

Registry Meeting Minutes

October 2017, EACTS Vienna

Members present: Hlubocky Jarosalan (VFN Prague, CZ), Jan Vojacek (Hradec Kralove), Igor Rudez (Univ Hosp. Dubrava, Zagreb Croatia), Josip Varvodic (Univ Hosp. Dubrava, Zagreb Croatia), Pouya Youssef (St georges Hosp. London, Hammersmith Hosp. London), Patrick Yiu (New Cross Hosp, Wilverhampton), Hanneke Takkenberg (Erasmus MC), Malapert Christian (CHU Dijon, France) Ismail El Hamamsy (Montreal Heart Institute), Peter Verbrugge (UZ Leven), Laurent de Kerchove (St Luc Bruxelles), Jolanda Kluin (AMC Amsterdam), Frederiek de Heer (AMC), Emmanuel Lansac (Institut Montsouris), Sarah Pousset (Institut Montsouris).

Agenda

1. Database update (summary report by Frederiek de Heer)

The database contains 57 centers in 17 countries and 4703 patients were enrolled by 49 active centers at 30 August 2017. Data completeness is presented for key variables. weight, heart rate, intention to repair, IDDM, creatinine, COPD, previous cardiac surgery, NYHA, reason for referral, pulmonary hypertension, dialysis are all more than 80% complete. Preoperative LVEF 68%, CTD 48,3% and urgency 46%. Date of surgery was not complete for all patients: in 47% of the patients the day of operation was missing. This makes it impossible to calculate precise postoperative date intervals for those patients (e.g. 30 days mortality, freedom from reoperation, follow-up duration). There is an imbalance between repaired and replaced valves: 4117 patients (88%) underwent valve repair compared to 340 patients (7%) with AV replacement. In total 8209 follow-up echo forms are created and 3236 patients (70%) do have at least one follow-up echo. The median follow-up duration is 1.8 years. Regarding variability of completeness, it was request to differentiate retrospective and prospective patients. Fredriek Heer explore this issue.

- How do we proceed to get more complete data?
 - Within CleanWeb there is a functionality to send queries to the centers. Sarah Pousset will further explore this function and send queries to all center
- How many patients do have at least 1 FU echo at 1 year?
 - *Answer dd. 29Nov2017: Of the patients with a known follow-up duration (which is 53% of the total AVIATOR population) 2113 patients have reached 1 year follow-up (365 patients were operated less than 1 year before 30 August 2017). Of the patients with 1 year follow-up 1514 (72%) patients have a follow-up echo in the database.*
- Suggestion to add "Unknown" as additional option for the question CTD yes/no. (=accepted)
- Discussion is started to simplify the registration of echo variables.
 - It was proposed to combine TTE and TEE in one preoperative echo. (=accepted)
 - It was proposed that Coaptation height/length, Effective height, Annulus (mm), Sinus (mm), STJ (mm) and Tubular aorta (mm) are optional variables .

- Echo will be consider as “complete” for multicentric clinical analysis if degree of AI and EF is precised.
- How many centers do enroll replacements?
- *Answer dd. 29Nov2017: 31 centers.*

2. Research proposals on the Aviator Database

There are 4 proposals submitted to the Scientific Committee (SC). Not all SC members have given comment before the EACTS meeting. The proposals were sent to all AVIATOR participants to be discussed at the EACTS meeting.

- **Proposal #1:** The role of aortic root remodeling with annuloplasty for the management of patients with connective tissue disorders.

PI : Ismail El-Hamamsy

Background

Valve-sparing aortic root replacement is the operation of choice in selected patients with connective tissue disorders. Root reimplantation has traditionally been the approach of choice because it stabilizes the aorto-ventricular junction. In recent years, root remodeling with annuloplasty has emerged as an alternative that combines the benefit of aorto-ventricular junction stabilization and optimal aortic valve and root dynamics. To date, there are limited data on the role of root remodeling in patients with connective tissue disorders (1). The aim of this study is to examine the role of aortic root remodeling with annuloplasty on aortic valve function, reoperation and survival in patients with connective tissue disorders.

Hypothesis

We hypothesize that addition of an aortic annuloplasty (extra-aortic ring or suture annuloplasty) to aortic root remodeling will result in stabilization of the aorto-ventricular junction and a low incidence of recurrent aortic regurgitation and/or reoperation.

Methods

Using the AVIATOR registry, retrospective analysis of all patients with a diagnosis of connective tissue disorder (Marfan syndrome, Loeys-Dietz syndrome, Ehlers Danlos syndrome and Turner syndrome) will be performed. Long-term actuarial survival, freedom from reoperation and freedom from 2+ or greater aortic regurgitation will be assessed. In addition, mixed effect models will be used to evaluate changes in aortic annular diameters measured by echocardiography. We will seek to determine predictors of reoperation, recurrent aortic regurgitation or expansion of aortic annular diameters in these patients.

