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Original Research Paper

Surgery

EARLY AND LONG-TERM OUTCOMES AFTER AORTIC SURGERY IN PATIENTS WITH MARFAN SYNDROME

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ABSTRACT

Background: The aim of this study is to determine the early- and long-term results after aortic surgery in Marfan syndrome patients.

Methods: Between January 2000 and December 2015, 36 patients affected by Marfan syndrome underwent open surgical aortic and root repair. Isolated ascending replacement, hemiarch replacement and total arch replacement was performed in 5 patients (14%), 14 patients (39%) and 17 patients (47%), respectively. Elephant trunk technique and frozen elephant trunk technique was performed in 10 patients (28%) and 3 patients (8%), respectively. The surgery was performed urgently in 16 patients (44%) and electively in 20 patients (56%). Hundred twenty-seven imaging studies were analyzed for segmental aortic diameter at our institution. Clinical data were prospectively entered into our institutional database. Mean late follow up for late survival was 5 ± 3 years and was 98 % complete.

Results: Thirty-day mortality was 6% (n=2). One patient died in the hospital. Intensive care unit stay was 3 ± 4 days. One patient (3%) experienced permanent neurologic deficits and 4 patients (11%) transient neurologic deficits. 5 Patients (14%) underwent redo surgery. Late survival and freedom from re-operation/re-intervention were 89 ± 2 % and 81 ± 3% at 6 years.

Conclusions: Marfan syndrome patients seem to benefit the most from total arch replacement with elephant trunk. We recommend rigorously adjust the systolic blood pressure less than 120 mmHg and a postoperatively treatment with ß-blockers and ACE inhibitors. The time of re-operation and the increase of the aortic size still unpredictably therefore a yearly follow-up lifelong is recommended.

KEYWORDS : Aorta; Marfan Syndrome; Cardiovascular diseases

Marfan syndrome (MFS) is a genetic disorder of the connective tissue with a reported incidence of 0.02% (Pepe et al., 2016). Beside the ocular and musculoskeletal manifestation, MFS leads essentially in the cardiovascular system to atrioventricular valve disorder and aortic dilatation inclusive aortic root (Pepe et al., 2016). The latter MFS may lead to rupture of aortic root aneurysm and aortic dissection, which are the most serious complications and determine the prognosis and survival of patients with MFS.

Thus prophylactic aortic surgery by MFS-patients is often recommended. The operation of choice for aortic root and valve disease in this patient cohort includes the Bentall procedure and in case of normal aortic valve leaflets the valve-sparing aortic root replacement (Patel et al., 2008; Birks et al., 1999, Rahnavardi et al., 2011; LeMaire et al., 2006). On the other hand the extention of the operative procedure in the aortic arch and descending aorta depends mainly from dispersion of the aortic dissection and accordingly aortic aneurysm (LeMaire et al., 2006).

The aim of this study is to determine our institutional results after aortic surgery in MFS-patients by focusing our interest in perioperative outcomes regarding mortality, morbidity, late survival, freedom from re-operation and finally optimal postoperative medical therapy.

Material and Methods

Between January 2000 and December 2015, 36 consecutive patients affected by Marfan syndrome underwent open aortic repair for annuloaortic ectasia at the Division of Thoracic and Cardiovascular Surgery, Johann Wolfgang Goethe University, Frankfurt am Main (Germany). The study was approved by the institutional review board, and individual patient consent for the study was waived.

Mean patients age was 37±17 years and 75% (n=27) of the patients were male. Arterial hypertension was detected in 39% (n=14) of the cohort. Almost half of the patients (47%, n=17) were preoperatively under ß-blockers therapy whereas 31% of the patients (n=11) took ACE-Inhibitors prior to surgery. Baseline clinical characteristics of the entire patient cohort are summarized in Table 1.

