by 7.65mm (AA) and 6.38mm (DA). Thus, a proportional estimate of 82.8% (AA) and 80.8% (DA) dissect at a size lower than the guideline recommended thresh-
old (55mm).

Conclusions: Aortic diameter increases substantially due to aortic dissection itself and thus, aortas are dissecting at clinically meaningfully smaller sizes than natural history analyses have previously suggested. These findings have important implications regarding at what size to intervene surgically (suggesting a shift toward smaller aortic sizes).

INITIAL EXPERIENCE IN DISSECTION OF AORTA IN NEPAL
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Introduction: Interventional cardiology including cardiovascular surgery is in its early phase of development in Nepal. Sahid Gangalal National Heart Centre is the only cardiology dedicated government hospital in Nepal and therefore, the main tertiary cardiac patient referral centre for the whole country. Surgery for aortic dissection has recently started in the country. We present our early experience with aortic dissection cases in the hospital.

Method: We did a retrospective descriptive analysis of aortic dissection cases requiring surgery over a period of 26 months between February 2014 and April 2016.

Results: Altogether 20 cases of dissection of aorta were operated during the period. Thirteen (65%) patients were males. Average age of the patients was 54 years (range: 25 to 81 years). Eighteen cases (90%) were of type A dissection: 17 with acute and 1 with chronic dissection, while the remaining two (10%) had type B dissection and required surgery because of complications like leak or rupture. Of the 18 type A dissection cases, two-third (12/18) underwent M Bentall’s procedure while 3 underwent Bentall’s with hemi arch replacement, 2 underwent ascending aortic replacement, and 1 underwent Bentall’s with proximal arch replacement. In addition, one of these patients had right coronary artery unroofing while another one had coronary artery bypass graft. Five of these 18 patients (27.8%) died. The two cases of type B dissection underwent surgery in an emergency basis due to ongoing leak and both expired post-operatively.

Conclusion: Our early experience with aortic dissection management shows a success rate of 65%. Studies that look into details of patient characteristics and health-provider related parameters can help improve success rate, and reduce mortality.

POSITIVE FAMILY HISTORY OF AORTIC DISSECTION DRAMATICALLY INCREASES DISSECTION RISK IN FAMILY MEMBERS
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Objective: Although family members of patients with aortic dissection (AoD) are believed to be at higher risk of aortic dissection, the prognostic value of a positive family history (FH) of aortic dissection (FHAD) in family members of patients with AoD has not been studied rigorously. We seek to examine how much a positive family history of aortic dissection may increase the risk of developing new aortic dissection among first-degree family members.

Methods: Patients with AoD treated at our institution between 1983 and 2015 were contacted to complete a questionnaire on FHAD. A family history was considered positive if AoD occurred in the index patient and one or more family members. The age at AoD, exposure years in adulthood before AoD, and annual probability of AoD among first-degree relatives were compared between patients with negative and positive FHADs.

Results: A total of 100 patients with AoD were identified. Mean age at dissection was 59.9 ± 14.7 years. FHAD was positive in 32 patients and negative in 68. Compared to patients with negative FHAD, patients with positive FHAD dissected at significantly younger age (54.7 ± 16.8 vs 62.4 ± 13.0 years, P = 0.013), had more AoD events in first-degree relatives (2.3 ± 0.6 vs 1.0 ± 0.0, P < 0.001), and shorter exposure years per AoD event (18.3 ± 6.7 vs 43.1 ± 8.5, P < 0.001). The annual probability of AoD per first-degree relative was 2.77 times higher in patients with positive than negative FHADs (0.0100 ± 0.0057 vs 0.0036 ± 0.0014, P < 0.001).

Conclusions: A positive FHAD confers a significantly increased risk of developing AD on family members.

OPEN SURGICAL CONVERSION AFTER TEVAR: INCIDENCE AND TREATMENT OPTIONS
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Background: To analyze indications, describe different approaches and report outcomes of patients undergoing late open conversion (LOC) after thoracic endovascular aortic repair (TEVAR).

Methods: From to 1999 to 2015, 65 patients at our Institution underwent redo procedures after TEVAR. Thirty of them underwent LOC. Average time from the index TEVAR to LOC was 57 months (range 2-98 months), indication to LOC was progression of distal aortic disease in nine patients (30%), stent-graft infection/fistulization in 10 (33.3%), retrograde dissection in 6 (20%), endoleak in 3 (10%), device migration/failure in 2 (6.7%). In 17 patients (56.6%) thoracic stent-graft was only partially removed and the proximal anastomosis was performed including native aorta, stent-graft and surgical graft. Left heart bypass and cerebrospinal fluid drainage were used in 22 (73.3%) and 16 (53.3%) cases, respectively. Biological flap coverage with intercostal muscle flap was used 6 six of infected cases.

Results: Overall perioperative mortality rate was 16.6% (5 patients) – 20% in the subgroup of patients with stent-graft infection/fistulization (2 patients) and 33% in the subgroup with retrograde dissection (2 patients). The most common postoperative complication was respiratory failure with seven cases (23.3%). Paraplegia was observed in 1 patient (3%). During a mean follow-up of 19 months (range, 5-63) was registered only one aortic-related death for aorto-esophageal fistula.

Conclusions: Open conversion after TEVAR is a technically demanding procedure but feasible leaving in site the proximal segment of thoracic stent-graft in most of the cases. Morbidity and mortality rates were higher in case of infection, fistula and retrograde dissection.

NEUROMONITORING USING MOTOR AND SOMATOSENSORY EVOKED POTENTIALS IN AORTIC SURGERY
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Background: Motor evoked potentials (MEP) and somatosensory evoked potentials (SSEP) are established methods of neuromonitoring aimed at preventing paraplegia after descending or thoracoabdominal aortic repair. However, their predictive impact remains controversial. The aim of this study was to evaluate our single center experience using this monitoring technique.

Methods: Between 2009 and 2014, 78 patients (mean age 66 ± 12, 53% male) underwent either descending or thoracoabdominal aortic repairs. Of these, 60% had an aortic aneurysm, 30% dissection and 10% other etiologies. Intraoperatively, MEPs and SSEPs were monitored and, if necessary, clinical parameters (blood pressure, hematoctrit, oxygenation) were adjusted in response to neuromonitoring signals. This analysis is focused on the neurological outcome (paraplegia, stroke) after the use of intraoperative neuromonitoring.

Results: Thirty-day mortality was 10 (12.8%). All patients with continuously stable signals or signals that returned after signal loss developed no spinal cord injury, whereas 2/6 of the evaluable patients with signal loss (without return) during the procedure suffered from postoperative paraplegia (one transient and one permanent). Sensitivity and specificity of use of MEP and SSEP were 100% and 94.20% regarding paraplegia, respectively.

Conclusions: (1) Preservation of signals or return of signals is an excellent prognostic indicator for spinal cord function. (2) Intraoperative modifications in direct response to the signal change may have averted permanent paralysis in the patients with signal loss without neurologic injury. We have found MEP and SSEP neuromonitoring to be instrumental in the prevention of paraplegia.

RADIATION PROTECTION FOR PATIENT AND STAFF DURING ROUTINE EVAR AND TEVAR PROCEDURES
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Endovascular aortic aneurysm repair require extended fluoroscopy guidance for the manipulation of endovascular devices, which is associated with biological risks for both physicians and patients. Potential consequences range from skin injuries to the development of solid cancers and leukemia. There is no absolutely safe amount of ionizing radiation and protection must be a priority for the endovascular therapist. When following good practices it is possible to keep the risks as low as reasonably achievable to commensurate with the medical purpose. Radiation protection can be achieved with the use of appropriate protective equipment and the reduction of the radiation dose. The use of shielding devices (lead aprons, thyroid shields, table suspended lead shields) is mandatory. The use of tables with a carbon fiber top instead of regular surgical tables is preferable. The distance between the patient’s body and the image receptor should always be minimized to avoid beam energy dispersion and the screen should always be collimated vertically and horizontally to the area of interest. Radiation dose reduction requires a strict application of the “as low as reasonably achievable” principle. The x-ray system should be by default set to low dose program and pulsed mode, while the pedal should be engaged only when information is required. Magnification should be avoided, while digital subtraction angiography should be replaced by fluoroscopy runs in most instances possible. Extreme angulations of the x-ray equipment should be avoided. Image fusion can facilitate endovascular navigation and reduce the dose needed, although have not been widely applicable. All interventionists should receive appropriate radiation protection training and always audit and review the outcomes of each procedure. The application of specific regulation of radiation protection during routine EVAR and TEVAR is mandatory. Optimized set-up of the fluoroscopy system, adherence to good clinical practice and adequate training are key points to ensure safety for both the patients and the staff during the procedure.

PATIENTS’ COMPLIANCE WITH POST-EVAR FOLLOW-UP AND ITS IMPACT ON THE OUTCOME
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Lifelong follow-up after Endovascular Aortic Aneurysm repair (EVAR) is recommended to monitor the effectiveness and durability of the treatment. Nevertheless, patients’ compliance with follow-up protocol is an important element that may be related to the outcome. We conducted a study to assess patients’ compliance with the follow-up imaging protocol, the presence of any factors associated with the patients’ compliance and the potential influence of imaging-protocol adherence on outcomes. This study was a systematic review of the existing literature by searching the MEDLINE, CENTRAL, and Cochrane databases and the related keys references.

One randomized control and nine retrospective studies were identified reporting on post-EVAR follow-up compliance. The studies included 36,119 patients with mean age of 76±3.1 years and the mean follow-up ranged from 25 to 73 months. Most of the patients were males (51%- 89%), white (51%- 97.7%) and the majority of them were living <100 miles from the treatment center. The data were too heterogeneous to perform a meta-analysis. Incomplete follow-up and complete loss of follow-up were ranging from 15% to 65% and 22% to 56%, respectively. Advanced age, symptomatic or ruptured aneurysm, history of chronic diseases, and social-economic issues were associated with poor follow-up compliance. Five of these studies suggested that complete follow-up did not offer any survival benefit, while only one study suggested that incomplete follow-up was associated with higher fatal complication rates.

Patients’ compliance with a post-EVAR follow-up imaging protocol is poor while patients’ age, social-economic issues, chronic comorbidities and operation undertaken as emergency appear to be factors associated with poor patients’ compliance. However, there is lack of solid evidence to show that this poor compliance results in worse outcomes. Prospective studies focused on the impact of follow-up adherence on the EVAR outcomes are needed.

EARLY AND LONG-TERM OUTCOMES AFTER OPEN OR ENDOVASCULAR REPAIR FOR ABDOMINAL AORTIC ANEURYSMS IN HIGH-RISK PATIENTS
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Introduction: The aim of this study was to evaluate the short and long term results of surgical or endovascular treatment for abdominal aortic aneurysms (AAA), stratifying patients according to preoperative risk.

Methods: A retrospective, observational study was performed. Data on preoperative risk factors were analyzed to stratify patients according to the SVS / ISCVS score. The patients were then classified in two groups according to the surgical risk (Group A SVS score 0-10, Group B SVS score 11-22). In the two groups of patients were evaluated postoperative complications, 30-day mortality and survival during follow-up.

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Results: From July 2011 to November 2014 at our unit were treated electively 374 patients with AAA. The analysis of the results was carried out only in 212 cases (24 females and 188 males) in which it was possible to collect clinical data. The mean age was 76.5 years (range 56-93 years); 135 (63.7%) patients underwent OR treatment, 77 (36.3%) underwent EVAR. The medium follow-up was 685 days (0-1420 days range). Open repair performed out in 75 and 60 patients in group A and B respectively. EVAR was done in 43 and 34 of the group A and B respectively. Mortality at 30 days was 1.7% and 3.2% in group A and B respectively. During follow-up the median survival was 91.9% for patients in the OR group, and 98.3% for patients undergoing EVAR in group A and 98.3% for patients subjected to OR and 79.4% for patients undergoing EVAR.

Conclusions: The results of our study showed a lower 30-day mortality in high-risk patients undergoing surgical or endovascular treatment. Analysis of the results showed that survival in high-risk patients during follow-up does not seem to be affected by the type of treatment and in fact was higher in patients undergoing OR compared with patients undergoing EVAR.

RENAL FUNCTION IS THE MAIN PREDICTOR OF ACUTE KIDNEY INJURY AFTER ENDOVASCULAR ABDOMINAL AORTIC ANEURYSM REPAIR
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Background: Postoperative acute kidney injury (AKI) may occur in up to 20% of elective endovascular abdominal aortic aneurysm repairs (EVAR) (1-3) and has been associated with poor outcome (1-4); however, it is not clear which patients are at highest risk, to target renal protection effectively. We sought to determine the predictive factors of AKI after elective EVAR.

Methods: Overall, 947 patients undergoing elective EVAR between January 2004 and December 2014 were analyzed, using prospective ly collected data. Postoperative AKI was defined by serum creatinine change within 48 hours, using the latest validated criteria (Acute Kidney Injury Network and Kidney Disease Improving Global Outcomes). Cardiovascular and kidney-disease risk factors were entered in univariate and multivariate analyses to assess influence on AKI development. Associations between AKI and long-term mortality, morbidity and cardiovascular events were sought using multivariate models.

Results: Overall, 167 (17.6%) patients developed AKI but only 2 patients required dialysis perioperatively. At multivariate analysis, adjusted for established AKI-risk factors and parameters that differed between groups at baseline, preoperative estimated glomerular filtration rate (eGFR; as per the chronic kidney disease epidemiology [CKD] formula); odds ratio (OR): 1.02 (per unit decrease); 95% confidence interval (CI): 1.003-1.041; P = 0.025; and chronic kidney disease (CKD) stage > 2 (OR: 1.28; 95% CI: 1.249-2.531, P = 0.001) were associated with development of AKI. During a median follow-up of 62 months, AKI was associated with CV events on adjusted analyses [Hazard Ratio (HR): 1.73, 95% CI 1.06-3.39, p=0.03] and mortality (HR: 1.84, 95% CI 1.01-4.22, p=0.01).

