The Preventive Surgery of Proximal Aortic Manifestations in Marfan Syndrome

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Background: Marfan syndrome (MFS) is a genetic connective tissue disease with an incidence of 2–3/10000 individuals resulting in multiple organ system affection, aortic dilatation, dissection and rupture the most severe cardiovascular complications according to natural history. These consequences can be prevented by prophylactic aortic surgery.
Methods: Results are presented of patients (N=22; mean age: 26.95±9.01, min: 9; max: 42; male/female ratio=16/6) underwent elective preventive surgery over a 11 years period.
Results: Preventive operations have zero 30 days mortality and still the best results in approaching normal population life extent compared to the survival of other indication groups. Secondary vascular complications should be monitored life-long after the succesful treatment of the diseased thoracic aorta of Marfan patients due to the systemic property of the extant syndrome.
Conclusions: After identifying the condition and registering people with MFS in a national database, the regular check-ups, preventive operations bear great importance. Timing is crucial for the preventive operation, because the underlying disease (MFS) exposes the aorta to be a "ticking" bomb that can lead to serious consequences like aortic dissection or rupture with possible fatal outcome. Preventive aortic operations at MFS patients enjoy the benefitial outcomes and nature of the management compared to other acute type, emergency or urgent operations. The effective prevention lays on carrying out the prophylactic surgery together with the continuous check-up of the predisposed and operated patients by the help of a professional nationwide register for people with MFS that, if not created yet, should be established as well.

Keywords: Marfan syndrome, aortic root, preventive surgery, prophylaxis

Introduction

Marfan syndrome (MFS) is a genetic connective tissue disease with an incidence of 2–3/10000 individuals resulting in multiple organ system affection, and aortic dilatation, dissection and rupture, the most severe cardiovascular complications according to the natural history [1]. Marfan's syndrome cannot be prevented but it is possible with early detection to watch for cardiovascular manifestations and treat, manage medically and apply the recommended preventive surgical therapy. These complications of the syndrome are mostly localized on the ascendent aorta, may on the aortic arch and descendent part in the thorax whereas the field of the intervention mainly belongs to cardiac, thoracic surgery specialists [2].

Objective

The aim of this article is to demonstrate the significance of the elective prophylactic surgery of cardiovascular complications in Marfan syndrome affecting the aorta and to emphasize the regular cardiologic control of the aorta. Demographics, perihospital care, indications for surgery, operation techniques, methods, survival and outcomes of the timed surgery performed are presented. Evaluation is made with particular highlights focusing on surgical prevention in the following parts. The main columns of the writing are primarily based on preventive aortic reconstruction, replacement according to the disease-involved part of the aorta.

Material and methods

Over an 11 years period 22 Marfan patients have been operated electively with preventive indication from 1999 to 2010 in the Department of Cardiac Surgery, Semmelweis University, Budapest, Hungary. Mean age of patients was 26.95±9.01 years, varying between 9 and 42 years, regarding gender distribution, there was a shifting towards male (16/22; 73%) versus female (6/22; 27%). All operations were carried out as timed elective aortic root reconstruction with prophylactic modality. The mean EuroScore value for the indicational group was 5.23±1.09.

Clinical diagnosis of Marfan's syndrome was established based on Ghent criteria. Eighteen out of the 22 patients (82%) were diagnosed with MFS previously and taking part in cardiologic follow-ups. Four patients (18%) were aware of the disease but were not under regular medical control and admitted to hospital based on symptoms and complaints. Family history was positive at 12 patients for aortic dissection at least at one member, parent or sibling (12/22; 54.5%). Skeletal and cardiovascular features were present at all patients (22/22; 100%), while ocular features (ectopic lenses, retineal detachment) at six patients (6/22; 27%) and pulmonary symptoms (spontaneous pneumothorax in childhood) at a 40 year old female (1/22; 4.5%). Furthermore two patients have been observed due to previous Stanford type B aortic dissection (2/22; 9%).

Regarding additional risk factors, alcohol abuse was present at two patients (2/22; 9%), nicotine abuse at three patients (3/22; 13%) and hypertension present at seven patients (7/22; 32%) treated with beta blockers and angiotensin II receptor antagonists.