Acute aortic dissection was diagnosed in 39% (n=14) of the patients, who has been urgently operated. Three patients (8%) were primary symptomatic with a neurologic disorder consisting of dysathria (n=2) and hemiplegia (n=1). Five patients (14%) had undergone an aortic redo surgery. Contrast computed tomography and transthoracic echocardiography were performed preoperatively in all patients. Transesophageal echocardiography was routinely performed in the operating room.

Operative techniques. The operation was performed from different surgeons during this period between 2000 and December 2015 and a substantial variability in the specific operative techniques of root and aortic surgery has been used. Operative data and surgical procedures are summarized in Table 2.

The standardized surgical and perfusion and temperature management protocols in Frankfurt am Main has been used for MFS-patients operated on aortic arch (86%, n=31) and is previously described in details (Zierer et al., 2012; Zierer et al., 2014; El-Sayed Ahmad et al., 2017; Zierer et al., 2017; El-Sayed Ahmad et al., 2016; El-Sayed Ahmad et al., 2015). Briefly, the left radial artery and one of the femoral arteries was cannulated for continuous blood pressure monitoring. Temperature probes were placed for esophago pharyngeal and rectal or bladder temperature monitoring. While we used a rectal temperature probe until 2007, we replaced it by bladder temperature monitoring thereafter. The patient was positioned on the operating table in the supine position. The right axillary artery was directly cannulated (18F-22F flexible arterial cannula; Edwards Lifesciences, Irvine, California) whenever possible (n=30; 83%) followed by cannulation of the right atrium in a standard fashion or bicaval cannulation in case of mitral valve repair. Alternatively, cardiopulmonary bypass (CPB) was established through ascending aorta (n=5; 14%) femoral artery cannulation (n=1; 3%) for isolated ascending replacement. The acid-base balance was maintained using the alpha-stat method. CPB was started, and cooling was limited to 28.8 ± 0.7°C rectal temperature. The innominate and left carotid artery were snared with vessel loops and occluded at the initiation of selective antegrade cerebral perfusion (ACP). After opening the aortic arch, the left subclavian artery was blocked by insertion of a Fogarty catheter (Edwards Lifesciences, Irvine, California). At that point, the elastomer loop snared around the left common carotid artery was temporarily loosened, and an arterial line was placed inside the vessel for bilateral ACP. This arterial line was simply connected as a side branch to the arterial CPB cannula. Bilateral ACP (28%, N=10) was the method of choice between 2000 and 2010. After 2010, there was a trend towards unilateral ACP (58%, N=21) to avoid the potential risk of creating cerebral emboli while manipulating on the arch vessels during insertion of the second arterial inflow cannula (Zierer et al., 2014). Selective ACP was conducted with a perfusate temperature of 29.1 ± 0.6°C in a pressure-controlled manner. The perfusion pressure was controlled on the pump unit and kept at 75 mm Hg, allowing for a mean flow of 1.4 ± 0.3 L/min. After completion of the arch aortic repair the Fogarty catheter was withdrawn from the left subclavian artery, the elastomer loops around the innominate as well as left common carotid artery were released, and the arch vessels were carefully deaired. Reconstitution of full-body perfusion via the right axillary artery was initiated after clamping the vascular graft. Subsequent proximal repair follows during the rewarming period. The decision regarding the strategy of proximal aortic repair was mainly based on the surgical inspection of the involvement of the aortic root, including the aortic valve leaflets as well as the coronary ostia. The standard operative Technique of Bentall, David and Yacoud were performed in case of aortic root surgery (Bentall and De Bono, 1968; David and Feindel, 1992; Sarsam and Yacoub, 1993). However, until 2004, we performed the standard David technique (David and Feindel, 1992). Later, we modified the procedure, initially by creating a pseudosinus to reduce leaflet stress (Aybek et al., 2005). Neurovascular monitoring consisted of cerebral saturation assessment using near-infrared spectroscopy. Details of perfusion management for the entire cohort are summarized in Table 3.

Postoperative aortic imaging. Of 34 operative survivors (94%), 33 underwent at least one follow-up imaging study (computed tomography [CT] or magnetic resonance imaging [MRI]) at our institution, which provided a review of aortic growth rates.

