

Imaging techniques in aortic valve and root surgery Regeer, M.V.

Citation

Regeer, M. V. (2017, April 18). *Imaging techniques in aortic valve and root surgery*. Retrieved from https://hdl.handle.net/1887/47977

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Title: Imaging techniques in aortic valve and root surgery

Issue Date: 2017-04-18

Chapter 9:

Comparison of left ventricular volume and ejection fraction and frequency and extent of aortic regurgitation after operative repair of type A aortic dissection among three different surgical techniques

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Am J Cardiol. 2016;117:1167-72.

Abstract

Background: Differences in recurrence rate of aortic regurgitation (AR) and extent of left ventricular (LV) remodeling across the different surgical options in patients operated for type A aortic dissection remain unknown. The present evaluation compared the AR recurrence rate and changes in LV volumes and systolic function among valve-sparing aortic root replacement (VSAR), supracoronary ascending aorta replacement (SCAR) and aortic valve and root replacement (AVAR).

Methods: A total of 97 patients (58±12 years, 62% men) with acute type A aortic dissection who underwent VSAR (n=24), SCAR (n=43) or AVAR (n=30) were evaluated. Changes in LV volumes and function between postoperative and follow-up were compared using linear mixed models.

Results: Postoperative AR grades were not significantly different between groups. However after median follow-up of 47 months, AR grade ≥2 was significantly more often observed in SCAR (55%) and VSAR (25%) compared to AVAR (0%, p<0.001). LV volumes remained stable in VSAR and AVAR but increased significantly in SCAR (LV end-diastolic volume: from 99±4 to 131±6 ml; p<0.001; LV end-systolic volume: from 49±3 to 66±5 ml; p=0.002). Among patients with recurrent AR grade ≥2 at follow-up, LV volumes increased whereas patients without recurrent AR did not show significant LV dilatation.

Conclusion: Patients with acute type A aortic dissection who underwent SCAR or VSAR showed more frequently AR grade ≥2 recurrence compared to AVAR. However, only patients who underwent SCAR experienced adverse LV remodeling at follow-up. Recurrence of AR grade ≥2 was associated with adverse LV remodeling.

Introduction

Acute type A aortic dissection is a life-threatening condition with 50% mortality within the first 48 hours if left unoperated. Resection of the primary intimal tear, stabilization of the aortic wall and prevention of aortic rupture are the surgical goals and can be achieved by performing a valve-sparing aorta replacement (VSAR), supracoronary ascending aorta replacement (SCAR) or aortic valve and aorta replacement (AVAR). Previous studies showed no difference in perioperative and mid-term survival between these surgical procedures. However, SCAR is associated with dilatation of the aortic sinuses and recurrence of aortic regurgitation (AR) at follow-up which may warrant a relatively high risk on reoperation. Furthermore, recurrence of AR at follow-up may lead to left ventricular (LV) dilation and systolic dysfunction. However, the effects of the type of surgery for acute type A aortic dissection on LV volumes and function during follow-up have not been evaluated. The aim of the present study was to assess differences in LV remodeling during follow-up for the several surgical procedures in patients with acute type A aortic dissection taking into consideration the differences in AR recurrence rates.

Methods

Patients

Patients with acute type A aortic dissection who underwent surgery at the Leiden University Medical Center between 1 July 1994 and 1 July 2013 and who survived the initial hospitalization were evaluated. Patients were included if postoperative transthoracic echocardiography was available. Ninety-seven patients were divided into three groups according to the surgical procedure performed: VSAR (n=24), SCAR (n=43) or AVAR (n=30). Patients with connective tissue disease were excluded.

Clinical and surgical characteristics were prospectively collected in the departmental Cardiology Information System (EPD-Vision®, Leiden University Medical Center, Leiden, The Netherlands) and retrospectively analyzed. LV volumes and function were evaluated with two-dimensional transthoracic echocardiography postoperatively and during follow-up (≥6 months after surgery, available in 53 patients). The institutional ethical committee approved this retrospective study and waived the need for informed consent in patients followed in the Leiden University Medical Center. Written informed consent was obtained when patients were followed in the referral hospital. Changes in LV volumes and function over time were assessed and compared between the three different surgical procedures. In addition, the incidence of recurrent AR over time was assessed.