Conclusions: AKI was common after elective infrarenal EVAR and preoperative renal function was the main predictor. Patients with a low eGFR need to be targeted with more aggressive renal protection, since AKI development is associated with poor outcomes.

References:

STRUCTURAL FINITE ELEMENT MODELLING OF THE BICUSPID ROOT TO UNDERSTAND DISEASE PROGRESSION
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Bicuspid aortic valve (BAV) is a congenital aortic valve disease where two out of the three leaflets are fused together. BAV is a recognized risk factor for pathologies affecting the aortic valve and the ascending aorta. Despite the genetic origin of BAV, the associated alterations in aortic root structural mechanics and fluid dynamics may play a relevant role in the progression of the mentioned degenerative processes, and hence in the timing for surgery. Currently, the evaluation of the progression of the disease, and hence prognosis and decision for surgery, largely rely on purely geometrical criteria, i.e. on the measurement of some key dimensions of the aortic root (AR) from clinical images. These criteria are empirical and sub-optimal; complementing them with new and biomechanically-driven ones could allow for more reliable prognosis and aid the decisional process. On this basis, we developed computational tools to assess the in vivo fluid dynamics and structural mechanics of the AR, aimed to the quantification of the biomechanical anomalies characterizing BAV disease. Here we focus on the finite element analysis of AR structural mechanics in presence of BAV through a novel approach that exploits the anatomical information yielded by magnetic resonance imaging and that allows for consistency between the image-based AR geometry and the pressure loads acting on it. We simulated AR function throughout the cardiac cycle for two preliminary cohorts of healthy volunteers (n=4) and BAV patients with normo-function al valves (n=3), and compared the corresponding biomechanical variables. Namely, we analyzed two features of potential clinical relevance in BAV patients. First, the increase in diastolic leaflet strains and stresses characterizing the abnormal closed leaf valve configuration, which may impact on the differentiation of valvular interstitial cells (VICs) and promote aortic valve calcification. Second, the increase in systolic aortic wall stresses in BAV patients in the tubular ascending aorta, which may be linked to aortic wall remodeling and to an increased risk for wall dilation and coarctation. Despite
the inter-subject variability within each cohort, differences were evident between healthy ARs and BAV-affected ones. When compared to healthy ARs, BAV-affected ones were characterized by i) altered diastolic leaflet stretches, which were notably reduced in the commissure-commissure direction and increased in the annulus-to-free margin direction, ii) increased diastolic leaflet stresses, and iii) aortic wall regions affected by elevated stresses in systole, which run from to sino-tubular junction to the convex side of the ascending aorta. When applied to a sufficiently wide and statistically robust population of subjects undergoing proper follow-up, our approach may yield detailed biomechanical data whose prognostic value could be evaluated, paving the way towards sounder criteria for the prognosis of BAV disease.

**IDENTIFYING CIRCULATING BIOMARKERS OF BAV AORTOPATHY RISK**

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The current knowledge of bicuspid aortic valve (BAV)-related aortopathy is recognized to be inadequate [1], especially in its pathogenetic and prognostic aspects. Patients are usually operated on electively, to prevent the risk of acute aortic events, namely aortic rupture and aortic dissection, on the basis of “dimensional” criteria of indication, i.e. aortic diameter and size progression rate [2]. However, it is now understood that dimensional criteria alone are not enough to adequately manage such a heterogeneous disease as BAV aortopathy, especially in terms of prognosis [3]: thus additional “non-dimensional” criteria for risk stratification are needed to the purpose of developing personalized medicine strategies [4, 5]. The search for putative risk markers of BAV aortopathy is particularly lively, however most studies have addressed imaging-based markers [6], while only few focused on the identification of biochemical markers [7-9]. Indeed, a biomarker of aortopathy should have pathogenetic significance, and ideally it should have limited correlation with aortic diameter, to provide additional information for prognostic stratification alongside this parameter. The issue of identifying possible biomarkers of BAV aortopathy has been addressed by few studies, with different approaches. Tzemos et al. previously reported higher MMP-2 serum concentration in BAV patients with aortopathy than in BAV patients without aortopathy (defined by aortic diameter >40mm and <35mm respectively) [10]. Later on, unique profiles of plasma MMPs, tissue inhibitors of MMPs and microRNAs were revealed in TAV versus BAV patients with aortic aneurysm [7], showing the possibility to predict the presence of specific etiologic subtypes (i.e. TAV or BAV) of aneurysm disease using a plasma multi-analyte regression strategy. Others [8] reported significant correlation between serum levels of the receptor for advanced glycation end-products (sRAGE) and its tissue expression, which was in turn associated with disrupted elastin and proteoglycan deposition, irrespective of the diameter. Hillebrand et al. [11] recently assessed the serum levels of TGF-β1 in an etiologically heterogeneous population, also including BAV patients: total serum TGF-β1 was higher in patients with aortic dilatation, however the only independent predictor in multivariable analysis was the presence of a genetic syndrome, and non-syndromic BAV patients had lower serum levels of TGF-β1 compared to the reference controls. The growing body of information on this topic will be systematically reviewed in this presentation and the unmet needs in the search for prognostically relevant biomarkers in BAV aortopathy will be appraised.

**References:**


**HOW TO INTEGRATE IMAGING AND BIOCHEMISTRY INTO RISK STRATIFICATION OF BICUSPID AORTOPATHY**

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Efforts over the past few years have focused on defining individual risk factors for disease progression in patients with bicuspid aortic valve (BAV) and aortopathy. The risks associated with BAV aortopathy may be less than previously believed. This statement is based on contemporary natural history studies and key comparisons to those with tricuspid aortic valve disease and genetic connective tissue aortopathies. More conservative and selective approaches to prophylactic aortic resection may be indicated, particularly in patients with BAV stenosis.

Using newer state-of-the-art imaging modalities (4D-flow MRI) with tissue correlation of molecular biomarkers, novel data supports
valve-mediated hemodynamics as a critical mediator of disease progression in BAV aortopathy. Recent studies by us and others indicate that altered aortic hemodynamics in BAV patients are directly associated with regional degradation of the aortic wall and the BAV aortopathy phenotype. Findings based on 4D flow MRI, which allows for the in-vivo measurement of aortic blood flow with full volumetric coverage of the aorta, have documented changes in transvalvular blood flow and their downstream impact on regional aortic wall shear stress (WSS) even for BAVs without valve dysfunction. WSS is a known stimulus for arterial mechanotransduction and can alter endothelial cell function resulting in outward vascular remodeling (e.g. dilation). A recent study from our group provides strong evidence for this proposed mechanism via the use of in-vivo 4D flow MRI and aortic tissue resection in BAV patients undergoing aortic repair. Correlation of aortic 4D flow MRI hemodynamics with resected aortic tissue histopathology showed that regionally elevated WSS patterns were closely associated with the severity of aortopathy.

There remains a substantial gap in knowledge with respect to BAV aortopathy in the pathophysiology and molecular mechanisms of disease progression. There is a critical need to develop individualized risk assessments beyond size and growth criteria to offer more precise and individualized strategies for surgical resection of the aorta in BAV patients. The integration of novel imaging and biomolecular markers of BAV aortic disease progression and severity may improve our management of individual patients who need prophylactic aortic resection.

References:

TWENTY-FIVE YEAR OUTCOME OF COMPOSITE GRAFT AORTIC ROOT REPLACEMENT: NEAR “CURATIVE” IMPACT ON AORTIC ROOT DISEASE

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Background: Operative choices for aortic root disease abound. We report our experience with traditional composite graft replacement in 449 patients focusing on long-term survival and freedom from late reoperation and adverse events.

Methods: The coronary button technique was used. Mean age was 56.1±14.0 years (range 14-87) with 83% males (373/449). Valve prosthesis was mechanical in 343 (76%) and bioprosthetic in 106 (24%). A modified Cabrol procedure (Dacron coronary graft) was employed in 10% (45/449) and concomitant CABG 10.9% (49/449). There were 15.8% (71/449) urgent/emergent and 8.2% (37/449) redo procedures. Survival follow-up was 100% averaging 7.0±5.1 years (range 0.1-24.8).

Results: Operative mortality occurred in 14 patients (3.1%) and was 2.2% (9/418) in non-dissection and 1.9% (7/361) in elective first-time operations. Stroke and re-exploration for bleeding occurred in 9 (2.0%) and 20 (4.5%) patients, respectively. Major late events included bleeding in 2.5% (11/435) and thromboembolism in 1.1% (5/435). At 5, 10 and 20 years, freedom from major events and reoperations on the root were 97.8%, 95.4% and 94.39%, and 99.0%, 99.0% and 97.9%, respectively. Survival in patients aged <60 years was 92.0%, 90.1% and 79.8% at 5, 10 and 20 years versus 88.4%, 67.9% and 42.6% in patients aged ≥60 years. Compared with age- and gender-matched controls, survival was not significantly different (p = 0.20).

Conclusions: Composite graft aortic root replacement is associated with low operative risk, excellent long-term survival, and low incidence of reoperation and late events. The favorable long-term results indicate an almost “curative” impact on aortic root disease.

HOW TO CLASSIFY THE DILATATIONS OF THE ASCENDING AORTA?

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While classification systems are available and currently used in the terminology to define aortic dissection and thoraco-abdominal aortic aneurysms, there is no such established method to classify the dilatative aortopathies that affect the ascending aorta. Several types of classifications have been proposed, in particular applied to the setting of bicuspid aortic valve-related aortopathy. They are based on different criteria for classification, including: 1) the pattern of dimensions (one segment relative to another); 2) the presence of dilatation in absolute terms (need for a cut-off); 3) the combination of both the previous criteria. These will be appraised in this presentation and their respective potential for a clinical usefulness will be commented. The hypothesis will also be issued that bicuspid aortopathy might be the testing ground for the identification of the best criterion to be then applied to all other tricuspid-aortic-valve-associated dilatations of the proximal tract of the aorta.
Complete replacement of the aortic arch remains one of the most complex vascular operative procedures. Open surgical repair is the reference standard but despite advances in surgical technology and techniques the mortality and neurological complication rates remain high. The arch branch endograft has been used in selective centers since 2009 and despite an initially steep learning curve, 30-day mortality rates are now similar to traditional open repair, despite taking on a significantly more morbid patient population. There are many challenges associated with this procedure, such as the integrity of the seal zones, the correct method for alignment of the device intra-operatively and consideration of the aortic valve. These will have an effect on the ease of implantation, the morbidity and mortality associated with the procedure and the long-term durability of the repair.

**CHOICE OF THE BEST TRANSASCATHETER SITE FOR TAVI IMPLANTATION**

Marc Radermeker, Christophe Martinez, Olivier Gach, Rodolphe Durieux, Jean-Olivier Defraigne, Victor Legrand

Department of Cardiothoracic Surgery and Cardiology, CHU Sart-Tilman, University of Liège, Belgium.

The least invasive access for the TAVI procedure is via the common femoral artery. However, among the patients actually referred for this procedure, this route is either impracticable or unwise in approximately 15-20% of the patients. Indeed, vascular complications and haemorrhage have a major negative impact on the outcome following this procedure.

We present the experience of the CHU of Liège over 215 cases of TAVI procedure using the Corevalve Medtronic(r) device. Our strategy implies the decision for the therapy and the selection of the vascular access in heart team. The past history of the patient, angio-CT data and the arteriography performed during the catheter evaluation are integrated.

The left axillary artery (20/215) and the right carotid artery (15/215) have been used successfully in our practice as respectively the first and third choice options. This versatility enabled us to treat in an antegrade or minimally invasive fashion virtually every patient.

**CRITICAL ANALYSIS OF RECENT REGISTRIES AND RANDOMIZED TRIALS**

Victor Legrand

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Clinical studies and registries supporting the safety and efficacy of Transcatheter Aortic Valve Implantation (TAVI) have been accumulated for the last two years. Additionally, randomized trials comparing TAVI with Surgical Aortic Valve Replacement (SAVR) showed non-inferiority and even superiority of TAVI over SAVR in moderate and high risk patients as defined by STS or Euroscore II scores. Results of four randomized trials comparing SAVR and TAVI are reviewed. Patient’s characteristics, early and late clinical outcomes of each trials are presented and discussed. TAVI was associated with a significant 13% reduction in mortality at 2 years, as compare to SAVR. Survival benefit of TAVI was significant for female patients (p=0.01) and for patients undergoing transfemoral access (p=0.004). The TAVI survival benefit was consistent across high-risk and lower-risk groups and was independent of device type. Of note that TAVI is not associated with survival benefit in male patients (p=0.95). TAVI procedures were associated with fewer kidney injury, new onset atrial fibrillation and major bleeding. Conversely, fewer major vascular complications, fewer new PCMK implantation and paravalvular regurgitation occurred among SAVR patients. Large US and European registries not only confirm the increasing use of TAVI for the treatment of aortic valve stenosis, but also aim to better define patients in whom the procedure may be futile. Patients with severe kidney or lung dysfunction, those with poor LV function (LVEF<50%, NYHA class IV) have worse outcomes. Presence of 3 or more major organ system compromises should be considered at prohibitive risk. Additionally, frailty index and cognitive functions should also be considered in decision making. Above all, it is now clear that the best treatment of aortic valve stenosis should be discussed by a valvular heart team which goal is to confirm the indication and decide the best procedure (TAVI or SAVR), according to clinical status of the patient and local experience.