Hundred twenty-seven imaging studies were analysed for segmental aortic diameter for an average of 4 scans per patient. The mean interval between consecutive scans was 13 months, and the mean time for scanning from the initial operation was 6 months.

Aortic outer diameter was measured using a calliper method with the reference measurement tool within the scan image. In the case of an elliptical cross section, the minor diameter of the ellipse was measured, regardless of orientation, to avoid convolution effect in an elongated, tortuous aorta.

Aortic diameter was measured at three predetermined segments:
(1) Aortic root,
(2) Aortic arch, and
(3) Descending aorta.

In case of aortic dissection, the measurements in the descending aorta were taken at the level of maximum segmental diameter, including both the true and false lumen, if present. A thrombosed false lumen was defined as the presence of a circumferential or crescentic nonenhancing-filling defect within the aortic lumen on contrast enhanced scans.

All imaging studies were analyzed retrospectively by one observer who was unaware of the patients' clinical details.

Follow- up.Clinical data from the initial hospitalisation were prospectively entered into our institutional database. Discharged patients were followed directly in our outpatient clinic yearly or by contacting the primary care physicians and patients or family members during a 4 months late closing interval ending in April 2016.

Clinical records from all operative survivors were reviewed for blood pressure (BP) control at late follow-up and medication history. Follow-up data on BP and medication history were available for 32 patients (89%). Patients and or primary care physicians categorized systolic BP (SBP) at late follow-up as less than 120 mm Hg, between 120 and 140 mm Hg, or greater than 140 mm Hg. Resulting late follow-up was 5±3 years and was 98% complete.

Data analysis. Hospital mortality was defined as the mortality rate within 30 postoperative days or before hospital discharge. Categorical variables are expressed as percentages, and continuous data are expressed as mean values ± SD. Comparisons of characteristics were calculated by using the χ^2 test. Cumulative survival rates and freedom from reoperation were estimated by the Kaplan-Meier method. Curves of freedom from reoperation were compared between groups using the log-rank test.

In all cases, missing data were not defaulted to negative, and denominators reflect only cases reported.

Multivariate analysis (stepwise backward regression) was used to determine preoperative, intraoperative, and postoperative risk factors that were significant, independent predictors of impaired long-term survival, increased segmental aortic enlargement, and diminished freedom from late reoperation. SigmaStat 2.03 software (SPSS Inc,Chicago, IL) was used for the analysis. Twenty variables were analyzed: age, year of operation, gender, hypertension, coronary artery disease, pulmonary disease, cerebrovascular disease, previous cardiac operation, cardiogenic shock, type A dissection, aortic aneurysm, aortic insufficiency, preoperative flow complications, aortic valve preservation versus replacement, ascending only versus hemiarch versus total arch replacement, initial segmental aortic diameter, SBP (< 120 mm Hg versus 120 to 140 mm Hg versus >140 mm Hg), diastolic BP (≤80 mm Hg versus >80 mm Hg), β-blockers, Statine, ACE-blockers. For important, significant factors in the multivariate analyses, standardized (β) regression coefficients (standardized to dimensionless values) are reported with standard error of the mean. Statistical differences were considered significant at a value of p ±0.05. All statistical analyses were performed with StatView (version 5.0) for Windows software (SAS Institute, Inc, Cary, NC).

Results

Operative data. Mean CPB time was 170 ± 71 minutes, and the mean myocardial ischemic time was 92 ± 64 minutes. ACP in moderate-mild systemic hypothermia was used in 31 patients (86%). Isolated cerebral perfusion time was 48 ± 25 minutes.