Two-dimensional transthoracic echocardiography

Transthoracic echocardiography was performed with commercially available ultrasound systems (Vivid 7, E9 or System 5, General Electric Healthcare, Vingmed, Horten, Norway) equipped with 3.5-MHz or M5S transducers. The echocardiographic data were digitally stored in cine-loop format and data analysis was retrospectively performed using EchoPac (112.0.1, GE Medical Systems, Horten, Norway). LV volumes were quantified at end-diastole and end-systole in the apical 2- and 4- chamber views using the Simpson's biplane method and LV ejection fraction was calculated.6 AR grade was assessed using a multiparametric approach that included the measurement of the jet width relative to the LV outflow tract width, vena contracta and/or the pressure half time of the regurgitant flow (if feasible) according to current recommendations.⁷

Surgery

The decision to perform VSAR, SCAR or AVAR was left at the discretion of the surgeon on duty. During VSAR, the native sinuses of Valsalva were resected and a graft was implanted using the reimplantation technique (modified David procedure, n=19) or the remodeling technique (Yacoub technique, n=5), as previously described. ^{8,9} Concomitant procedures (leaflet triangular resection, leaflet resuspension and plication of the free edge of the leaflet) were performed if needed. For SCAR, the ascending aorta was resected until the sinotubular junction and replaced by a Hemashield tubular graft. ¹⁰ If necessary, resuspension of the commissures (n=15) and/or restoration of the sinuses of Valsalva using bioglue (n=24) or gelatin-resorcinformalin glue (n=5) was performed. ¹¹ During AVAR, the native sinuses of Valsalva and valve were excised and replaced by either a biological (n=18) or mechanical prosthesis (n=12). ^{12,13} In every patient the distal ascending aorta and arch were inspected under deep hypothermic circulatory arrest. If a (re)entry tear was present in the arch, concomitant (hemi-)arch replacement was performed.

Follow-up

All patients underwent transthoracic echocardiography postoperatively before discharge. Transthoracic echocardiography at follow-up was performed at the discretion of the treating cardiologist. Follow-up echocardiography was available in 53 patients and was included in the present study when it was performed at least 6 months after surgery. The median echocardiographic follow-up duration was 47 months (interquartile range: 18-76 months) and comparable between the 3 groups (VSAR: 49 months, interquartile range: 19-74 months. SCAR: 55 months, interquartile range: 31-77 months. AVAR: 24 months, interquartile range: 12-56 months; p=0.150).

Statistical analysis

Data analysis was performed using SPSS software version 20 (SPSS, Chicago, IL). Continuous variables were reported as mean±standard deviation or median and interquartile range (IQR) when appropriate. Categorical variables were reported as numbers and percentages. Differences between the 3 different surgical procedures were analysed using analysis of variance test, Kruskall-Wallis test or Chi-square test. Survival and freedom from reoperation were analyzed using the Kaplan-Meier curves and differences among surgical procedures were assessed with the log-rank test. Linear mixed model analysis was used to assess the differences in change in LV volumes and LV ejection fraction over time among the groups. Type of surgery (VSAR, SCAR or AVAR) and timing of transthoracic echocardiography (postoperative or late follow-up) were incorporated in the model as fixed variables as well as the interaction between type of surgery and timing of transthoracic echocardiography. An unstructured covariance matrix was applied. The estimated marginal mean ± standard error of the mean was presented. Post-hoc analyses were performed using the Bonferroni test to correct for multiple comparisons. Subgroup analysis was performed to compare LV remodeling in patients with and without recurrent AR grade ≥2. All statistical tests were two-sided. A pvalue<0.05 was considered statistically significant.

Table 1. Baseline clinical and surgical characteristics.

	VSAR (n=24)	SCAR (n=43)	AVAR (n=30)	p-value
Age (years)	50±7	62±11	58±14	<0.001
Male gender	20 (83%)	22 (51%)	18 (60%)	0.033
Diabetes mellitus	0 (0%)	0 (0%)	2 (7%)	0.087
Hypertension	6 (25%)	26 (60%)	12 (40%)	0.018
Dyslipidemia	0 (0%)	4 (9%)	2 (7%)	0.374
Critical preoperative state	0 (0%)	2 (5%)	2 (7%)	0.460
EuroSCORE II (%)	4.7 (4.1-6.4)	5.3 (3.4-7.2)	6.0 (4.8-8.0)	0.069
Bicuspid aortic valve	1 (4%)	0 (0%)	6 (20%)	0.004
CPB time (min)	267±75	191±48	253±66	< 0.001
AoX time (min)	209±66	119±38	178±48	< 0.001
Aortic (hemi-)arch replacement	14 (58%)	16 (37%)	15 (50%)	0.299
Mitral valve surgery	0 (0%)	1 (2%)	0 (0%)	0.530
Coronary bypass	0 (0%)	1 (2%)	2 (7%)	0.345

Data are presented as mean ± standard deviation, median (interquartile range) or as number (percentage). AoX time: Aortic cross clamp time. AVAR: Aortic valve and aorta replacement. CPB time: Cardiopulmonary Bypass time. EuroSCORE II: European System for Cardiac Operative Risk Evaluation. SCAR: Supracoronary ascending aorta replacement. VSAR: Valve sparing root replacement.