**HIGH HERITABILITY OF ABDOMINAL AORTIC ANEURYSMS – A POPULATION-BASED TWIN-STUDY**

Trine Maria Mejnert Joergensen

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Introduction: First-degree relatives of patients with abdominal aortic aneurysm (AAA) have an increased risk of developing AAA; however, despite intensive investigation, the specific genetic factors involved in the development of the disease are still largely unknown. In twin studies the influence of genetic and environmental factors can be assessed by comparing concordance rates between monozygotic (MZ) and dizygotic (DZ) twins. Higher phenotypic similarity between MZ than DZ twins indicates a genetic attribution to the aetiology. Overall heritability can be calculated using structural equation modelling.

Aim: To investigate the heritability of AAA among Danish twins using concordance rates and heritability estimates.

Materials/methods: The Danish Twin Registry was used to identify all Danish twin pairs where both twins were alive January 1, 1977. We then identified AAA-cases using the National Patient Registry and the Registry of Cause of Death. Probandwise concordance rates were calculated and heritability estimated using structural equation modelling.

Results: We identified 414 twins with AAA; 69.8% (289/414) men and 30.2% (125/414) women. The probandwise concordance rate in MZ twins was 30% (95% CI:20.3;43.3%) compared with 12% (95%CI:7.0;20.1%) in DZ twins. In the heritability analysis 77% (95%CI:67.8%;85%) of the total variance was explained by additive genetic components and 23% (95%CI:15.3%;33%) was explained by non-shared environmental factors.

Conclusions: We found a probandwise concordance rate 2.5 times higher in MZ twins compared with DZ twins and an overall heritability of 77% which suggests a substantial genetic component in the development of AAA.

**GLOBAL AND GENE SPECIFIC DNA METHYLATION IS ASSOCIATED WITH ABDOMINAL AORTIC ANEURYSMS**

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University of Leicester, Leicester, United Kingdom

Introduction: Abdominal aortic aneurysm (AAA) is a degenerative cardiovascular disease characterised by the gradual, irreversible dilation of the abdominal aorta. There is strong evidence of genetic
predisposition in the development of AAA but only a small number of low-effect risk loci have been identified. It is feasible that DNA methylation, one cause of altered gene-regulation, may contribute to AAA. We recently identified that global DNA hyper-methylation was associated with large AAA and increasing aneurysm diameter. These associations were independent of ethnicity, gender, age and smoking, highlighting the potentially pathogenic effects of chronic inflammation on methylation.

**Aim:** To identify gene specific CpG methylation changes in the promoters of genes already known to be associated with AAA.

**Work summary:** Candidate gene promoters (SORT1, LDLR, IL6R, LRP1, CDKN2B and MMP9) were isolated in DNA derived from the peripheral blood mononuclear cells of 48 people with large AAA and 48 controls using DNA bisulphite conversion and bisulphite-specific PCR, then sequenced using next-generation sequencing technology. Data was analysed using open source bioinformatics software specifically designed for methylation sequencing.

**Results:** Changes in levels of CpG methylation were observed in people with large AAA vs controls. The LDLR and SORT1 promoters were consistently hyper-methylated across large sections in 48 AAA vs 48 controls. 21 individual CpGs were hyper-methylated in AAA at the LDLR promoter locus, with an average increase of 5.4% (+/-1.08) (P=0.002). 4 CpG sites were significantly hyper-methylated in AAA in the SORT1 promoter locus, with an average increase of 4.8% (+/-0.35) (P=0.004).

**Conclusion:** We have now identified that global and gene specific DNA methylation is associated with AAA. Functional corroboration is needed, but it is possible that these methylation differences are biological determinants of altered gene expression, and that DNA methylation does play a role in the disease. These genes also represent viable meQTL candidates.

**References:**

**END-STAGE HUMAN ANEURYSM DISEASE IN DIFFERENT ARTERIAL POSITIONS IS SIMILAR - ANEURYSM INDUCTION IN MOUSE MODELS HOWEVER NOT**

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3 Institute for Radiology, Würzburg, Germany
4 Clinical for Visceral, Vascular and Pediatric Surgery, Würzburg, Germany

**Introduction:** Aneurysm disease can occur throughout the arterial tree, with abdominal aortic aneurysms (AAA) being the most frequent central - and popliteal artery aneurysms (PAA) the most frequent peripheral one. The pathology has been well examined, yet, very little is understood regarding AAA development. Leaving aside secondary vessel enlargement due to dissection, inflammation and genetic disorders, aneurysm disease has distinct features like angiogenesis and phenotypic switching of vascular smooth muscle cells (VSMC). However, little is known about these characteristics in other than AAA.

**Material and Methods:** From a surgical biobank of aneurysm tissue we compared 42 AAA, 15 PAA, three ascending aortic, five iliac, three femoral, two brachial, one visceral and one carotid artery aneurysm on morphologic, protein and miRNA-expression levels. Two multi-stage mouse models of aneurysm disease, porcine pancreatic elastase infusion (PPE) and topic application of elastase (EPA), were applied to test the response to arterial aneurysm induction in different locations within the arterial system.

**Results:** AAAs show a wide variety in histomorphologic appearance, which can not be detected in PAA. All investigated aneurysm entities show characteristic VSMC phenotypic switching, angiogenesis, matrix remodeling, T-cell inflammation and M1-like macrophage homing. AAA and PAA, despite being of elastic and muscular artery origin respectively, have similar involvement of key transcription factors, like i.e. Kruell-liked factor 4 or myocardin. To further investigate these conditions in inducible aneurysm models, we applied the PPE procedure to a juxtarenal aorta and the EPA model to a thoracic, abdominal and femoral location.

**Conclusion:** Despite different arterial morphogenesis, advanced aneurysm disease from human intraoperative specimen shows similar characteristics of end-stage disease that are best mimicked by the murine PPE model of aneurysm induction.

**PHENOTYPIC SWITCHING OF SMCS IS A POTENTIAL THERAPEUTIC TARGET IN POPLITEAL ANEURYSMS**

**Hultgren**1, **Lars Mægdesfeldt**1

1 Karolinska Institute, Stockholm, Sweden
turnover in the aneurysmal neck area suggests evaluation of alternative treatment strategies, targeting key processes in its pathogenesis.

**RESVERATROL INHIBITS AORTIC ROOT DILATATION IN THE FBN1C1039G/+ MARFAN MOUSE MODEL**

Stijnje Hibender, Romy Franken, Cindy van Rooijen, Ingeborg van der Made, Maarten Groenink, Aelko Zwierdeman, Barbara Mulder, Carole de Vries, Vivian de Waard

Academic Medical Center, Amsterdam, The Netherlands

**Objective:** Marfan syndrome (MFS) is a connective tissue disorder caused by mutations in the fibrillin-1 gene. MFS patients are at risk for aortic aneurysm formation and dissection. Usually blood pressure lowering drugs are used to reduce aortic events, however, this is not sufficient for most patients. In the aorta of smooth muscle cell-(SMC) specific sirtuin-1 (SIRT1)-deficient mice, spontaneous aneurysm formation and senescence is observed. Resveratrol is known to enhance SIRT1 activity and to reduce senescence, which prompted us to investigate the effectiveness of resveratrol in inhibition of aorta dilatation in the Fbn1C1039G/+ MFS mouse model.

**Approach and Results:** Aortic senescence strongly correlates with aortic root dilatation rate in MFS mice. However, while resveratrol inhibits aortic root dilatation, it only shows a trend towards reduced aortic senescence. Resveratrol enhances nuclear localization of SIRT1 in the vessel wall and, in contrast to losartan, does not affect leukocyte infiltration, nor activation of SMAD2 and ERK1/2. Interestingly, specific SIRT1 activation (sirtinol) or inhibition (sirtinol) in MFS mice does not affect aortic root dilatation rate even though senescence is changed. Resveratrol reduces aortic elastic breaks, and decreases miRNA-29b expression coinciding with enhanced anti-apoptotic Bcl-2 expression and decreased number of TUNEL positive cells. In cultured SMCs, the resveratrol effect on miR-29b downregulation is endothelial cell- and NF-kB-dependent.

**Conclusion:** Resveratrol inhibits aortic root dilatation in MFS mice by promoting elastin integrity and SMC survival, involving downregulation of the aneurysm-related miR-29b in the aorta. Based on these data, resveratrol holds promise as a novel intervention strategy for MFS patients.

**IMMUNOPATHOLOGY IN PATIENTS WITH AAA**

Miroslav Prucha, Petr Stadler, Petr Sedivy, Pavel Zdrahal

Na Homolce Hospital Prague, Czech Republic

Aortic aneurysm (AAA) is a serious condition with unclear pathogenic mechanism which has a high mortality rate in case of the occurrence of the most serious complication - a ruptured aneurysm. One of the discussed pathogenic factors which might be involved in the development of AAA are immunological mechanisms. Patients and methodology: We examined a total of 58 patients with AAA requiring surgery and 20 patients treated for lipid metabolism disorder without AAA in the control group. Demographic and clinical characteristics of both groups are shown in Table 1. The following parameters were examined in both groups: IgG, IgG1-IgG4, pentraxin 3, fractalkine, IL-8, IL-10, IL-15, IL-18, IL-1b, M-CSF, MPC-1, RANTES, SAP, TNF, MMP-2, MMP-3, MMP-9, MMP-12. Results: In the AAA group of patients, statistically significantly higher concentrations of IgG4 were detected as compared to the control group. There were no significant differences in the concentration of fractalkine, IL-10, IL-15, IL-18, IL-1b, MPC-1 and TNF in both groups. RANTES concentration, as well as the concentrations of MMP 2 (p=0.02), MMP 3 (p=0.04) and MMP 9 (p=0.009) were significantly higher in the group of patients with AAA (p=0.0004). Conclusion: Significantly higher concentrations of bio-markers related to immune mechanisms and inflammatory activity were detected in the group of patients with AAA. A higher frequency of increased IgG4 concentrations in patients with AAA is a reason why some AAAs are considered to be a disease associated with IgG4. A higher inflammatory activity detected in the group of patients with AAA as compared with the control group of patients with treated atherosclerosis provides a possibility to potentially use a targeted treatment in patients with AAA.

**HOW DOES IT FEEL TO HAVE AN ABDOMINAL AORTIC ANEURYSM – A PATIENT-CENTERED VIEW**

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1. Leiden University Medical Center, Leiden, The Netherlands
2. Leiden University, Leiden, The Netherlands

**Aims:** An abdominal aortic aneurysm (AAA) is a potentially lethal disease, which is relatively common in elderly men. As repair has only proven benefit above 5.5cm, quite a large group of patients with smaller aneurysms do not receive specific treatment. These patients are in a watchful-waiting period and have little contact with their vascular specialist. Qualitative data from patients with small AAAs is scarce and little is known about the psychological impact of living with an aneurysm. More insights into patients’ view on diagnosis and disease burden of an abdominal aneurysm is needed to provide patients with additional support in coping this disease.

**Methods:** For this purpose we perform ten in-depth semi-structured qualitative interviews with AAA patients who are in a watchful-waiting period. After the interview patients are asked to fill in a few questionnaires assessing: health related quality of life (SF-36), illness perceptions (IPQ), anxiety and depression (HADS). All interviews will be audio taped and transcribed verbatim. Interview transcripts are then coded and contents will be analyzed.

**Results:** Preliminary analyses of data derived from ten interviews shows that patients often have little knowledge on AAA-disease and treatment options. However, they accept the conservative watchful-waiting plan proposed by the surgeon. In addition, patients rated their own health and quality of life as highly positive, despite severe comorbidity and sometimes uncertain life expectancy. In these patients, the disease burden of an AAA was very low due to the absence of symptoms and active intervention. Aneurysm patients feel they have little control over their AAA and largely rely on the surgeon for judgment.

**Conclusions:** Patients with small AAA are generally content with a conservative treatment plan and consider themselves to enjoy a good health despite comorbidity. In addition, patients depend on their specialist to take control in AAA treatment.

**META-ANALYSIS OF THE CURRENT PREVALENCE OF SCREEN-DETECTED ABDOMINAL AORTIC ANEURYSM IN WOMEN**

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2. Department of Public Health and Primary Care, University of Cambridge, Cambridge, United Kingdom
3. Department of Cardiovascular Sciences and NIHR Leicester Cardiovascular Biomedical Research Unit, University of Leicester, Leicester, United Kingdom
Background: Although women represent an increasing proportion of those presenting with abdominal aortic aneurysm (AAA) rupture, the current prevalence of AAA in women is unknown. The contemporary population prevalence of screen-detected AAA in women was investigated by both age and smoking status.

Methods: A systematic review was conducted, according to the PRISMA guidelines, of studies screening for AAA, including over 1000 women, aged at least 60 years, done since the year 2000. Studies were identified by searching MEDLINE, Embase and CENTRAL databases until 13th January 2016. Study quality was assessed using the Newcastle–Ottawa scoring system for cross-sectional studies.

Results: Eight studies were identified, including only three based on population registers. The largest studies were based on self-purchase of screening. Altogether, 1,537,633 women were screened. Overall AAA prevalence rates were very heterogeneous, ranging from 0.37% to 1.53% pooled prevalence 0.74% (95%CI 0.53 to 1.03). The pooled prevalence increased with both age (1% for women aged over 70 years) and smoking (>1% for ever smokers and >2% in current smokers).

Conclusion: The current population prevalence of screen-detected AAA in women is subject to wide demographic variation. However, in ever smokers and those over 70 years, the prevalence is 1%.