One third of the patients (33%, N=12) underwent partial upper sternotomy were as the remaining 24 patients (N=67%) were operated through median sternotomy. The aortic root was reconstructed, glued and remained untouched in 21 patients (55%), 3 patients (8%) and 4 patients (11%), respectively. Eight patients (22%) who have the Bentall operation underwent aortic root replacement with composite grafts using standard methods. David Procedure, Yacoub procedure and aortic valve replacement was performed in 9 patients (25%), 3 patients (8%) and 2 patients (6%), respectively. Hemiarch replacement has been performed in 14 patients (39%) whereas 17 patients underwent total arch replacement (47%). (Table 2)

Perioperative mortality and morbidity. Thirty day mortality was 6% (N=2). Mean chest tube drainage within first 24 hours was 479 ± 251 ml and re-exploration for bleeding was necessary in 3 patients (8%). Mean intensive care unit stay was 3 ± 4 days and hospital length of stay among surviving patients was 7 ± 6 days.

Transient neurologic deficit was detected in 4 patients (11%). Among them 3 patients revile temporary delirium and one temporary motor deficit. One further patient (3%) was discharged from hospital with a postoperative permanent neurologic deficit based on stroke (Ranklin-Scale 3). Table 4 summarizes perioperative mortality and morbidity.

Long-term survival and freedom from reoperation. Kaplan-Meier estimates for late survival at 6 years were 89 ± 2 %. Figure 1 illustrates the Kaplan–Meier curve for survival.

During follow-up time, 5 patients (one after ascending wrapping, one after David procedure with hemiarch replacement, two after Yacoub procedure with isolated ascending replacement and one after aortic valve replacement with isolated aortic ascending replacement) required reoperation. These patients required a surgical approach to replace the residual pseudoaneurysm of ascending aorta and aortic arch. Two reoperations involved ascending and totally arch replacement and 3 totally arch replacement using elephant trunk technique. Overall freedom from reoperation among operative survivors was 92 ± 1% at 1year and 81 ± 3% at 6 years (Figure 2). Freedom from redo/re-intervention in MFS-patients underwent hemiarch replacement was 64 ± 5% and 91 ± 3% for total arch replacement (p = 0.04) (Figure 3).

Multivariate regression analysis. Multivariate regression analysis identified 3 factors to be independent predictors of enlargement of aorta during the follow up time.

Preoperative aortic diameter greater than 5 cm (p <0.001; OR: 4.1; 70%CI: 2.8 to 3.3); Systolic blood pressure greater than 140 mmHg at late follow-up (p = 0.04; OR: 2.3; 70%CI: 2.2 to 3.2) and hemiarch replacement (p = 0.05; OR: 5.1; 70%CI: 2.9 to 3.7).

Independent predictors for late reoperations were isolated ascending repair (p < 0.001; OR: 3.4; 70%CI: 3.3 to 4.0); Systolic blood pressure greater than140mmHg (p = 0.008; OR: 2.7; 70%CI: 2.4 to 3.9) absence of postoperative β-blockers therapy (p = 0.02; OR: 3.3; 70%CI: 2.1 to 5.3) and absence of postoperative ACE-Inhibitor therapy (p = 0.01; OR: 4.3; 70%CI: 2.6 to 4.3).

Finally isolated ascending therapy (P= 0.001; OR: 3.3; 70%CI: 2.6 to 3.2), systolic blood pressure greater than 140 mmHg (p=0.001; OR: 3.7; 70%CI: 2.1 to 4.5) and absence of postoperative β-blockers therapy (p=0.04; OR: 2.5; 70%CI, 1.8 to 3.6) were identified to be independent predictors of late mortality.

Discussion

In patients with MFS cardiovascular complications such as dilatation and dissection of the aortic root and other segments of the thoracic aorta have been described to be the leading cause of morbidity and mortality. The prime cause of aortic disease includes impaired synthesis and deposition of fibrillin-1 protein, resulting from various gene mutations (Pepe et al., 2016). Thus aortic root and thoracic aorta are especially prone to dilatation and dissection. Both in elective and in emergent cases, the operative management regarding operative treatment of the aortic root and thoracic aorta remains a big challenge. Postoperative care including optimal medical therapy and imaging follow-up seems to play a fundamental role in the postoperative management of the disease.