References

- (1) Kuniyama T, Aicher D, Rodioncheva S, et al. Outcomes after valve-preserving root surgery for patients with Marfan syndrome. *J Heart Valve Dis* 2012;21:615-22.
- (2) David TE, David CM, Manlhiot C, et al. Outcomes of Aortic Valve-Sparing Operations in Marfan Syndrome. *J Am Coll Cardiol* 2015;66:1445-53.

- Reimplantation will be included to the study population
- Valve sparing patients: look for the centers whom haven't completed CTD, contact them in order to complete the data. Sarah In charge
- Hanneke Takkenberg advised for the methodology to look closer at a publication on longitudinal data and mixed models for the analysis of the AI data. (*Andrinopoulou et. al. An Introduction to Mixed Models and Joint Modeling: Analysis of Valve Function Over Time. Ann Thorac Surg 2012;93:1765–72*)
- Conclusion: proposal #1 accepted

- **Proposal #2:** Annular stabilization in aortic root remodeling – comparison between eternal aortic ring annuloplasty and PTFE suture annuloplasty.

PI : Jochen Schäfers

Background

Root remodeling was proposed by Sarsam and Yacoub (1) as valve-preserving root replacement in patients with aortic root aneurysm. They hypothesized that aortic regurgitation was solely due to aortic dilatation and the goal was to normalize valve function by replacing all dilated aortic root tissue. A dilated aortic annulus has been identified as a risk factor for repair failure (2, 3), thus root remodeling was recently modified by additional annular stabilization. For this, different techniques have been proposed such as external aortic ring annuloplasty (4) and suture annuloplasty (5).

Objectives

For both approaches an improved valve stability has been shown (4, 5). The techniques for annular stabilization differ in several aspects while the surgical approach for root remodeling and concomitant valve repair is quite similar. So far, no comparison between both populations regarding the influence and related complications of the annuloplasty has been performed. The purpose of this study is to analyze the short- and long-term results for patients who had undergone root remodeling including annuloplasty with either an expansible ring or a PTFE suture annuloplasty.

Methods

This study should include a retrospective analysis incorporating all patients registered in the AorticValve repair InternATIOnal Registry (AVIATOR) who had undergone root remodeling and concomitant suture annuloplasty or external ring annuloplasty. By Kaplan-Meier analysis and log-rank test the influence on survival, freedom from reoperation and recurrent aortic regurgitation and differences between the groups could be evaluated.

Literature

1. Sarsam MA, Yacoub M. Remodeling of the aortic valve anulus. *J Thorac Cardiovasc Surg.* 1993;105:435-8.
2. Kuniyama T, Aicher D, Rodioncheva S, Groesdonk HV, Langer F, Sata F, Schäfers HJ. Preoperative aortic root geometry and postoperative cusp configuration primarily determine long-term outcome after valve-preserving aortic root repair. *J Thorac Cardiovasc Surg.* 2012;143:1389-95.
3. Schäfers HJ, Raddatz A, Schmied W, Takahashi H, Miura Y, Kuniyama T, Aicher D. Reexamining remodeling. *J Thorac Cardiovasc Surg.* 2015;149(2 Suppl):S30-6.
4. Lansac E, Di Cerna I, Sleilaty G, Lejeune S, Berrebi A, Zacek P, Debauchez M. Remodeling root repair with an external aortic ring annuloplasty. *J Thorac Cardiovasc Surg.* 2017;153(5):1033-1042.
5. Schäfers HJ, Aicher D. Root remodeling for aortic root dilatation. *Ann Cardiothorac Surg.* 2013;2(1):113-6.

- Concern is the balance of patients over the centers. Strong point of AVIATOR is that it is multi center and a comparison of one center compared to another center should be avoided.
- In the subset will be looked at the distribution between “suture annuloplasty” and “external ring” over the centers.
- Are we looking at the right endpoint?
 - o Primary endpoint: echo annulus diameter, preop vs FU
 - o Secondary endpoints: degree of AI, reoperation, complication
- Primary gros analysis of the multicentric population will be provided by Fredereik and Sarah in order to detail final study

• For the sake of time other proposals were not plenary discussed. The other proposals were:

• **Proposal #3:** Determinants of conversion to aortic valve replacement in patients selected for valve repair.

PI : Jolanda Klin

Background

Whether patients with aortic regurgitation and/or a dilated ascending aorta undergo valve repair or replacement highly depends on the center in which the patient is treated. In specialized repair centers surgeons can correctly predict the suitability of repair of the aortic valve in the vast majority of cases. In 4326 patients in the AVIATOR registry, information on the intention to repair before and after cusp analysis was complete. The vast majority receives repair (89%) as the prior intention was. At the other side of the spectrum: ninety-one patients receive a replacement when it was clear that the valve could not be repaired. In between are the cross-overs. The objective of the current study is to give further insight in the patient and valve characteristics that determine a repair or replacement strategy and to assess determinants that predict valve repair failure (conversion to aortic valve replacement or early reoperation).

Research questions

- Which patient and valve characteristics determine valve repair or replacement in specialized repair centers?
- Does patient selection - for aortic valve repair - differ among specialized repair centers?
- Are there determinants that predict aortic valve replacement after initial aortic valve repair?