Registration: PROSPERO database of systematic reviews (http://www.crd.york.ac.uk/PROSPERO) CRD42015020444

Pooled prevalence of abdominal aortic aneurysm in women aged at least 60 years: eight studies with screening performed between 2001 and 2012. Values in parentheses are 95 per cent confidence intervals.

<table>
<thead>
<tr>
<th>Study</th>
<th>Estimate (95% CI)</th>
<th>Weight</th>
</tr>
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<tbody>
<tr>
<td>Forsdahl (2009)</td>
<td>1.53 (1.07, 2.13)</td>
<td>12.12</td>
</tr>
<tr>
<td>Ogata (2006)</td>
<td>1.46 (0.94, 2.28)</td>
<td>11.20</td>
</tr>
<tr>
<td>Hupp (2007)</td>
<td>0.94 (0.71, 1.25)</td>
<td>12.78</td>
</tr>
<tr>
<td>Savji (2013)</td>
<td>0.44 (0.43, 0.45)</td>
<td>14.11</td>
</tr>
<tr>
<td>Hupp (unpublished)</td>
<td>0.92 (0.63, 1.32)</td>
<td>12.01</td>
</tr>
<tr>
<td>Svensjo (2013)</td>
<td>0.37 (0.24, 0.35)</td>
<td>10.23</td>
</tr>
<tr>
<td>Palombo (2010)</td>
<td>0.31 (0.28, 0.35)</td>
<td>13.48</td>
</tr>
<tr>
<td>Bulbulia (2013)</td>
<td>0.35 (0.28, 0.35)</td>
<td>15.36</td>
</tr>
<tr>
<td>Pooled Overall (I−squared = 96.26%)</td>
<td>0.74 (0.53, 1.03)</td>
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</tr>
</tbody>
</table>

Figure 1. Pooled prevalence of abdominal aortic aneurysm in women aged at least 60 years: eight studies with screening performed between 2001 and 2012. Values in parentheses are 95 per cent confidence intervals.

References:
1. PRISMA: Transparent reporting of systematic reviews and meta-analyses. Available from: www.prisma-statement.org

DIASTOLIC GROWTH RATE AND FUTURE INDICATION FOR SURGERY CAN BE PREDICTED WITH FINITE ELEMENT ANALYSIS AND SEMI-AUTOMATIC DIAMETER MEASUREMENTS IN SMALL ABDOMINAL AORTIC ANEURYSMS

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Objective: For small abdominal aortic aneurysms (AAA), it is difficult to predict which aneurysms will require surgery and which will remain stable. We aimed to evaluate if semi-automatic diameter measurements and finite element analysis were superior at predicting the four-year progression rate and indication for surgery of AAAs compared to standard diameter measurements.

Methods: Thirty-three small AAAs with a baseline diameter of 40-50 mm were identified. ‘Standard diameters’, measured by radiologists or vascular surgeons, were collected from patient records. The aneurysms were subsequently recreated into digital, three-dimensional (3D) models by semi-automatic segmentation from the CTAs. Maximal diameter orthogonal to the aneurysms’ centerline was automatically measured and finite element analysis, yielding peak wall rupture index (PWRI), was performed. Further, growth rate between two standard diameters was studied in an overlapping group of 39 AAAs that had been measured once more after the initial CTA (baseline diameter of 40-60 mm).

Results: Diameter growth rate displayed a good correlation with baseline semi-automatic diameter (r=0.53, p=0.0006) and PWRI (r=0.44, p=0.0055) but only a trend could be observed for baseline standard diameter (r=0.31, p=0.052). After four years, 20 AAAs had received surgery or had reached indication for surgery, ie standard diameter of 55 mm, and 13 AAAs remained intact with a standard diameter of < 55 mm. Baseline semi-automatic diameter and PWRI could specifically identify aneurysms that would require surgery within four years, n=6 (30%) and n=9 (45%), respectively, whereas the baseline standard diameter could not (n=0, 0%).

Conclusion: Finite element analysis and precise diameter measurements may improve AAA growth rate predictions and allow early aortic repair in selected patients with AAA.
TRANSDIFFERENTIATION OF HUMAN DERMAL FIBROBLASTS TO SMOOTH MUSCLE LIKE CELLS: A NOVEL METHOD TO STUDY THE EFFECT OF MYH11 AND ACTA2 VARIANTS IN THE AORTIC ANEURYSM WALL

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Introduction: Research on the pathogenesis of aortic aneurysms has revealed mutations in genes encoding the smooth muscle cell contractile proteins as key underlying causes. Mutations associated with familial aortic aneurysms have been found in MYH11 (myosin heavy chain 11), ACTA2 (smooth muscle actin alpha 2) and MYLK (myosin light chain kinase) genes, which encode integral proteins of the contractile apparatus.

Experimental Aim/Problem Definition: Currently, SMC can only be obtained by an invasive aortic biopsy. Therefore, the aim of this study is to transdifferentiate skin fibroblasts into SMC-like cells to provide a less invasive diagnostic test to study SMC function and mutations.

Work Summary: Dermal fibroblasts from 7 healthy donors and 7 patients with MYH11 or ACTA2 variants were transdifferentiated into SMC-like cells within 2 weeks by using 5ng/mL TGFβ1 and a scaffold containing collagen and elastin (matriderm). As control, cells were cultured without TGFβ1. SMC-specific markers were analyzed via qPCR, western blot and immunofluorescence. To investigate and classify the pathogenicity of the variants, cDNA sequencing was performed.

Results: The induced SMC-like cells were comparable to primary human aortic SMC in the expression of SMC specific markers on mRNA and protein level (Fig.1): ACTA2 (αSMA), SMTN (smoothelin) and CNN1 (calponin). Importantly, in patients with MYH11 or ACTA2 variants the effect on splicing was demonstrated on the mRNA level in the induced SMC, allowing classification into pathogenic or non-pathogenic variants. Moreover, the pathogenic MYH11 variants showed overexpression of contractile proteins accompanied by defective F-actin cytoskeleton formation if compared to transdifferentiated SMC from the healthy donors.

Conclusions: Direct conversion of human dermal fibroblasts into SMC-like cells is a highly efficient method to investigate the pathogenic effect of variants in genes encoding the proteins of the SMC contractile apparatus. Our findings suggest the role of defective cytoskeleton formation and disturbed contraction of SMC in aortic aneurysm formation.
tiodiol and cut into cubes. Subsequently, cubes were submerged in agarose, glued on an anvil, and cut into slices of 150 μm. Slices were cultured at 37°C Celsius in media supplemented with antibiotics. Viability analysis was performed up to 92 days after harvesting using LIVE/DEAD® Viability/Cytotoxicity Kit. Cell type characterization was achieved by staining for CD45, CD68, α-SMA/smoothelin to identify leukocytes, macrophages and fibroblasts/smooth muscle cells (SMC) respectively. Additionally, tissues were digested using collagenase to study individual cells and analyze cellular populations in live tissues.

Tissue slice analysis showed a stable viability of 40% until 7 days (graph 1) and after improvement of the protocol up to 92 days after harvesting (with outgrowth of new cells). Live cells were mainly seen centrally in the tissue, while dead cells were observed at cutting edges. Live cells were differentiated by qualitative analysis based on cell morphology and specific marker expression. The majority of studied live cells were fibroblasts/SMC. Furthermore, leukocytes and macrophages were observed. These findings were in accordance with the findings in cells of digested tissues.

Vitality and organization of tissue sections of aneurysmal and non-aneurysmal vascular tissue can be preserved until 92 days after harvesting. This study provides a solid base for further experimental research on pathophysiological mechanisms underlying aneurysms and possibly other vascular diseases.

Figure 1. Viability of human aortic tissue slices.

References:

INHIBITION OF PATHOLOGICAL VASCULAR SMOOTH MUSCLE CELL REMODELLING AS A TREATMENT STRATEGY FOR ABDOMINAL AORTIC ANEURYSM
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Introduction: Pathological vascular smooth muscle cell (VSMC) remodelling in abdominal aortic aneurysm (AAA) drives eventual VSMC senescence, loss and luminal dilation. The VSMC have not been a major target for novel AAA treatment approaches. We hypothesise that strategies to reduce this VSMC remodelling response may be beneficial in the context of novel AAA therapeutics and provide evidence for this idea using a novel small-molecule inhibitor of VSMC remodelling in murine models of AAA.

Methods: For the study we used a small-molecule inhibitor of PDGF induced VSMC remodelling delivered to mice via subcutaneous osmotic mini pump. In the first set of experiments, AAA was induced by AngII infusion to ApoE/-/- mice, peri-aortic CaCl2 or peri-aortic elastase application to C57BL6/J mice. Novel treatment was delivered at the time of aneurysm induction. In the second protocol, the novel inhibitor was given only after AAA had formed in the AngII model to investigate AAA progression. The aortic lumen was visualised with 3D in-vivo ultrasound and tissue evaluated by histology and immunohistochemistry.

Results: Histological evidence of pathological VSMC remodelling was apparent in all three murine models investigated. Treatment of animals with the novel inhibitor throughout the experiment reduced VSMC remodelling and aneurysm size. The effect was particularly apparent on aortic lumen area. When the inhibitor was applied to ApoE/-/- mice with established AAA following AngII infusion, no further aortic dilation occurred suggesting effectiveness against AAA progression and translational potential.

Conclusion: Pathological VSMC remodelling is apparent in multiple murine models of AAA. Inhibition of the VSMC remodelling response with a small molecule inhibitor is possible and attenuates AAA progression. Translational efforts to further understand and modulate VSMC remodelling in human AAA should be explored.

CANONICAL TGFSS-SIGNALING IS TRIGGERED BY INFLAMMTION IN HUMAN NON-SYNDROMIC ANEURYSM DISEASE, BUT IS NOT REFLECTED BY INDUCIBLE AAA MOUSE MODELS
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2 Clinical for Visceral, Vascular and Pediatric Surgery, Würzburg, Germany
Introduction: Transforming growth factor β (TGFβ) signaling has been demonstrated to be crucially involved in aneurysm pathogenesis since mutations in its receptors have been revealed to be responsible for multicollateral aneurysm formation in patients with Loeys-Dietz syndrome. Despite TGFβ’s central role in cell signaling, its specific regulation in non-syndromic aneurysm formation is yet of unclear significance.

Material and Methods: We explored a biobank of human AAA and popliteal artery aneurysms to elucidate the function of different components of the TGFβ pathway by immunohistochemistry, gene expression analysis and western blot. Additionally the TGFβ-connectorive tissue derived growth factor (CTGF) axis was analyzed in a new mouse model of inducible juxtarenal acute aneurysm.

Results: Canonical TGFβ signaling with increased activation of phosphorylated SMAD 2/3 was discovered independently of the grade of inflammation or the type of artery. This process was triggered by mononuclear infiltrates in the arterial media. While collagen production increased, other downstream effects like CTGF signaling appeared not elevated. Inducible murine models of AAA mimic an earlier time point of aneurysm development and demonstrate enhanced canonical TGFβ signaling in infrarenal, juxtarenal and thoracic position, as seen in two different models.

Conclusion: Canonical TGFβ signaling is elevated in human aneurysm disease. The TGFβ-CTGF-axis seems to be of lesser importance. In vivo experiments with murine inducible models can only partly reflect these conditions due to the specific role of this pathway during aneurysm development and progression.

PHENOTYPING OF TRANSGENIC PIGS TO DETERMINE THE SUITABILITY OF XENOGRAFTS IN THE TREATMENT OF AORTIC DISEASES

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Abdominal aortic aneurysm and aortoiliac occlusive disease are the two most common vascular diseases in which surgical treatment requires the implantation of aortic prosthesis. The synthetic materials can cause graft infection, a distal potentially fatal complication of surgical treatment. This is connected with the necessity of patient reoperation and the replacement of prosthesis with biological material, such as auto- or allografts. Due to the shortage of multiorgan donors, many patients with infection of the prosthesis cannot be treated successfully. The domestic pig may be the perfect donor of easily accessible blood vessels for transplantation. Under the MEDPIG project a series of „humanized“ pigs were generated by genetic engineering and breeding, to omit species incompatibility.

We focus on the ex vivo studies of biological material harvested from several genetic variation of humanized pigs. Tissue samples are tested to identify modification the least immunogenic to human. We established over 20 primary endothelial aortic cells lines, isolated from thoracic aorta of transgenic pigs and comparable number of cell lines from control, wild type animals. In vitro studies include several cytotoxicity assays to evaluate response to the human complement and other components of human immune system. Biomechanical properties studies focus on comparative analysis of a transgenic pig and human vessels, in order to identify anatomical resemblance and ability to function in different hemodynamic conditions. Biomechanical, histological and molecular evaluation of arteries were performed before and after cryopreservation. The level of inbreeding of pigs was also evaluated genetically. In a pilot study functionality of the aortic grafts was tested in vivo through cross transplants.

Our studies demonstrate the application of transgenic pig tissue in modeling and therapy of human aortic diseases. Funded by the NCRD (grant n. INNOMED/I/17 /NCBR/2014) from the Innovative Economy Operational Programme funds, in the framework of the ERDF.