Aortic complications in Marfan's requiring surgical intervention are pathologic dilatation of the great vessel, annulo-aortic ectasia, dissection, pseudoaneurysm due to

Table I. MFS patients in the indicational subgroups for elective prophylactic aortic surgery

Subgroups of indicating prophylactic aortic surgery in MFS	Patient No.	Percentage
I: (40 mm ≤ aortic bulb diameter + positive family history)	6	27.3 %
II: (50 mm ≤ aortic bulb diameter)	12	54.5 %
III: (40 mm ≤ aortic bulb diameter ≤ 50 mm + a 5 mm/year growth)	4	18.2 %
Total	22	100 %

various causes, aortic valve insufficiency and regurgitation [1].

Aortic dilatation occurs in about 75–85% of the patients, it may be asymptomatic but can cause regurgitational murmur, secondary congestive cardiac failure, superior vena cava syndrome, dyspnea, caughing, haemoptysis, recurrent pneumonia (due to tracheal compression and dislocation), dysphagia (due to esophagus compression), hoarseness (by explicating pressure on the recurrent laryngeal nerve), chest pain in 37% of the cases and back pain at 21% of the patients [3].

Regurgitation through the aortic valve goes at the beginning unsymptomatically, later paplpitation, tiredness, angina pectoris and at the end stage heart failure can develop. Heart murmurs can help on establishing the diagnosis [4]. Physically, diastolic regurgitational murmur was described at six, while systolic at one patient totalling 32% of the whole patient count.

The aorta is not only a structural but dynamic element as well of the circulatory system with conduiting and modulational functions [3]. The appropriate application of any surgical or other treatment should depend on the estimation of medically induced advantages, risks and disadvantages compared to the natural course of the specific disease. If left untreated, the history of certain diseases (dilatations, aneurysms, dissections) on the thoracic aorta often concludes with patient death [5].

The timed preventive surgery was initiated in cases of the following indicational subgroups to prevent further potential lethal cardiovascular consequences of MFS:

- If the diameter of the aortic bulb (measured at the level of the sinus of Valsalvae) reaches 40 mm and family history of the patient is positive for aortic dissection (Subgroup I), or
- in every case when the diameter of the aortic bulb reaches or exceeds 50 mm (Subgroup II), or
- the diameter value of the aortic bulb is measured between 40 and 50 mm in every case if the dilatation rate of the bulb reaches or exceeds 5 mm per year (Subgroup III), elective prophylactic aortic root surgery is indicated [11] (Table I).

Imaging techniques used for mapping the dimensions of the aorta and function of the aortic valve were transthoracal echocardiography (TTE) and computer tomography (CT). Average aortic bulb diameter size was 50.54±7.29 mm. To measure proper functional intactness and sparability of the aortic valve, transesophageal echocardiography (TEE) examinations have been conducted. Physiologic or mild (Grade 0 and I) aortic valve insufficiency, regurgitation were present at 11 patients (11/22; 50%), moderate (Grade II) regurgitation at eight patients (8/22; 36.4%), moderately severe (Grade III) at two patients (2/22; 9%) and severe aortic regurgitation was present at one patients (1/22; 4.5%).

Results

To repair the ascendent aorta — according to the involvement of the valve and root, mostly Bentall procedures have been performed (17/22; 77%), when the mitral valve also involved in two cases replacement of the valve and Bentall operation was done (2/22; 9%) [6]. Bentall procedure with aortic arch replacement was done in one case out of 22 (4,5%). Tirone David aortic valve-sparing operation was carried out in 2 cases (2/22; 9%) [7]. Bentall procedures have been performed with the use of composit grafts in 19 cases (86.4%), in one case at a 21 years old female, biological valve has been implanted. Coronary artery reimplantation was done with button technique in 9 cases (40.9%).

Femoral artery cannulation for extracorporeal bypass circulation (ECC) during the surgery was used in five cases (5/22; 22.7%) while aortic cannulation as arterial endpoint for the ECC in 17 cases (77.3%). As for perfusion time, the following data were counted for the 22 operations divided into femoral and aortic arterial groups. In the femoral group average operation (OP) time was 280±40.16, extracorporeal circulation (ECC) time was 192±38.18, aortic clamping (Ao clamp) time was 101.4±22.13 and total circulatory arrest (TCA) time was 14±4.83 minutes. In the aortic group average operation time was 239.06±48.48, extracorporeal circulation time was 151.56±41.64, aortic clamping time was 127.25±34.70 (Figure 1, 2). Cannulation associated tem-