Results

A total of 97 patients (mean age 58±12 years, 62% men) who underwent emergent surgery for acute type A aortic dissection and survived the index hospitalization were evaluated. Table 1 shows the baseline clinical and surgical characteristics of the patients. Patients who underwent VSAR were significantly younger and more often male than patients who underwent SCAR or AVAR. Hypertension was more often present in patients undergoing SCAR compared to patients treated with VSAR or AVAR. The EuroSCORE II was slightly higher among patients who underwent AVAR compared to VSAR and SCAR. In SCAR, the cardiopulmonary bypass and aortic cross clamp times were significantly shorter compared to VSAR and AVAR.

Survival and reoperation during follow-up

The 5-year survival in this cohort was 91±4% and was not significantly different between the surgical procedures (VSAR: 100%, SCAR: 90±6%, AVAR: 82±10%; log rank p=0.653; Figure 1A). Reoperation at follow-up on the proximal and/or distal thoracic aorta was performed in 2 VSAR, 8 SCAR and 4 AVAR patients. The freedom from reoperation on the proximal and or distal aortic after 5 years follow-up was 86±5% and comparable between the groups (VSAR: 95±5%, SCAR 83±8%, AVAR: 77±13%; log rank p=0.516; Figure 1B).

However, when considering only reoperation on the proximal aorta, aortic valve replacement was performed in 2 and 7 patients treated initially with VSAR and SCAR respectively, while none of the patients treated with AVAR required reoperation of the proximal aorta. Reasons for reoperation were severe recurrent AR in 7 patients, dilatation of the sinuses of Valsalva without AR in 1 patient and aortic valve stenosis in 1 patient. Therefore, the 5-year freedom from proximal reoperation after SCAR (88±7%) was slightly less favorable compared with VSAR and AVAR (95±5% and 100%, log rank p=0.060; Figure 1C).

Aortic regurgitation after surgery

The prevalence of significant AR directly postoperatively and during follow-up is displayed in Figure 2. Postoperative AR grade ≥ 2 was present in 13% of patients who underwent VSAR compared to 8% in patients who underwent SCAR and 4% of patients who underwent AVAR (p=0.136). In contrast, at long-term follow-up, there was a significant difference in AR grade between the surgical procedures: in patients who underwent VSAR or SCAR, AR grade ≥ 2 was observed in 25% and 55% of patients, respectively, whereas none of the patients who underwent AVAR showed AR grade ≥ 2 (p<0.001).

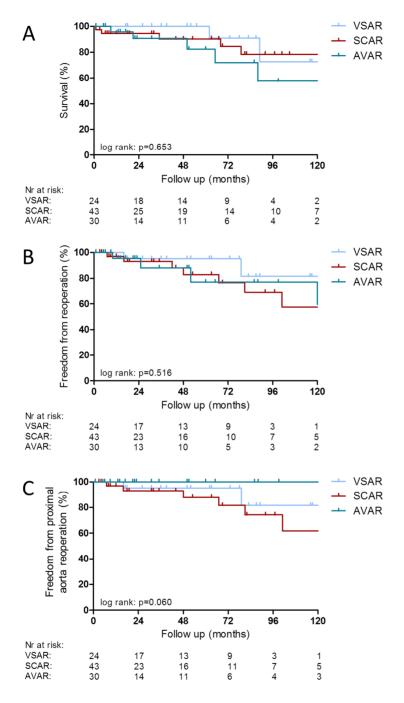
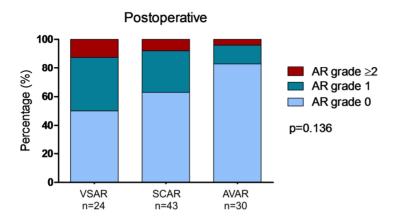


Figure 1. Kaplan-Meier curves for survival, survival-freedom from reoperation and survival-freedom from proximal aorta reoperation.

AVAR: Aortic valve and aorta replacement. SCAR: Supracoronary ascending aorta replacement. VSAR: Valve sparing aorta replacement.