According to the actuarial literature aortic root aneurysm in MFS-patients should be prophylactic replaced when the aortic root diameter is larger than 4.5cm, when aortic root growths more than 2mm per year or in presence of positive family history of aortic dissections (Groenink et al., 1999). However up to 70% of patients with Marfan syndrome develop thoracic aortic dissection, which is type A in 64–86% of cases and type B in 14–36% (LeMaire et al., 2006). According the registry data for aortic dissection, 21% of MFS-patients presenting with aortic dissection die in consequence of dissection (Januzzi et al., 2004). Therefore, the purpose of aortic root surgery is to preempt the risk of dilatation and dissection thus saving the patient from aortic regurgitation and death due to aortic dissection.

Thirty-day mortality following aortic surgery in MFS-patients in a large multicenter study published from Coselli et al reported to be 1%, which is almost in line with our in hospital mortality of 2%.

In our series 12 patients had aortic valve-sparing procedure whereas in 8 patients aortic root replacement has been performed. Isolated aortic valve replacement was performed only in 2 patients. During follow-up time, 3 patients with root repair required redo surgery because of root dilatation (two after Yacoub procedure and one after isolated aortic valve replacement) whereas none of the Bentall treated patients was reoperated. Similar results have been reported previously from Patel et al. (Patel et al., 2008) and Karck et al. (Karck et al., 2004). They reported by the comparison between Bentall operation and valve-spare root in MFS-patients higher rates of reoperation among valve-spare root repair patients.

Bachet et al. reported 2007 that the aortic arch replacement in MFS-patients is not indicated during the initial procedure (Bachet et al., 2007). Our results are not in line with Bachet et al once in our series isolated ascending aorta replacement was detected as an independent predictor of late reoperation and mortality indicating more aggressive approach toward the aortic arch during initial surgery. Based on that data our institutional management of aortic arch surgery in MFS-patients changed and includes since 2002 arch- or at least hemiarch-replacement both in elective and emergent cases.

DeBakey, McCollum, Crawford, Morris, Howell, Noon and Lawrie (1982) described first a relationship between postoperative blood pressure control and progression of aneurysmal disease in long-term follow-up. In their classic 1982 series of 527 patients with acute and chronic aortic dissections, the authors noted that aneurysms developed in about 50% of patients with uncontrolled hypertension compared with only 15% with blood pressure control. Moreover, Zierer, Voeller, Hill, Kouchoukos, Damiano and Moon (2007) demonstrated that Ideal BP control not only decreased the incidence of aortic expansion from 34% to 14% but also decreased the incidence of late reoperation from 35% to 8% if the SBP was maintained below 120 mm Hg. Our findings in the enlargement progress and late reoperation of the aorta on MFS-patients support DeBakey's and zierer´s original contentions. The current report demonstrated the relationship of elevated systolic blood pressure at late follow-up and its management with both aortic enlargement and late reoperation in cardiosurgical treated MFS-patients.

To avoid the risk of aortic dissection or rupture medical therapy with ß-blockers (Tahernia, 1993), ACE inhibitors (Ahimastos et al., 2007) or angiotensin II-receptor blockers (Brooke et al., 2008) in MFS-patients is fundamental. We found that the impact of postoperative ß-blocker and ACE inhibitors medication was substantial, once absence of the above mentioned medication was associated with an increased rate of late reoperation and mortality. Furthermore systolic blood pressure greater that 140 mmHg was an independent predictor for aortic enlargement and consecutively of late reoperation.

Thus, in our hands it is imperative that we reinforce to our patients and their primary care physicians the importance of long-term BP control; that is, maintaining SBP below 120 to 140 mm Hg, and the impact specifically of ß-blockers and ACE inhibitors therapy in the long-term management of cardiosurgical treated MFS-patients.