MANAGEMENT OF VISCERAL ARTERY ANEURYSMS: A 20-YEAR SINGLE CENTRE EXPERIENCE

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1 Division of Cardiac Surgery University of Palermo, Palermo, Italy
2 Division Of Vascular Surgery Ospedale Civico, Palermo, Italy

Visceral artery aneurysms (VAA), including renal and splanchic lesions, are rare (0,01% up to 2% in general population) but life-threatening disease. The natural history is unknown but rupture occurs frequently particularly when vessel dimension exceeds 2 cm that, to date, represent the threshold to intervene in asymptomatic patient. Unfortunately, when rupture occurs, mortality rate is consistent ranging from 21% when the complication is located at the hepatic artery site up to 100% when is located at the celiac artery site. Object of this study is to review our experience with VAA treatment. Between January 1995 and August 2015, 28 VAA were treated, (21 males, 7 females) with mean age of 56 years (range 25-87). Intraoperative data included surgical approach, type of reconstruction and associated procedure. N=19 patients were asymptomatic, n= 6 symptomatic and n=3 presented on emergency due to rupture. The most common locations were renal artery (n=10), splenic artery (n=8), hepatic artery (n=4), celiac trunk (n=3). Four patients underwent endovascular treatment (1 on emergency), 23 patients underwent open surgery (2 on emergency) and 1 patient was operated on in Minimally Invasive approach. Overall early mortality was 7.14% (2 patients in surgical group operated on emergency due to the rupture of renal aneurysm). Perioperative morbidity was 3.5% (1 patient operated on splenectomy). Late mortality was 25% (1 patient in endovascular group). We believe that surgical VAA treatment is a safe and effective procedure irrespective if it will be done open or percutaneous, mortality and morbidity are low outweighing dismal expectancy of life in untreated patients.

References:

AORTIC SIZE INDEX COULD IMPROVE SURVEILLANCE OF WOMEN AND MEN WITH ABDOMINAL AORTIC ANEURYSM

5th International Meeting on Aortic Diseases
Rebecka Hultgren, Hedvig Lofdahl, Joy Roy
Dep Vascular Surgery A2:01, Karolinska University Hospital and Karolinska Institutet, Stockholm, Sweden

Background: Abdominal aortic aneurysm (AAA) predominantly affects men, however the risk of rupture is higher in women resulting in a poorer outcome. Recent studies have shown that the correlation between body surface area and aortic diameter (aortic size index) could be a better predictor than aortic diameter for rupture in women, however there is a lack of knowledge within the field. This study aims at investigating the correlation between body surface area and aneurysm diameter in women and men with non-ruptured AAA.

Methods: A retrospective population based cohort study. Patients with AAA followed at the Karolinska University Hospital in Stockholm, Sweden between January 2012 and December 2014, with at least two imaging examinations performed were eligible for inclusion, 120 women and 120 men were included in the study. Data was collected through review of medical records. Means were compared using independent t-test and Mann Whitney test for continues variables. Pearson’s chi-square and Fischer’s exact test was used for categorical variables.

Results: Women had a higher mean age, but did not differ from men regarding comorbidities. The aortic diameter was similar between women and men (41.5mm versus 43.0mm, p=0.21). Women had a smaller body size area and a larger aortic size index (2.4 versus 2.1, p<0.05). Older patients had a higher aortic size index compared to younger patients. The median growth rate for the cohort was 2.2 mm per year. No difference in growth rate was shown between women and men. Larger aneurysms (median 45.0 mm) had a higher growth rate compared to smaller aneurysms (2.7 mm versus 1.6 mm, p<0.05). No difference in growth rate was shown between women and men. Larger aneurysms (median 45.0 mm) had a higher growth rate compared to smaller aneurysms (2.7 mm versus 1.6 mm, p<0.05).

Conclusion: The results supports previous reports showing that aortic size index, combined with aortic diameter could be a useful tool for improved surveillance, especially in women and older patients with small AAA. Further prospective analysis must be performed in order to define the predictive value of ASI for rupture risk.

Rebecka Hultgren, Joy Roy
Department of Vascular Surgery, Karolinska institutet and Karolinska University Hospital, Stockholm, Sweden

Introduction: Ruptured abdominal aortic aneurysm (rAAA) is a life threatening condition with mortality around 70-90 %. Diagnostics is still depending on identification of a classic diagnostic triad of pain, hypotension and pulsatile mass. The literature is scarce regarding the true occurrence of the classic triad of symptoms in patients with RAAA [1-3]. Primary Aim: To investigate how many of admitted patients with rAAA that had the classic triad. Secondary Aim: To investigate whether a correlation between number of triad-symptoms and time to treatment and outcome can be found.

Material and Methods: Records of 283 patients with ICD code 171.3 (rAAA) diagnosed between 2009-2013 in the Stockholm County has been identified, for this analysis only patients subjected to the Karolinska University Hospital in Stockholm were reviewed retrospectively, 52 were included.

Results: The classic triad was present in 13 (25 %) of the patients with rAAA. Back or abdominal pain was present in 49 (94 %) and hypotension in 43 (83 %). Pulsating mass was found in 14 (27 %), but only in one (4 %) of the overweight patients (p=0.004). Patients with 3 out of 3 symptoms of the classic triad did not have shorter time to treatment (p=0.72) or lower 30 day mortality (p=0.41) compared to patients with less than 3 symptoms.

Conclusions: Only one fourth of the patients with RAAA have the classic triad of symptoms, which correlates with the few reports within the field. The diagnostic value of the classic triad can be discussed in the present form, however adding ultrasound for evaluation of aortic diameter would probably increase the validity.

References:

SURVIVAL DISPARITY FOLLOWING AAA REPAIR HIGHLIGHTS INEQUALITY IN SOCIOECONOMIC STATUS
Manar Khashram1, Suzanne Pitama2, Jonathan Williman3, Greg Jones4, Justin Roake5
1 Department of Surgery, University of Otago, Christchurch, New Zealand
2 Maori/Indigenous Health Institute University of Otago, Christchurch, New Zealand
3 Department of Population Health, University of Otago, Christchurch, New Zealand
4 Department of Surgical Sciences, Dunedin School of Medicine, University of Otago, Dunedin, New Zealand
5 Department of Vascular Endovascular and Transplant Surgery Christchurch Hospital, Christchurch, New Zealand

Background: Determinants of survival following abdominal aortic aneurysm (AAA) repair are well documented and are predominantly co-morbidity driven. Other patient factors such as socioeconomic status (SES) have also been suggest-
ed as factors influencing mortality. The aim of this study was to report if deprivation influences survival after AAA repair.

**Methods:** Consecutive patients undergoing AAA repair between July 2000 and December 2013 were identified from the national database. SES was defined as recorded on health records. A score of 1 indicates those least deprived and 10 representing the most deprived. Multivariate logistic regression model was used along with confounders included as independent variables to calculate odds ratios (OR) and survival analysis using Cox proportional model to report adjusted hazard ratios (HR).

**Results:** 5824 patients with a mean age (standard deviation, SD) of 74 (7.7) years and 78.7% males were included. The mean (SD) deprivation score was 6.1 (2.7). Deprivation categories 7-8 and 9-10 were associated with OR 1.54 (95%CI: 1.07-2.23) and 1.61 (95%CI: 1.10-2.36) respectively. The median survival follow up period was 5 years and after adjusting for confounders, deprivation categories 9-10 was associated with a higher risk of death HR 1.25 (95%CI: 1.10-1.42).

**Conclusions:** Patients with a lower SES have an independent risk of reduced short and long-term survival. Identifying deprivation status may represent a mechanism through which cardiovascular risk modification is initiated and maintained during follow-up. This may help reduce outcome disparities for people with lower SES and highlights the need for more emphasis on targeting at-risk groups.
ic and hormonal changes in vascular structure increase wall tension and intimal shear forces, on an aortic media more susceptible to injury, making pregnancy an independent risk factor for dissection [3]. Advanced maternal age and diffusion of assisted reproductive technology to overcome age related infertility increase risk of pregnancy related hypertension, consequently dissection [4].

**Work Summary:** We reviewed PubMed database to identify aortic dissection cases in which pregnancy was the only reported risk factor, excluding fibrillopathies, Turner syndrome or bicuspid aortic valve.

**Results:** 41 cases of aortic dissection without known risk factors were reported from 1995 to 2015. Of these, 63% occurred during pregnancy (56.1% third trimester); 36.5% in postpartum. Hypertension was the mostly reported comorbidity (36.7%), including chronic and gestational hypertension, pre-eclampsia and eclampsia, followed by obesity and smoking. According to Stanford classification, 28 were type A and 17 type B, in 9 cases lesion consisted in aneurysm on dissection. Organ ischemia complicated dissection in 7 cases. Thoracic pain (73.2%) was main symptom at diagnoses, followed by neurological impairment, back and abdominal pain, dyspnea, nausea. Differential diagnosis was challenging in 14 cases (34.2%), pulmonary embolism being most frequently misdiagnosed. In three cases diagnosis was autopsic. Treatment consisted in open surgery (53.6%), endovascular (19.5%), hybrid approach (12.2%). Of five cases managed conservatively, 4 required surgery. Time from onset to treatment ranged from <24 h (63.4%) up to 1 week. As for fetal management, emergency cesarean section was performed in 41.5% of cases, 1 surgery during pregnancy and 1 therapeutic abortion were reported. Maternal outcome was successful in 73.2%, perioperative death being 17.1%. Fetal outcome was favorable in 26 cases, 3 autopsic findings, 2 stillbirths, 1 growth restriction recorded on follow up. **Conclusions:** Aortic dissection can occur in normal pregnancy and postpartum. High index of suspicion is necessary, and it must be included in differential diagnosis in acute setting, because of high maternal-fetal mortality of this condition.

**Table 1: Aortic dissection in pregnancy. Clinical aspects, management and outcome of 41 cases reported in literature.**

<table>
<thead>
<tr>
<th>Timing</th>
<th>N</th>
<th>%</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy</td>
<td>26</td>
<td>63.4%</td>
<td>1st semester</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2nd semester</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3rd semester</td>
<td>23</td>
</tr>
<tr>
<td>Postpartum</td>
<td>15</td>
<td>36.6%</td>
<td>1st week</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2nd week</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3rd week</td>
<td>1</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>N</th>
<th>%</th>
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</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obesity</td>
<td>3</td>
<td>7.3%</td>
</tr>
<tr>
<td>Smoke</td>
<td>2</td>
<td>4.9%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Dislipidemia</td>
<td>0</td>
<td>0%</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Dissection type</th>
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<tbody>
<tr>
<td>Type a</td>
<td>24</td>
<td>58.5%</td>
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<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type b</td>
<td>17</td>
<td>41.5%</td>
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<thead>
<tr>
<th>Clinical aspects</th>
<th>N</th>
<th>%</th>
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</thead>
<tbody>
<tr>
<td>Neurologic</td>
<td>8</td>
<td>19.4%</td>
</tr>
<tr>
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<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Back pain</td>
<td>14</td>
<td>34.1%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thoracic pain</td>
<td>26</td>
<td>63.3%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyspnea</td>
<td>13</td>
<td>31.7%</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>7</td>
<td>17.1%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>7</td>
<td>17.1%</td>
</tr>
</tbody>
</table>

**Figure 1.** Physiopathology of aortic dissection in pregnancy.
Table 1. (cont.)

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organ ischemia</td>
<td>7</td>
<td>17</td>
</tr>
<tr>
<td>cardiac (IMA)</td>
<td>3</td>
<td>7.3%</td>
</tr>
<tr>
<td>mesenteric</td>
<td>2</td>
<td>4.9%</td>
</tr>
<tr>
<td>stroke</td>
<td>1</td>
<td>2.4%</td>
</tr>
<tr>
<td>multiple</td>
<td>1</td>
<td>2.4%</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>4</td>
<td>9.8%</td>
</tr>
<tr>
<td>eclampsia</td>
<td>1</td>
<td>2.4%</td>
</tr>
<tr>
<td>renal stones</td>
<td>1</td>
<td>2.4%</td>
</tr>
<tr>
<td>gallstones</td>
<td>1</td>
<td>2.4%</td>
</tr>
<tr>
<td>cesarean pain</td>
<td>1</td>
<td>2.4%</td>
</tr>
<tr>
<td>embolic stroke</td>
<td>1</td>
<td>2.4%</td>
</tr>
<tr>
<td>HELPP syndrome</td>
<td>1</td>
<td>2.4%</td>
</tr>
<tr>
<td>IMA</td>
<td>1</td>
<td>2.4%</td>
</tr>
</tbody>
</table>

Timing of management

Autopsy finding                  | 3 | 7.3% |
Treatment < 24 h                 | 26 | 63.4% |
> 24H/no treatment              | 15 | 36.6% | 24-48 h       | 4 | 9.8% |
> 48 < 1 week                    | 4 | 9.8% |
> 1 week                         | 1 | 2.4% |
planned treatment               | 3 | 7.3% |

Management

Pharmacological                  | 5 | 12.1% | successful     | 1 | 2.4% |
unsuccessful                    | 4 | 9.7% |
Open surgery                     | 22 | 53.6% | primary        | 19 | 46.3% |
after conservative failure      | 3 | 7.3% |
Endovascular surgery            | 8 | 19.5% | primary        | 7 | 17.1% |
after conservative failure       | 1 | 2.4% |
Hybrid surgery                   | 5 | 12.2% |

Maternal outcome

Well after treatment             | 30 | 73.2% |
Mortality                        | 11 | 26.8% | sudden death    | 4 | 9.8% |
preoperative                     | 1 | 2.4% |
intraoperative                   | 2 | 4.9% |
postoperative                    | 4 | 9.8% |

Fetal management

Therapeutic abortion             | 1 | 2.4% |
Surgery in pregnancy             | 1 | 2.4% |
Emergency cesarean preop         | 17 | 41.5% |
Fetal outcome

Alive                            | 35 | 85.3% | born before event | 8 | 19.5% |
well on follow up                | 26 | 63.4% |
growth restriction               | 1 | 2.4% |
Mortality                        | 6 | 14.6% | therapeutic abortion | 1 | 2.4% |
stillbirth                       | 2 | 4.9% |
autopsy finding                  | 3 | 7.3% |

References:


SMAD2 MUTATIONS CAUSE ARTERIAL ANEURYSMS AND DISSECTIONS; A NEW PLAYER IN AN OLD STORY

Dimitra Micha1, Dong-chuan Guo1, Natalija Bogunovic1,2, Yvonne Hilhorst-Hofstee2, Fop van Kooten1, Dian Atmaj1,4, Eline Overwater2,7,7, Ferdy Cayami1,4, Ellen Regalado2, René van Uffelen2, Hanka Venselaar2, Sultana Faradze2, Gerrit Vriend2, Marjan Weiss2,3, Erik Sierstensmans3, Alessandra Maugeri2, Dianna Milewicz2, Kak Khee Yeung2, Fleur van Dijk1,3, Gerard Pals1

1 Department of Clinical Genetics, Center for Connective Tissue Research, VU University Medical Center, Amsterdam, The Netherlands
INCIDENCE, TREATMENT AND LONG-TERM CLINICAL OUTCOME IN PATIENTS WITH AORTIC GRAFT INFECTIONS

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Department of Vascular Surgery, Karolinska University Hospital, Stockholm, Sweden
Section of Vascular Surgery, Department of Surgery, Södersjukhuset; Institution of Clinical Science and Education, Karolinska Institutet, Stockholm, Sweden

Introduction: Aortic graft infections are relatively rare, with an incidence of 0.6-3%. High mortality rates continue to be a major concern in this patient category. The primary aim of this study was to identify the incidence of postoperative aortic graft infection and assess the long-term clinical outcome of different treatment modalities in a population-based cohort.