Methods

A random mixed model will be developed with preoperative patient and valve characteristics as determinants (predictors) and conversion to aortic valve replacement as outcome variable. Potential determinants are, for example: left ventricular function, age, connective tissue disease, NYHA, detailed aortic valve morphology, aortic root dimensions, main reason for referral. Conversion to aortic valve replacement will be defined as conversion to valve replacement in an additional clamp session after initial repair or as reoperation during follow-up. As treatment decisions could be dependent on center specific factors, we will model ‘center’ as random co-variate in the model.

Data selection

We would like to select all patients where the question 'intention to repair' is complete as well as before as after the cusp analysis. More in detail, we would like to select the following data variables from the AVIATOR registry: subject ID, center ID (anonymised), gender, DOB, reason for referral, dissection, endocarditis, height, weight, HR, LVEF, COPD, IDDM, dialysis, poor mobility, extracardiac arteriopathy, recent myocardial infarction, critical state, creatinine value, pulmonary hypertension, CTD, urgency of operation, intention to repair before and after cusp analysis, operation date, age, hegar, AV morphology, cusp analysis, operation type, repair type, replacement type, graft, clamp duration, additional clamp session needed, operation type during additional clamp session, all pre-op and intra-op ECHO variables, operation type during follow-up.

Planning

November/December: receive data set

January-March: data analysis

April: writing (draft) manuscript

● **Proposal #4:** Early and mid-term clinical and echocardiography outcomes in patients undergoing aortic valve repair / replacement for isolated aortic regurgitation from AVIATOR database

PI : Maciej Matuszewski, Patrick Yiu

Background

The patients who undergo aortic valve repair for isolated aortic regurgitation are usually fewer in numbers than those who undergo concomitant aortic surgery, and their data are usually published alongside the latter. The objective of this study is to determine the early and mid-term outcomes in these patients, and to examine if they are improved by the use of various repair techniques.

Research questions

- What is the early and mid-term mortality of patients who undergo aortic valve repair for isolated aortic regurgitation?
- What is the reoperation rate in patients who undergo aortic valve repair for isolated aortic regurgitation?
- What are the early and mid-term ECHO outcomes of patients who undergo aortic valve repair for isolated aortic regurgitation?
- Are there any determinants that predict good mid-term outcomes after aortic valve repair for isolated aortic regurgitation?
- What are the clinical and ECHO outcomes and the reoperation rate of patients who underwent aortic valve replacement during the initial surgery because valve repair was not possible?

Methods

Using the AVIATOR registry, retrospective analysis of all patients with a diagnosis of isolated aortic regurgitation will be performed. Operative mortality, mid-term actuarial survival, freedom from reoperation and freedom from 2+ or greater aortic regurgitation will be assessed. We will seek to determine predictors of reoperation and recurrent aortic regurgitation.

Data selection

We would like to select all patients with isolated aortic regurgitation. More in detail, we would like to select the following data variables from the AVIATOR registry: subject ID, center ID (anonymised), gender, DOB, reason for referral, endocarditis, height, weight, HR, LVEF, COPD, IDDM, dialysis, poor mobility, extracardiac arteriopathy, recent myocardial infarction, critical state, creatinine value, pulmonary hypertension, CTD, urgency of operation, intention to repair before and after cusp analysis, operation date, age, hegar, AV morphology, cusp analysis, operation type, repair type, annuloplasty and its type, STJ band, replacement type, clamp duration, additional clamp session needed, operation type during additional clamp session, all pre-op and intra-op ECHO variables, operation type during follow-up.

Planning

November/December: receive data set

January-April: data analysis

May writing (draft) manuscript

How to proceed: for each proposal an overview should be given of the data completeness (descriptive statistics) for the PI and the Scientific Committee.

3. Aviator Kids update (Dr. Jolanda Kluin)

- Paper CRF is finalized
- Jolanda asked Catalyze (small Dutch company which supports scientist/doctors with grant applications) to look for suitable grants. They suggested to write to the Agency for Healthcare Research and Quality (AHRQ). Call PA-17-246: Health Information Technology (IT) to improve Health Care Quality and Outcomes.
- Deadline: 16 February 2018
- Award Budget: \$200,000 per year or \$300,000 for the entire project period
- Project duration 2 years.
- Catalyze can write the proposal for € 30 000.

Suggestion from Emmanuel: combine financing for building e-CRF of Aviator kids, aviator medical, and 'empowering the patient' module for Aviator in general.

4. Any other business (AOB)

- Emmanuel announced that we need extra budget for the upgrade of CleanWeb safety levels as consequence of new European regulation, which will be effective on 25 May 2018 in all European countries.

- Ismail suggests to look at Redcap. He has good experience with it. The software itself is free to use. You do need a server to host the data. We will explore the advantages and disadvantages of Redcap.
- In the Scientific Committee Gebrine El-Khoury will be replaced by Laurent de Kerckhove.