Finally based on our data and findings for long-term serial imaging after successful treatment of an aneurysm or an acute type A aortic dissection by MFS-patients depends on aortic size and operation technique. Patients with aortic diameter less than 5cm and with hermiarch or arch replacement can be followed up safely at 12-month intervals, whereas MFS-patients with large aneurysms greater than 5 cm and only aortic root or/and aortic ascending replacement in the initial surgery should be monitored at radiographic intervals of 6 months or less.

We conclude that MFS-patients seem to benefit from initial total arch replacement with elephant trunk or frozen elephant trunk techniques. Furthermore we recommend rigorous adjustment of systolic blood pressure below 120 mmHg and postoperative medical treatment including ß-blockers and ACE-inhibitors in MFS-patients.

Appendix A

Figure 1. Kaplan–Meier survival curve of MFS-patients after aortic surgery.

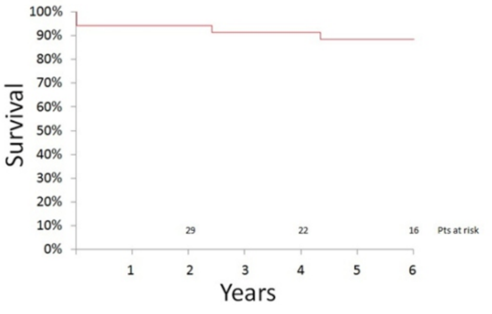


Figure 2. Kaplan–Meier curve demonstrating freedom from re-operation/re-intervention after surgery in MFS-patients.

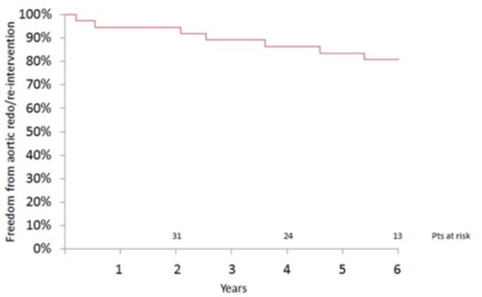
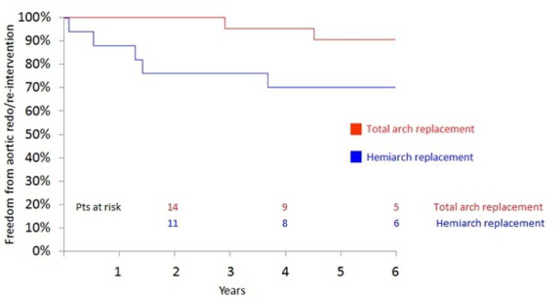


Figure 3. Kaplan–Meier curve demonstrating the difference of freedom from re-operation/re-intervention between MFS-patients undergoing total aortic arch replacement and hemiarch replacement.



Appendix B

Table 1: Patient Characteristics

Characteristic	
N (%)	
Number of patients	36 (100%)
Acute type A dissection	14 (39%)
Aortic aneurysm	22 (61%)
Age (years ± SD)	37 ± 17
Male	27 (75%)
Arterial hypertension	14 (39%)
chronic obstructive pulmonary disease	2 (6%)
Aortic valve regurgitation ≥2°	12 (33%)
Aortic valve stenosis	1 (3%)
Mitral valve regurgitation	7 (19%)
Coronary artery disease	3 (8%)
Preoperative neurologic dysfunction	3 (8%)
Previous cardiac surgery	2 (6%)
Previous aortic surgery	5 (14%)
Preoperative treatment with ß-Blockers	17 (47%)
Preoperative treatment with ACE-Inhibitors	11 (31%)

Table 2: Operative Data and Surgical Procedures

Variable	N (%)
Cardiopulmonary bypass time (min)	170 ± 71
Crossclamp time (min)	92 ± 64
Partial upper sternotomy	12 (33%)
Median sternotomy	24 (67%)
Isolated ascending replacement	5 (14%)
Hemiarch replacement	14 (39%)
Total arch replacement	17 (47%)
Elephant trunk technique	10 (28%)
Frozen elephant trunk technique	3 (8%)
David procedure	9 (25%)
Bentall procedure	8 (22%)
Yacoub procedure	3 (8%)
Aortic valve replacement	2 (6%)
Coronary artery bypass grafting	2 (6%)
Mitral valve reconstruction	3 (8%)