Methods: Using the in-hospital electronic patient registry and the Swedish Vascular Registry (Swedvasc), 2026 patients treated for aortic aneurysms and aortoiliac occlusive disease in Stockholm county region (pop. 2.2 million) during the period 2005-2015 were identified. Review of the patients’ records provided information on type of infection, treatment and outcome.

Results: 219 suspected cases of infection were reviewed, yielding 29 patients (26 males, 3 females) with aortic graft infections. The mean age was 68.9 ± 10.7 years. Mean follow-up time was 81.4 ± 66.3 months from primary surgery (EVAR 51.3 ± 44.7; open repair 98.6 ± 71.8). The overall incidence of graft infection was 1.4% (29/2026). Ten patients had emergency surgery at the time of primary intervention.
Mikhail Generalov, Dmitry Maystrenko, Igor Panov, Anna

The incidence of graft infection for both non-emergent and emergent cases was 1.4%. In the non-emergent group (n = 19), 11 patients were treated conservatively, seven patients underwent surgical reconstruction and there was one missing case. In the emergent group (n = 10), seven patients were treated conservatively and three underwent surgical reconstruction. There were five deaths due to graft infection in the conservatively treated group but none in the surgically treated group. All-cause mortality for the non-emergent group was 53% and for the emergent group 80%. Mortality rates based on treatment method were 78% for conservatively treated patients and 40% for surgically treated patients. In the conservatively treated group 5.6% were free of infection compared to 30% in the surgically treated group.

Conclusion: There were no significant differences between the emergent and non-emergent groups in terms of incidence of graft infection or time to infection. Surgically treated patients had better rates of eradication of infection and survival than the conservatively treated patients.

References:

ABDOMINAL AND ILIAC ANEURYSMS REPAIR USING VARIOUS IMPLANTATION TECHNIQUES OF STENT-GRRAFTS MODULES: A FIRST EXPERIENCE IN RUSSIA
Mikhail Generalov, Dmitry Maystrenko, Igor Panov, Anna Oleschuk, Alexander Ivanov
Russian Research Center of Radiology and Surgical Technologies, Saint Petersburg, Russia

Target: To evaluate the feasibility and midterm results of a new (for the Russian market) stent-graft for suprarenal and infrarenal and iliac endovascular aneurysm repair (EVAR). METHODS: Twenty six patients (21 men, 5 women; mean age 71 years, range 59-87) with suprarenal (n=2) and infrarenal (n=21) abdominal aortic aneurysms (AAA) and iliac (n=3) aneurysms (IAA) suitable for EVAR were treated with various modular stent-grafts of JOTEC company (Germany). The maximum AAA diameter was 56 mm (48-81), mean diameter of IAA was 44 mm (38-52). The complex vascular anatomy (hostile neck and tortuous iliac artery) were in 11 (42%) cases. Most of the patients (79%) were ASA grade 3 or higher. All procedures were primary implantation.

Results: All stent-grafts were implanted at the intended position; no conversions to open surgery were necessary and no type I endoleaks were noted. Two constructs were made using the Chimney technique. Abdominal bifurcation stent-grafts have been established in 21 patients. Sandwich technique has been applied in three cases of iliac aneurysms. There was no 30-day mortality. In the mean 12-month follow-up (range 8-17), no stent fractures, migrations, or secondary endoleaks were noted. The diameter of the aneurysm was reduced in 12 (46%) and remained unchanged in the 14 (54%) cases. One patient required open surgery at 3 months for thrombotic occlusion of the stent-graft branch. Two octogenarian patients died during the observation period.

Conclusion: Modular stent-grafts of JOTEC company appear safe and effective in this initial mid-term clinical experience. This devises are especially suitable for complex aneurysm anatomy, such as hostile aneurysm necks or tortuous and dilated iliac arteries.

SEX DIFFERENCES IN OUTCOMES AFTER AAA REPAIR IN THE UNITED KINGDOM
David Sidloff, Athanasios Saratzis, Michael Sweeting, SWAN Collaborators, Matthew Bown
1 University of Leicester, Leicester, United Kingdom
2 University of Cambridge, Cambridge, United Kingdom
3 United Kingdom

Introduction: AAA screening in men is cost-effective and reduces mortality. There is no evidence that screening women is effective. However, women are four times more likely to rupture and account for 33.6% of all ruptured AAA deaths, therefore may be disadvantaged by current policies.

Problem Definition: Peri-operative risk is critical in determining the effectiveness of screening and contemporaneous estimates of these risks are lacking. We therefore aimed to compare outcomes for men and women undergoing AAA in the UK.

Work Summary: Anonymised individual data from the UK National Vascular Registry for patients who had undergone AAA repair 2010-2014 were analysed. Relevant covariates were extracted for further analysis by sex. Analyses were stratified by 5-year age bands and the primary outcome measure was in hospital mortality by gender, indication and operation. Multi-variate regression was performed to adjust for co-morbidities.

Results: 33,069 patients were included. For elective open surgical AAA repair, in hospital mortality was 4.0% in men and 6.9% in women (OR 1.77, 95%CI 1.33-2.35, P=0.0001) whilst for EVAR in hospital mortality was 0.7% in men and 1.7% in women (OR 2.51, 95%CI 1.57-4.03, P=0.0001). No differences were seen in mortality after ruptured AAA repair. Elective morbidity was higher in women who were more likely to develop cardiac complications (4.3% versus 5.7%, OR 1.34 95%CI 1.09-1.68, P=0.004) and renal failure (7.0% versus 9.3%, OR 1.37, 95%CI 1.07-1.75, P=0.007) after OSR and haemorrhage (1.0% versus 1.7%, OR 1.70, 95%CI 1.07-2.71, P=0.02) and cerebral complications (0.2% versus 0.5%, OR 2.53, 95%CI 1.01-6.36, P=0.05) after EVAR. Female gender remains a significant risk factor for death (P=0.028) after adjustment.

Conclusion: Women have worse outcomes after elective AAA repair. This highlights the need for sex specific pre, peri and post-operative strategies to reduce the differences seen and may erode any benefit of screening for AAA in women.

EXPLANTATION OF A FENESTRATED ABDOMINAL ENDOGRaFT WITH AUTOLOGEOUS VENous RECONSTRUCTION FOR INFECTION
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Case Report: A 72-year old man underwent a three-vessel EVAR for an asymptomatic thoraco-abdominal aneurysm of 64 mm. The
Aortic valve: a process beyond normal cardiovascular ageing

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Introduction: Patients with a bicuspid aortic valve (BAV) carry an increased risk for aortic dilation as compared to patients with a tricuspid aortic valve (TAV). During cardiovascular development the second heart field (SHF) and neural crest progenitor cells (NCC) guide and contribute to numerous processes such as semilunar valve formation and differentiation of vascular smooth muscle cells (VSMCs). It is therefore plausible that an altered NCC and/or SHF contribution not only can lead to the development of a BAV but is also associated with a structurally different aortic wall leading to pathology.

Methods: Ascending aorta biopsies of BAV (n=36) and TAV (n=23) both with and without dilation were investigated with classical stainings (MOVAT pentachrome, resorcin fuchsin and hematoxylin eosin). Differentiating and mature VSMCs, lamin A/C, and progerin were studied by immunohistochemistry and with western blot. A pathology score was developed based on seven histopathological criteria: mucoid extracellular matrix accumulation, inflammation, loss of smooth muscle cell nuclei, smooth muscle cell differentiation, intimal thickness, elastic fiber degradation and atherosclerosis.

Results: We found a significant difference in the structure and maturation of the aortic wall in BAV, persisting in the dilated aortic wall, presenting with a thinner intima, lower expression of several VSMC markers (p<0.05) and lowered lamin A/C expression in BAV (p<0.05) as compared to TAV. The dilated TAVs showed significantly increased progerin expression (p<0.05) as well as increased periaortic inflammation (p<0.01).

Conclusion: Our findings indicate that the structure of the non-dilated and dilated aortic wall in BAV and TAV is intrinsically different, with the latter having more aspects of ageing. In BAV there is a VSMC differentiation defect possibly linked to an altered NCC and/or SHF contribution to the aortic wall. These findings are clinically relevant, indicating the requirement for different treatment modalities for aortic dilation in TAV and BAV patients.

The role of hemodynamics and shear stress on the ascending aortic wall in patients with a bicuspid aortic valve

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Background: A bicuspid aortic valve (BAV) is the most common congenital cardiac malformation and is associated with ascending aortic dilation in 60-80%. Structural differences have earlier been noted between patients with BAV and a tricuspid aortic valve (TAV). The purpose of this study was to analyze the correlation between hemodynamics and shear stress on aortopathy in BAV patients.

Methods: BAV (n=36) (mean age 55.8 ± 8.7 years, 72% male) and tricuspid aortic valve (TAV) (n=17) (mean age 60±9 years, 82% male) patients undergoing aortic valve replacement underwent pre-operative cardiac phase-contrast cine magnetic resonance imaging (4D flow MRI) assessment to detect the area of maximal flow-induced stress in the proximal aorta. Based on these MRI data paired aortic wall samples (i.e. area of maximal shear stress (jet sample) and the opposite aortic wall (control sample)) were collected during surgery. The jet and control sample were graded by histopathology in the tunica intima, media and adventitia for the pathology score features: mucoid extracellular deposition, inflammation, elastic fiber fragmentation, smooth muscle cell differentiation, loss of smooth muscle cell nuclei, intimal thickness and atherosclerosis.

Results: Earlier described differences in the pathology score between all BAV and TAV patients were confirmed in this study [1]. Comparing the jet and control samples in both BAV and TAV, regions of maximal shear stress did not show any difference in the pathology score in the tunica media and adventitia even if corrected for aortic stenosis/ regurgitation, aortic dilation and raphe position. At the jet side all BAV and TAV patients, however, showed changes in endothelial phenotype from squamous to cuboid, an increase of the subendothelial elastic lamellae and intimal elastic lamellae and increased intimal extracellular matrix deposition.

Discussion: Increased wall shear stress leads to intimal pathology with observed activation of the endothelium in both BAV and TAV patients.

References:
DEEP HYPOTHERMIA WITH RETROGRADE CEREBRAL PERFUSION – AS METHOD OF BRAIN PROTECTIONS IN ASCENDING AORTA AND ARCH ANEURYSMS SURGERY

Vitalii Kravchenko, Ivan Kravchenko, Bogdan Cherpak, Valerii Ltvinenko, Olena Rybakova, Yurii Tarasenko, Vasylly Vitalii Kravchenko, Ivan Kravchenko, Bogdan Cherpak, Oleksandr Tretyak, Vasyly Lazorishinets

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Introduction: Antegrade and retrograde perfusion for cerebral protection are controversial approaches in the surgery of ascending aorta and arch. In some cases retrograde cerebral perfusion (RCP) is preferable because of technical simplicity and it allows to reach a good result.

AIM: Selection of efficient technology for RCP on the basis of clinical experience, instrumental and laboratory researches.

Materials and Methods: 253 patients with ascending aortic and arch aneurysms were operated on during 1994 - 2015 (205 (81.0%) males, 48 (19.0%) females), age ranged 27 – 79 years, mean 53,4±8,2; acute (subacute) dissection took place in 224 (88,5%), chronic – in 12 (4,8%), without dissection – 17 (6,7%) pts. The main reason of aneurysms forming was: arterial hypertension, atherosclerosis – in 151 (59,7%); Marfan syndrome – 32 (12,6%); bicuspid aortic valve disease – 26 (10,3%); cystodemionecrosis – 22 (8,7%); lues – 12 (4,7%); Takajasu arteritis – 3 (1,2%); falling from height – 2 (0,8%); unknown – 5 (2,0%).