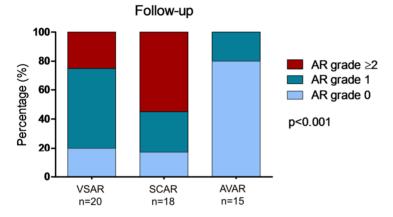
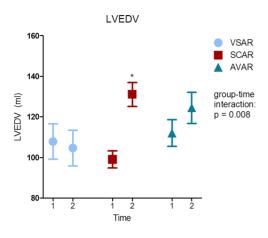


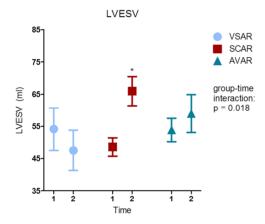
Figure 2. Aortic regurgitation grade postoperatively and during follow-up.

AR: Aortic regurgitation. AVAR: Aortic valve and root replacement. SCAR: Supracoronary ascending aorta replacement. VSAR: Valve sparing root replacement.

LV remodeling after surgery

The immediately postoperative LV end-diastolic volume, LV end-systolic volume and LV ejection fraction were comparable among the 3 groups (Figure 3). However, there was a significant difference in the LV end-diastolic volume and LV end-systolic volume at late follow-up among the surgical procedures. In the VSAR group, the LV end-diastolic volume (108±9 vs. 105±9 ml; p=0.756) and LV end-systolic volume (54±7 ml vs. 47±6 ml; p=0.387) remained stable. In contrast, the LV end-diastolic volume increased during follow-up in SCAR (99±4 vs. 131±6 ml; p<0.001). The LV end-systolic volume also increased significantly in the SCAR group from 49±3 to 66±5 ml (p=0.002). After AVAR, the volumes remained stable.





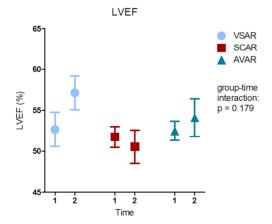


Figure 3. Left ventricular volumes and function over time.

Left ventricular volumes and function over time in VSAR, SCAR and AVAR. Data are displayed as estimated marginal means ± standard error of the mean. Time 1 represents measurement directly postoperatively and time 2 represents measurement during follow-up. * p<0.05 compared to postoperative. Group-time interaction p-value is given per variable. AVAR: Aortic valve and aorta replacement. LVEDV: left ventricular end-diastolic volume; LVEF: left ventricular ejection fraction; LVESV: left ventricular end-systolic volume. SCAR: Supracoronary ascending aorta replacement. VSAR: Valve sparing aorta replacement.

The LV ejection fraction tended to improve in VSAR patients (53 ± 2 vs. $57\pm2\%$; p=0.074), while it remained stable in both SCAR (52 ± 1 vs. $51\pm2\%$; p=0.546) and AVAR (52 ± 1 vs. $54\pm2\%$; p=0.489). The group-time interaction effect on LV end-diastolic volume (p=0.008) and LV end-systolic volume (p=0.018) indicated a significant effect of the type of surgery on the change in LV volumes over time.

Effect of recurrent AR on LV remodeling

A subgroup analysis was performed in 53 patients with late follow-up echocardiography available to compare LV remodeling in patients with recurrent AR grade \geq 2 versus patients without recurrent AR during follow-up (Table 2). Patients with recurrent AR grade \geq 2 experienced significant increase in the LV end-diastolic volume and LV end-systolic volume whereas the LV volumes remained stable in patients without recurrent AR. Furthermore, the LV ejection fraction improved in patients without recurrent AR compared to deterioration in patients with recurrent AR grade \geq 2.

Table 2. LV remodeling in patients with and without recurrent aortic regurgitation.

	Recurrent aortic regurgitation			
	No (n=38)	Yes (n=15)	p-value	
LV end-diastolic volume (ml)			0.001	
Postoperative	112±6	89±7		
Late follow-up	115±6	132±9*		
LV end-systolic volume (ml)			0.001	
Postoperative	55±4	43±5		
Late follow-up	52±4	69±7*		
LV ejection fraction (%)			0.003	
Postoperative	53±1	53±3		
Late follow-up	56±1*	49±3*		

Data are presented as estimated marginal means \pm standard error of the mean. Within groups: *p<0.05 vs postoperative, LV: left ventricular.