Table 3: Details of cerebral perfusion and temperature management

Variable	N (%)
Antegrade cerebral perfusion	31 (86%)
Antegrade cerebral perfusion time (min)	48 ± 25
Antegrade cerebral perfusion flow (L/min)	1.4 ± 0.3
Unilateral antegrade cerebral perfusion	21 (58%)
Bilateral antegrade cerebral perfusion	10 (28%)
Perfusate temperature (°C)	29.1 ± 0.6°C
Perfusion pressure during Antegrade cerebral perfusion (mm Hg)	75
Core temperature (°C)	28.8 ± 0.7

Table 4: Perioperative mortality and morbidity

Variable	N (%)
Intensive care unit stay (day)	3 ± 4
Ventilation time (hour)	17 ± 12
Chest tube drainage (ml/24h)	479 ± 251
Reexploration for bleeding	3 (8%)
Hospital length of stay (day)	7 ± 6
Thirty-day mortality	2 (6%)
Transient neurologic deficit	4 (11%)
Temporary delirium	3 (8%)
Transient motor deficit	1 (3%)
Permanent neurologic deficit	1 (3%)
Stroke	1 (3%)

REFERENCES

1. Ahimastos AA, Aggarwal A, D'Orsa KM, Formosa MF, White AJ, Savarirayan R, Dart AM, Kingwell BA. (2007). Effect of perindopril on large artery stiffness and aortic root diameter in patients with Marfan syndrome: a randomized controlled trial. JAMA 298(13):1539-47.
2. Aybek T, Sotiriou M, Wöhleke T, Miskovic A, Simon A, Doss M, Dogan S, Wimmer-Greinecker G, Moritz A. (2005). Valve opening and closing dynamics after different aortic valve-sparing operations. J Heart Valve Dis. 14:114–20.
3. Bachet J, Larrazet F, Goudot B, Dreyfus G, Folliguet T, Laborde F, Guilmet D.(2007). When should the aortic arch be replaced in Marfan patients? Ann Thorac Surg 83(2):774-9.
4. Bentall H, De Bono A. 1968. A technique for complete replacement of the ascending aorta. Thorax 23:338–9.
5. Birks EJ, Webb C, Child A, Radley-Smith R, Yacoub MH. 1999. Early and long-term results of a valve-sparing operation for Marfan syndrome. Circulation 100:II-29–II-35.
6. Brooke BS, Habashi JP, Judge DP, Patel N, Loeys B, Dietz HC 3rd. (2008). Angiotensin II blockade and aortic-root dilation in Marfan's syndrome. N Engl J Med 358(26):2787-95.
7. David TE, Feindel CM. 1992. An aortic valve-sparing operation for patients with aortic incompetence and aneurysm of the ascending aorta. J Thorac Cardiovasc Surg 103:617–22.
8. DeBakey ME, McCollum CH, Crawford ES, Morris GC Jr, Howell J, Noon GP, Lawrie G.(1982). Dissection and dissecting aneurysms of the aorta: twenty-year follow-up of five hundred twenty-seven patients treated surgically. Surgery 92: 1118–1134.
9. El-Sayed Ahmad A, Papadopoulos N, Detho F, Srndic E, Risteski P, Moritz A, Zierer A.(2015). Surgical repair for acute type A aortic dissection in octogenarians. Ann Thorac Surg 99:547–51.
10. El-Sayed Ahmad A, Papadopoulos N, Risteski P, Moritz A, Zierer A.(2017). The Standardized Concept of Moderate-to-Mild (≥28°C) Systemic Hypothermia During Selective Antegrade Cerebral Perfusion for All-Comers in Aortic Arch Surgery: Single-Center Experience in 587 Consecutive Patients Over a 15-Year Period. Ann Thorac Surg. 104(1):49-55.