Operations’ were fulfilled with heart-lung bypass, deep hypothermia and RCP through superior vena cava (SVC). Femoral artery was utilized for arterial cannulation. The following methods were used for correction: supracoronary grafting of ascending aorta with hemiarch(arch) – 179(4) (70,8%); Bentall’s operation with hemiarch (arch) – 56(4) (22,1%); isolated arch grafting – 9 (3,5%); Wheat operation with arch grafting – 5 (2,0%); aortic arch plastic – 4 (1,6%).

Results: Group I (1994-2001) – 25 operations with deep hypothermia (16-18°C), perfusion blood flow – 500-750 ml/min/m², pressure in SVC – 15-25 mmHg. Mortality – 7 (28%) pts., in 2 cases the cerebral complications were the cause of death. Group II – 63 operations fulfilled in 2002-2007 yy., with deep hypothermia (12,5-14°C), blood flow rate – 250-500 ml/min/m², pressure in SVC – 10-12 mmHg. Mortality – 11 (17,4%) pts. Pulmonary complications were in 5 cases, 3 (4,8%) of them died. Lethal brain injury were 1 pts (1,6%). Group III – 125 operations fulfilled in 2008-2015 yy., with deep hypothermia (18-20°C), blood flow rate – 250-500 ml/min/m², pressure in SVC – 10-12 mmHg. Perfusion through femoral artery during the RCP stage was maintained permanently in group II and III. 30-day mortality – 9 (7,2%) pts. Pulmonary complications was lethal in 1 (0,8%) patient and brain lesion -1 (0,8%) pts. Overall 30-day mortality composed 10,7%. Better clinical results in Group III were confirmed by analysis of arterial and venous blood, thermography, EEG and MRI of the brain.

Conclusion: RCP with deep hypothermia (18-20°C), pressure in SVC – 10-12 mmHg, blood flow rate – 250-500 ml/min/m² with continually perfusion through femoral artery is safe method of brain protection during ascending aortic and arch correction.

ANEURYSM AT THE SITE OF REPAIR OF COARCTATION OF AORTA: FREQUENCY, METHODS OF TREATMENT, RESULTS

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5th International Meeting on Aortic Diseases

Meeting Abstracts
Results: The main findings from this study are that only 20% of patients in surveillance proceeded to elective surgical repair. Patient factors did not predict rupture, which occurred in <4% of patients, of whom 41% had a last recorded MAPD <5mm. Those with MAPD growth >4.6mm/year were more likely to rupture, although only 37% of ruptures proceeded to surgery. Most patients who die in surveillance do so from non-AAA related causes, most commonly malignancy. 

Conclusions: Significant numbers of patients are kept under AAA surveillance inappropriately and there is room for significant service improvement. Specifically, it is important not commence surveillance in patients who are very unlikely to ever grow to a point where AAA surgery would be contemplated on grounds or age and/or co-morbidity. Similarly, patients need to be discharged from surveillance when this likelihood becomes apparent.

OVERVIEW ABOUT THE VALUE OF FUNCTIONAL IMAGING IN THE MANAGEMENT OF AORTITIS

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Background: Aortitis is defined as an abnormal inflammatory condition of infectious or non infectious origin involving the aortic wall. Aortitis may be related to multiple causes with variable prognoses. Because of the nonspecific clinical presentation, aortitis is often overlooked and patients frequently undergo multiple tests and imaging to reach the final diagnosis. However, it is important to establish an early diagnosis as soon as possible. Indeed, this inflammatory process may deteriorate the aortic wall, resulting in potentially life-threatening vascular complications. Compared to conventional imaging tools that provide anatomical and morphological information, Positron Emission Tomography/Computed tomography (PET/CT) provides important additional information.

Methods and Results: During a 4-year period, 428 consecutive patients referred to our cardiovascular surgery department for aortic diseases underwent FDG PET/CT examinations. Among these, 19 (4.4%) patients with suspected to have aortitis. All of them had an initial positive FDG PET/CT uptake occurring in the aorta and major branches as evaluated by visual analysis of images and assessed with the final diagnosis of aortitis. During follow up, after surgery and/or starting immunosuppressive treatment, each patient undergoes PET/CT which was compared with the initial evaluation. In all cases, normalisation of FDG uptake was correlated with clinical improvement.

Conclusions: Although relatively rare, major anomalies of the renal veins and perirenal vena cava should be borne in mind when operating on the abdominal aorta. Retroaortic left renal vein is a malformation in which the left renal vein courses dorsal to the abdominal aorta. In patients with abdominal aortic aneurysm, an aorto-left renal vein fistula can form if the left renal vein is sandwiched between the aneurysm wall and lumbar vertebrae. A caution is required to control bleeding from this type of fistula when an incision is made in the aortic aneurysm. In conclusion, the possibility must be entertained that the aorto-left renal vein fistula in abdominal aortic aneurysms often correlate to the retro-aortic left renal vein. This clinical condition can cause severe renal dysfunction, in spite of which an enhanced contrasted CT scan would be extremely informative preoperatively.

ADVENTITIAL ADIPOGENIC DEGENERATION: AN UNIDENTIFIED CONTRIBUTOR TO AORTIC WALL WEAKENING IN THE ABDOMINAL AORTIC ANEURYSM.


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Objectives: To determine additional pathophysiological mechanisms driving AAA growth.

Background Data: The processes underlying abdominal aortic aneurysm (AAA) growth and ultimate rupture are complex and poorly understood. AAA is accepted as an inflammatory response with an accompanying proteolytic imbalance, however clinical intervention studies consistently fail to show a benefit from interference with these processes. There are striking associations between AAA and popliteal artery aneurysms (PAA); yet while AAAs will eventually rupture, PAA’s have a low propensity for rupture. We reasoned differences between AAA, PAA and normal aorta’s provide critical clues towards other processes involved in critical debilitation of AAAs.

Methods: Tissue was harvested during elective open aneurysm repair or kidney transplantation for control aortas. Tissue was handled correctly and used for qPCR, microarray, IHC and in vitro studies.

Results: Histological evaluation of AAA, PAA and control aorta showed不影响eurysm rupture. The literature series of ALRVF, updated here to about 30 reported cases, demonstrates that patients with ALRVF present with a unique clinical syndrome characterized by abdominal or left flank pain (84%), a pulsatile abdominal mass (63%), abdominal bruit or murmur (63%), hematuria (100%), and nonfunction of the left kidney on functional imaging studies (100% of patients studied).

Matherial and Method: We report the case of a patient who was transferred to our facility after a CT scan obtained at a local hospital revealed a leaking abdominal aortic aneurysm. Review of the scan showed an aorto-left renal vein fistula. Knowing this fistula was present, made the operative repair of the aneurysm and control of the fistula much more straightforward than might otherwise have been the case. Because of the critical condition and evident clinical signs of ruptured AAA, the patient was operated on immediately without any other diagnostic procedure. Transperitoneal approach was used. Intraoperative findings were consistent with the rupture of the frontal aneysmal wall into retroperitoneal space. The operation consisted of the closure of the defect in the retroaortic left renal vein and the repair of the aneurysm. The aneurysm was replaced with impregnated tubular Dacron graft 16 mm.

Results: The postoperative recovery was successful. The patient survived the necessary surgical correction and was followed-up for 18 months, and there were no signs of cardiac or renal failure and arterio-venous insufficiency of legs.

Conclusions: Although relatively rare, major anomalies of the renal veins and perirenal vena cava should be borne in mind when operating on the abdominal aorta. Retroaortic left renal vein is a malformation in which the left renal vein courses dorsal to the abdominal aorta. In patients with abdominal aortic aneurysm, an aorto-left renal vein fistula can form if the left renal vein is sandwiched between the aneurysm wall and lumbar vertebrae. A caution is required to control bleeding from this type of fistula when an incision is made in the aortic aneurysm. In conclusion, the possibility must be entertained that the aorto-left renal vein fistula in abdominal aortic aneurysms often correlate to the retro-aortic left renal vein. This clinical condition can cause severe renal dysfunction, in spite of which an enhanced contrasted CT scan would be extremely informative preoperatively.
extensive fibrous changes in AAA and PAA and identified presence of large adventitial adipocyte aggregates as a unique and consistent feature of AAA (P < 0.01). The combination of fibrosis and adipogenic degeneration characterize AAA as dystrophic disorder. Adipogenic differentiation is controlled by transcription factors from C/EBP family, KLF5 and PPARy. Immunohistochemistry revealed abundant expression of these factors in AAA disease indicating the transcriptional machinery required for adipogenic differentiation is present. qPCR data confirms upregulation of KLF-5 (P < 0.05) and PPARy (P < 0.05), two factors crucial in the final stages of adipogenic differentiation. Furthermore, microarray analysis between ruptured and stable AAA’s reveals upregulation of both adipogenesis (P < 0.001) and PPAR (P = 0.002) pathways. Adipogenic potential of AAA and control adventitial cells were underwent adipogenic differentiation in vitro showing the capability of normal cells adapt an adipogenic phenotype. AAA cells have a higher propensity to do so (P < 0.05).

**Conclusions:** Systemic evaluation of AAA and PAA tissues shows adventitial fatty degeneration in the context of dystrophy as an additional pathophysiologic mechanism. These results should be considered in the light of failing pharmaceutical therapies and provide new avenues for pharmaceutical AAA stabilization.

**PET-TC utility to assess the abdominal aortic aneurysm growth and its relationship with changes in energetic metabolism**

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**Introduction:** PET-CT utility to assess AAA growth remains controversial. Factors involved in the increased metabolic activity that leads to its inflammatory activity remain unknown.

**Experimental aim:** to check the 18-FDG uptake by PET-CT in AAA, evaluate its correlation with diameter and growth and determine differences in those processes involved in the energetic metabolism

**Work Summary:** The 18-FDG PET-CT was performed in 20 patients with AAA before elective open surgery. A SUVmax > 2.5 was considered as increased 18F-FDG uptake. The aneurysm wall samples collected during surgery (in case of increased uptake, two sample were collected, one of them from the highest uptake site). The expression of following proteins involved in the cellular metabolism were analyzed: aerobic (lactate-dehydrogenase, pyruvate-dehydrogenase), anaerobic (malate- dehydrogenase), beta-oxidation of fatty acids (acetyl-coenzyme A-dehydrogenase [acilCoADH], carnitine-palmitoyltransferases [CPTs]), oxidative phosphorylation (uncoupling-protein 1 [UCP-1]), ATP-synthase.

**Results:** 5 patients showed an increased uptake. Therefore 25 samples were collected. There was a statistical significant difference regarding demonstrated growth of the AAA (80% in uptake group vs 20%, P = 0.018) with a RR 7.4 (CI 95% (1.02-54.31)). The uptake group showed a lower aortic diameter without statistical significance (53.80±9.09 mm vs 60.87 ± 8.48 mm). We observed no differences regarding to the expression of proteins related to aerobic or anaerobic metabolism. Levels of expression acilCoADH (32.80±8.05UA vs 55.58 ± 4.28 , p = 0.049) and CPT-II (12.68±4.73UA vs 38.30±3.78 , p = 0.001) were significantly lower in the group. Significantly higher levels of expression of UCP-1 were observed in the uptake group (138.64±26.57UA vs 55.05±11.12 , p = 0.005), with lower levels of ATP synthase (10.17±2.67 UA vs 20.11 ± 4.01).

**Conclusions:** metabolic changes in AAA with increased 18-FDG uptake is related to an uncoupling of the oxidative phosphorylation chain and a diminished ATP synthesis. PET-CT could be considered a potential biomarker to detect those AAA with recent growth, but further studies are required to confirm its validity.

**Evidence of intimal tear in aortic intramural hematoma.**

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Aortic Intramural Hematoma (IMH) represent Class II of Acute Aortic Syndrome (AAS); this group of virulent lesions share the presence of an intimal tear but original description of IMH is reported as a “dissection without intimal tear” due to vasa vasorum rhexis. Moreover, as per Acute Dissection (AD) timing of surgery is well codified, for IMH this issue is controversial ranging from watchful waiting, eventual surgery up to emergency. Related to this the natural history described IMH as a dynamic entity with associated tendencies (regression, progression to AD, expansion or rupture) that vary geographically. To date only sporadic reports emphasize the prevalence in IMH of a tear, lesion that may contribute to justify a change in the policy protocol considering the causative role of vasa vasorum as questionable because the pressure generated by the rupture is too low to overcome the counterpressure exerted from the inner lumen. We review retrospectively our data on a group of patients with diagnosis of AAS during a period between July 2013 to March 2016 focusing on natural history, radiographic follow-up and intraoperative findings of subset of patients (12,12%) affected by IMH. All IMH patients, both type A-type B, were operated on as eventual surgery, except one IMH type A that was operated on as emergency. Pre-operative and/or intraoperative findings showed in one-third of all cases the evidence of an intimal lesion. There was no intraoperative death, one patient was complicated with retrograde TAAD during Tevar procedure and was the one that suffered for permanent neurologic disorder and account for late death. Our data review, due to IMH high rate of worsening during follow-up, the coexistence of an intimo-medial tear and the favourable surgical results, led us to consider for IMH a more aggressive timing for intervention.

**References:**


**The application of metabolic profiling to aneurysm research**

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**Background/Objective:** Metabolomics is a top-down systems biology approach [1] involving high resolution spectroscopic profiling of small (<1kDa) molecules (representing endpoints of metabolism) combined with computational data modeling that may be used to determine biomarkers of disease presence, unravel pathophysiological pathways, confer prognostic information, or map response to treatment. There is considerable uncertainty regarding the aetiological development and optimal management of aneurysmal disease. This study aimed to explore the diversity and outcomes of existing metabolomic research as applied to the clinical challenges for patients with abdominal aortic aneurysm (AAA).