Discussion

The main findings of the present evaluation can be summarized as follows: patients who underwent SCAR for acute type A aortic dissection had more adverse LV remodeling and recurrent AR grade ≥ 2 at follow-up as compared with patients who underwent VSAR or AVAR. Furthermore, recurrent AR grade ≥ 2 at follow-up was associated with more adverse LV remodeling and deterioration of LV function.

Selection of operative technique in acute type A aortic dissection

Surgical treatment reduces the mortality of acute type A aortic dissection from 90% to 30% and therefore is considered the treatment of choice. ^{1,14} The optimal operative technique will

depend on the underlying pathophysiology (pre-existing aortopathy associated with connective tissue), extent of the proximal dissection towards the aortic valve, aortic valve competence, aortic annulus dimensions and associated patient's comorbidities. While the SCAR approach is the quickest technique, it is well known that in patients with diseased aortic tissue (i.e. Marfan syndrome), this technique is associated with increased risk of redissection, aneurysm formation and subsequent significant AR because of aortic dilatation (incidence between 25-45%). 15,16 In contrast, AVAR replaces the ascending aorta with a valved tubular graft and has shown excellent results.³ However, this technique (when performed using a mechanical prosthesis) is associated with the need of lifelong anticoagulation and increased risk of bleeding and thromboembolic complications. ¹⁷ Accumulating data have shown the feasibility and safety of the VSAR procedure with excellent results at short- and long-term follow-up. 3,18-20 Although the VSAR procedure is more time-demanding, several registries have shown lower early mortality and similar long-term survival for this technique compared with SCAR and AVAR. 3,18 In addition, VSAR and AVAR resulted in comparable AR recurrence rates. 21 Early mortality is one of the main factors to choose the appropriate surgical technique in patients with acute type A aortic dissection. According to previous series, the 5-year survival of initial hospital survivors is comparable between the 3 surgical procedures ranging between 65%-88% after AVAR, 64%-81% after SCAR and 65%-89% after VSAR. 3,18-20, 22-24 The present study showed comparable 5-year survival rates for each surgical technique. However, the long-term outcomes of the surgical techniques differ significantly among the 3 surgical techniques in terms of reoperation due to aneurysm formation and significant AR recurrence. Similarly to previous series, the present study showed increased risk of reoperation due to significant AR among patients treated with SCAR.^{3,5}

However, to date, the effects of recurrent significant AR on LV dimensions and function have not been evaluated. The present study showed significant adverse LV remodeling after SCAR. Furthermore, adverse LV remodeling was present in patient with recurrent AR grade ≥2 compared to stable LV volumes in patients without recurrent AR. Aiming at restoring aortic valve competence and performing a durable repair is an important goal in surgical techniques for acute type A aortic dissection in order to avoid AR recurrence and further deterioration of the left ventricle at follow-up.

Clinical perspective

The present study provides additional information to be taken into consideration when selecting the surgical approach in patients with acute type A aortic dissection. Patients who undergo SCAR benefit from shorter cardiopulmonary bypass and aortic cross clamp times, which is therefore often performed in older patients.³ However, SCAR is associated with higher rates of AR recurrence, adverse LV remodeling during mid-term follow-up and higher

reoperation rate on the aortic valve and proximal aorta. Therefore, the risk of the initial surgery should be weighed against long-term outcome when selecting the surgical procedure. Whether LV remodeling after surgery for acute type A aortic dissection is associated with worse clinical outcome should be elucidated in future clinical research.

Limitations

Some limitations should be acknowledged. This was a retrospective study with a limited number of patients. Patients who survived the initial hospitalization and who underwent transthoracic echocardiography before discharge were included introducing an important selection bias. The applied surgical technique was not randomly assigned. Preoperative transthoracic echocardiography was not systematically available and therefore preoperative AR grade, LV volumes and LV function, which could be different between the groups, were not included in the analysis. Furthermore, late follow-up echocardiography could only be performed in patients who survived the first 6 months after surgery. The present study was performed in a tertiary care hospital to which patients were referred from other hospitals. Follow-up echocardiograms were performed at the discretion of the treating cardiologist and were retrieved from the referring hospital when possible. Therefore, late follow-up echocardiography was available in only 53 patients of the complete cohort of 97 patients. In addition, computed tomography data of the aorta were not systematically available. The small number of patients limited further multivariate analyses to assess independent predictors of AR recurrence after surgery for acute type A dissection. Furthermore, the impact of changes in LV volumes and function at follow-up on the clinical outcome was not evaluated.

Conclusion

Patients with acute type A aortic dissection who underwent SCAR showed more frequently AR grade ≥2 recurrence which was associated with adverse LV remodeling.

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