11. El-Sayed Ahmad A, Risteski P, Papadopoulos N, Radwan M, Moritz A, Zierer A. (2016). Minimally invasive approach for aortic arch surgery employing the frozen elephant trunk technique. Eur J Cardiothorac Surg 50(1):140-4.
12. Groenink M, Lohuis TA, Tijssen JG, Naeff MS, Hennekam RC, van der Wall EE, Mulder BJ. (1999). Survival and complication free survival in Marfan's syndrome: implications of current guidelines. Heart 82(4):499-504.
13. Januzzi JL, Marayati F, Mehta RH, Cooper JV, O'Gara PT, Sechtem U, Bossone E, Evangelista A, Oh JK, Nienaber CA, Eagle KA, Isselbacher EM. (2004). Comparison of aortic dissection in patients with and without Marfan's syndrome (results from the international Registry of Aortic Dissection). Am J Cardiol 94:400–2.
14. Karck M, Kallenbach K, Hagl C, Rhein C, Leyh R, Haverich A.(2004). Aortic root surgery in Marfan syndrome: Comparison of aortic valve-sparing reimplantation versus composite grafting. J Thorac Cardiovasc Surg 127(2):391-8.
15. LeMaire SA, Carter SA, Volguina IV, Laux AT, Milewicz DM, Borsato GW, Cheung CK, Bozinovski J, Markesino JM, Vaughn WK, Coselli JS.(2006). Spectrum of aortic operations in 300 patients with confirmed or suspected Marfan syndrome. Ann Thorac Surg 81: 2063–2078.
16. Patel ND, Weiss ES, Alejo DE, Nwakanma LU, Williams JA, Dietz HC, Spevak PJ, Gott VL, Vricella LA, Cameron DE. (2008). Aortic Root Operations for Marfan Syndrome: A Comparison of the Bentall and Valve-Sparing Procedures. Ann Thorac Surg 85:2003–11.
17. Pepe G, Giusti B, Sticchi E, Abbate R, Gensini GF, Nistri S. (2016). Marfan syndrome: current perspectives. Appl Clin Genet. 9:55-65.
18. Rahnavardi M, Yan TD, Bannon PG, Wilson MK. (2011). Aortic valve-sparing operations in aortic root aneurysms: remodeling or reimplantation?. Interact Cardiovasc Thorac Surg 13(2):189-97.
19. Sarsam MA, Yacoub M. (1993). Remodeling of the aortic valve annulus. J Thorac Cardiovasc Surg 105:435-8.
20. Tahernia AC. (1993). Cardiovascular anomalies in Marfan's syndrome: the role of echocardiography and beta-blockers. South Med J 86(3):305-10.
21. Zierer A, El-Sayed Ahmad A, Papadopoulos N, Detho F, Risteski P, Moritz A, Diegeler A, Urbanski PP.(2017). Fifteen years of surgery for acute type A aortic dissection in moderate-to-mild systemic hypothermia. Eur J Cardiothorac Surg 51(1):97-103.
22. Zierer A, El-Sayed Ahmad A, Papdopoulos N, Mortiz A, Diegeler A, Urbanski PP. (2012). Selective antegrade cerebral perfusion and mild (28C-30C) systemic hypothermic circulatory arrest for aortic arch replacement: results from 1002 patients. J Thorac Cardiovasc Surg 144:1042–50.
23. Zierer A, Risteski P, El-Sayed Ahmad A, Moritz A,Diegeler A, Urbanski PP. (2014). The impact of unilateral versus bilateral antegrade cerebral perfusion on surgical outcomes after aortic arch replacement: a propensity-matched analysis. J Thorac Cardiovasc Surg 147:1212–8.
24. Zierer A, Voeller RK, Hill KE, Kouchoukos NT, Damiano RJ Jr, Moon MR. (2007). Aortic enlargement and late reoperation after repair of acute type A aortic dissection. Ann Thorac Surg 84(2):479-86.