**Method:** A systematic review has been performed adhering to PRISMA guidelines. All original research articles applying metabolic profiling to samples collected from patients with aneurysms were included. Non-human studies and reviews were excluded.

**Results:** Seven articles relevant for inclusion were identified [2-8] examining plasma/serum or tissue. All studies utilised mass spectrometry (MS) and one additionally incorporated Proton Nuclear Magnetic Resonance Spectroscopy (‘H-NMR) [5]. Aminomalonic acid (GC-MS) [5], guanidinosuccinic acid (HPLC-MS) [2] and glycerol (‘H-NMR) [5] emerge as biomarkers of large aneurysm presence. Results from targeted metabolic lipid profiling suggest that preferential incorporation of adipocytes into aneurysm adventitia may occur, decreasing tensile strength, thereby increasing the risk of rupture. Temporal relationships between chemical mediators of inflammation and resolution in patients undergoing open AAA repair imply differential responses in early and late healers, generating hypotheses for targeted perioperative adjunctive therapy. Limitations encountered include small study sizes, single time-point sampling, and lack of statistical correction for the likelihood of false positive discovery.

**Conclusion:** Current studies demonstrate the utility of metabolomic science in identifying potential biomarkers of aneurysm presence and elucidating mechanisms underlying dilating arterial disease. Further translational longitudinal studies incorporating larger, matched cohorts are required for validation of the metabolites identified, to determine metabolic variations associated with aneurysm growth and generating targets for drug design and development.

**References:**

**PREOPERATIVE FIBRINOGEN LEVELS AND EARLY OUTCOME FOLLOWING ENDOVASCULAR REPAIR OF RUPTURED ABDOMINAL AORTIC ANEURYSMS**

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**Aim:** To investigate the potential association between preoperative levels of fibrinogen and early outcome following endovascular aortic repair (EVAR) of ruptured abdominal aortic aneurysms (RAAAs).

**Methods:** Consecutive patients undergoing EVAR for RAAA between March 2010 and May 2016 were recruited from a single vascular centre. Patient details including fibrinogen levels on admission were extracted from case files and 30-day mortality was recorded. Fibrinogen levels were compared between survivors and fatal cases using the independent samples t-test.

**Results:** Twenty-one patients (20 males, median 71 years) with a RAAA receiving EVAR and available preoperative fibrinogen levels were included in this study. There were 16 patients with a de novo RAAA and 5 with free rupture after a previous EVAR. Of these, 3 patients died within 30 days (14.3%), one intra-operative and two within 24 hours due to multiple organ failure. Fibrinogen levels on admission were significantly higher in the group of survivors when compared to those who died (mean ± standard deviation 456.36±183.72 versus 192.57±52.26; p=0.026).

**Conclusion:** This study suggests a possible relationship between fibrinogen levels on admission and early mortality in patients undergoing EVAR for a RAAA. Higher fibrinogen levels, which may indicate a preoperative hypercoagulable profile, seemed to be associated with better chances of early survival in our small series. Further and larger studies are needed to clarify this issue and possible future therapeutic implications.

**INFLAMMATION AS A PREDICTOR OF ABDOMINAL AORTIC ANEURYSM GROWTH AND RUPTURE: A SYSTEMATIC REVIEW OF IMAGING BIOMARKERS**

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**Background:** Methods are required to identify abdominal aortic aneurysms (AAA)s at increased risk of rupture. Inflammatory characteristics of AAA can be visualised using advanced imaging techniques and have been proposed as potential predictors of aneurysm progression. The objective of this review was to determine which inflammatory imaging biomarkers are associated with AAA growth and rupture.

**Methods:** A systematic review was carried out in accordance with the
BIOMECHANICAL IMAGING MARKERS AS PREDICTORS OF ABDOMINAL AORTIC ANEURYSM GROWTH OR RUPTURE: A SYSTEMATIC REVIEW

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Objectives: Biomechanical characteristics, such as wall stress, are important factors in the pathogenesis of abdominal aortic aneurysms (AAA) and can be visualised and quantified using imaging techniques. This systematic review aims to present an overview of all biomechanical imaging markers that have been studied in relation to AAA growth and rupture.

Methods: A systematic review was carried out in accordance with the PRISMA guidelines. A search in Medline, Embase and the Cochrane Library identified 1503 potentially relevant articles. Studies were included if they assessed biomechanical imaging markers and their potential association with growth or rupture.

Results: Twenty-seven articles comprising 1730 patients were included. Eighteen studies performed wall stress analysis using Finite Element Analysis (FEA), thirteen of which used Peak Wall Stress (PWS) to quantify wall stress. Ten of thirteen case-control FEA studies reported a significantly higher PWS for symptomatic or ruptured AAAs than for intact AAAs. However, in some studies there was confounding bias due to baseline differences in aneurysm diameter between groups. Clinical heterogeneity in methodology obstructed a meaningful meta-analysis of PWS. Three out of five FEA studies reported a significant positive association between several wall stress markers – such as PWS and 99th percentile stress – and growth, one study reported a significant negative association and one other study reported no significant association. Studies assessing wall compliance, the augmentation index and wall stress analysis using Laplace’s law, computational fluid dynamics (CFD) and fluid-structure interaction (FSI) were also included in this systematic review.

Conclusions: PWS is significantly higher in symptomatic or ruptured AAAs in most FEA studies. However, confounding bias, clinical heterogeneity and lack of standardisation limit the interpretation and generalisability of the results. Also, there is conflicting evidence on whether increased wall stress is associated with growth.

References:
Georgios Makrygiannis, Evanthia Mourmoura, Konstantinos MMP13 (p=0.034) and allele frequencies for SNP (-77A/G). The G allele was more frequent in patients with AAA than in control group (142 vs. 108, p=0.034, OR (95% CI) 1.41 (1.03–1.93)). No significant differences in genotype or allele frequencies for the MMP9 polymorphism were detected.

Conclusion: Significant genotypic and allelic associations were observed between MMP13 (-77A/G) polymorphism and AAA in a Greek population, supporting its potential involvement in AAA pathogenesis, while no correlation was identified between MMP9 and AAA.

CAN AORTIC ROOT REPLACEMENT WITH A GRAFT AFFECT CARDIAC FUNCTION IN PATIENTS WITH MARFAN SYNDROME?
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Background: Marfan syndrome (MFS) is a heritable connective tissue disorder characterized by skeletal, ocular and cardiovascular manifestations. The most know and life-threatening cardiovascular condition is aortic root dilation and dissection. Different surgical techniques to replace the aneurysmatic or dissected aorta with a graft are possible. Recently, decreased left ventricular function, leading to cardiomyopathy in some cases, and arrhythmias have also been identified as an important cause of mortality in these patients. Furthermore, abnormal myocard has been shown in different mice models of MFS. Nevertheless, risk factors favouring the development of ventricular dysfunction and arrhythmias are not well known.

We, therefore, wanted to investigate the effect of aortic surgery by inserting a rigid graft on cardiac function in patients with MFS. Methods: We selected all patients from our cohort who underwent aortic root replacement (AoRR). We retrospectively collected demographic and clinical data and we reviewed systolic and diastolic parameters on echocardiography at 3 different time points: before surgery, 6 months after surgery and during the last follow up. Results: Thirty-three MFS patients underwent AoRR. Twenty-eight patients (84.9%) had an aortic valve sparing surgery (6 of which with associated aortoplasty). The rest underwent a Bentall procedure. Median aortic root before surgery was 52.5mm (IQR 49-56) and 13 patients (39,4%) had at least moderate aortic regurgitation. Median time of follow up was 5 years (IQR 2-10,5). Left ventricular end diastolic and systolic diameters (LVEDD, LVESD) decreased significantly during the first 6 months after surgery (56,75 vs 52,75mm; p<0,001 and 37,16 vs 32,16mm; p=0,018 respectively). At the last follow-up, LVEDD was similar to 6 months after surgery, but LVESD significantly increased (36,1mm, p=0,02). Increase of LVESD lead to decreased left ventricular ejection fraction (LVEF) (59,57 at 6months vs 52,86% at follow-up, p=0,016). No changes in diastolic parameters were observed.

Right ventricular function was also affected by AoRR: TAPSE decreased after surgery to a suboptimal value and remained like this during follow-up (22,3mm before surgery, 17mm at 6m and 16,52mm during last FU, p< 0,001).

Conclusion: These results support the hypothesis that the placement of a rigid graft might influence cardiac function on long term. Our study is limited in the fact that it was retrospective and that no comparison group has been used.

References:

CHOLESTEROL PRECURSORS IN PATIENTS WITH AAA
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Introduction: Abdominal aortic aneurysm (AAA) is a serious condition with unclear pathogenetic mechanism. One of the discussed factors involved in its pathogenesis is arteriosclerosis. We focused in our study on the detection of biomarker concentrations which are far more precise in monitoring the balance between cholesterol synthesis and absorption, namely campesterol, sitosterol and lanosterol as markers of cholesterol absorption, and desmosterol and lathosterol as markers of cholesterol synthesis.

Patients and Methods: We examined a total of 58 patients with AAA requiring surgery and 20 patients treated for lipid metabolism disorder without AAA in the control group. Demographic and clinical characteristics of both groups are shown in Table 1. The following parameters were examined by means of mass spectrometry: campesterol, sitosterol, lanosterol, desmosterol, and lathosterol. In addition, lipoprotein-associated phospholipase A2 (Lp-PLA2) and hsCRP serum concentrations were examined.

Results: The difference of Lp-PLA2 concentrations in both groups was not statistically significant. hsCRP concentration was significantly higher in the group of patients with AAA (p=0.007). No differences between both groups were found for cholesterol absorption markers - campesterol and sitosterol (p=0.96 and 0.65 respectively). By contrast, cholesterol synthesis markers - lanosterol, desmosterol and lathosterol - were significantly higher in the AAA group of patients as compared to the control group (p=0.004; p=0.0005 and p=0.0002 respectively, Table 1).

Conclusion: In the AAA group of patients, statistically significantly higher concentrations of hsCRP were detected as compared to the control group. Cholesterol synthesis markers were statistically significantly higher in the AAA group while cholesterol absorption markers were not statistically significantly different in both groups. It suggests an imbalance in cholesterol synthesis in patients with AAA and a potential possibility of targeted adjustment of hypercholesterolemia therapy in patients with AAA who are treated with statins.

GENE EXPRESSION SIGNATURE IN PATIENTS WITH ABDOMINAL AORTIC ANEURYSM
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Introduction: Abdominal aortic aneurysm (AAA) is a serious condition with unclear pathogenetic mechanism and progression. Etiology is clearly multifactorial in nature and is being further investigated. In our study, we compared gene expression in abdominal aortic aneurysm tissue and unaffected tissue of the same patient.

Patients and Methods: A total of 48 patients with AAA in whom surgery was necessary were included into the study. Two samples (5x5 mm) of the entire arterial thickness were collected from each patient during AAA surgery. One sample was collected from the aneurysm at the site with the largest dilation seen macroscopically while the second sample was collected from the aneurysm neck where the tissue had no aneurysm changes. Subsequently, the gene expression profiles using microarrays (Illumina) were compared in RNA extracted from samples. Demographic and clinical characteristics of the patients is seen in Table1.

Results: Altogether, 2185 genes were found to be upregulated and 2100 downregulated. Analyzing the gene list based on the biological pathways they belong to and using Panther and Nature pathway revealed that regulation of inflammation mediated by chemokine and cytokine signaling pathway, "integrin signaling pathway", "T and B cell activation" were the the most important pathways.

Conclusion: We demonstrated different gene expression in the tissue with aneurysm changes and the sample of healthy vessel. The changes related to inflammation regulation by means of immunity mechanisms comprising T and B lymphocyte subpopulations. Understanding these mechanisms may potentially aid in better understanding etiopathogenetic mechanisms of aneurysm and its treatment.

THE NATURAL HISTORY OF A LARGE AORTA IS GREATER CARDIOVASCULAR RISK
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Introduction: Ultrasound screening for AAA is cost effective and reduces AAA related mortality. Excess cardiovascular morbidity and mortality is well recognised in patients with AAA, however, AAA screening has no formal role in cardiovascular risk reduction which may be an opportunity missed.

Figure 1. Cardiovascular survival from time of screening.
Problem Definition: The aim of this study is to characterise the association of cardiovascular mortality with aortic diameter utilising a single screening cohort.

Work Summary: Consent was gained to analyse the NHS AAA screening cohort (2013-2014) and the UK Health Episode Statistics/Office for national statistics deaths dataset. Patients who did not attend screening were excluded. Data relating to maximum AP aortic diameter, study date, date of death and cause of death (ICD-10) were extracted. Cardiovascular death included those ICD codes pre-specified by the Global Burden of Disease studies. Relative risks were calculated to compare groups and log-rank survival analysis performed.

Results: 240,954 patients were included and mean aortic diameter was 18mm (SD 3mm). 3,235 patients (1.34%) had a sub-aneurysmal aorta (25-29mm) and 2,981 (1.24%) had an AAA (>30mm). At three years 34 patients in the sub-aneurysmal group (1.1%, RR 2.25, 95% CI 1.61 – 3.14, P=0.0001) and 61 in the small AAA group (5.3%, RR 4.2 95%CI 3.34-5.47, P=0.0001) had a cardiovascular related death compared to those with a normal aorta (<24mm). Overall cardiovascular survival decreased with progressive aortic dilation (Figure 1, Log Rank P=0.0001).

Conclusion: The natural history of an enlarging aorta is progressive cardiovascular risk. Aortic screening is currently an opportunity missed to address this risk in those with and without AAA.

Comment on this Article or Ask a Question

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