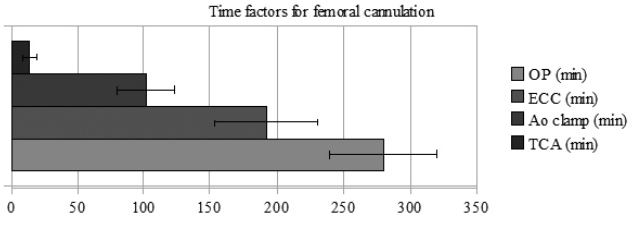

Fig. 1. Time factors for femoral artery cannulation in minutes

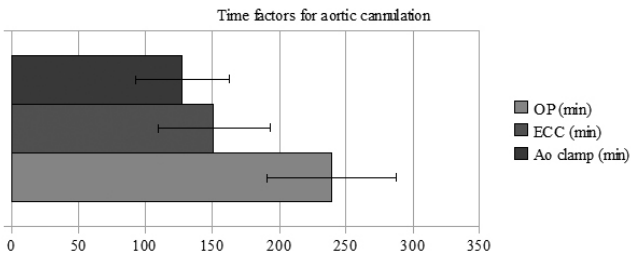

Fig. 2. Time factors for aortic cannulation in minutes

Table II. Listing of the general consensual surgical paradigms regarding proximal aorta operations

Planned operation with electivity; the application of the requirements of open heart surgery
Extracorporeal circulation (cardiopulmonary bypass); considering the total surgery, pump and circulatory arrest time; pre-, intra- postoperative monitoring
Avoidance of cerebral complications, minimizing risk factors
Antibiotics, antithrombotics, neuroprotection, myocardium protection and the corresponding specific treatments
Supportive, drug therapy, controlled hemodynamics

perature was in the femoral group 18.25±6.24 °C and in the aortic artery group 32.5±1.73 °C.

When going off the ECC pump, to start the heart in 13 cases (59%) was needed defibrillation in average 1.85±0.99 times when the temperature was 33.25±1.51 °C. Glue was used in 5 cases to protect the sutures of the aortic wall (5/22; 22.7%), while for protection of the distal anastomoses in nine cases a vascular graft left-over was used as a protective ring against bleeding or distal anastomosis dilatation according to Szabolcs (9/22; 40.9%) [8].

Reoperations occurred only at two patients, at a 18 years old male due to postoperative bleeding, the surgical source was found to be at the sternum wires pin through and at a 17 years old male on the 16th postoperative day pericardial puncture was done due to increasing pericardial fluid. At a 42 years old female operated due to severe annulo-aortic ectasia and aortic regurgitation grade III with 8 EuroScore points, postoperatively intra-aortic balloon pump had to be used to provide mechanical and additional pharmacological circulatory support.

Average postoperative time spent on the surgical intensive care unit was 2.9±1.1 days while the mean value of overall postoperative hospitalization duration was 12.5±3.6 days. There was no postoperative mortality in the first 30 days. All patients were sent to cardiac rehabilitation institute for recovery after the surgery procedure. Drugs used at emission were mainly acenocumarol, beta blockers, calcium channel blockers, angiotensin converting enzyme inhibitors and - II receptor blockers plus non-steroid anti-inflammatory agents to relieve postoperative pain.

Discussion

Primary prevention orientates towards preserving and promoting the development of health. Secondary prevention focuses on screening diseases and early detection, tertiary prevention is about inhibiting deterioration and improving life quality of patients with chronic disease. Preventive operations are secondary type of prevention, while medical management by using anti-hypertensive drugs may refer to primary or secondary type of prevention – depends on the viewpoint of the avoided event. General requirements of aortic surgery are listed in the following table below (Table II).

In the strategy of surgical prevention of aortic dissection (AD) and aortic rupture (AR) in case of root dilatation, certain diagnostic and therapeutic algorithms are followed:

For screening purposes the different sizes of the aortic root are obtained through 2-Dimensional echocardiography. Preventive operations are carried out in the following group of indications: escalation of the symptoms, complaints; widening of the mediastinal shadow; the premature signs of rupture; growing aortic insufficiency; increasing severity of angina symptoms and vascular neurological signs. Aortic root dilatation in case going with complaints for the patient is an aggressive surgical indication. Surgery is indicated if the dilatation goes without complaints and the aortic root size at the level of the bulb is over 50 mm or between 40 and 50 mm and any of the following occurs: dissection in family history, a yearly growth rate reaching or exceeding 5 mm in measured diameter, mitral insufficiency of IIIrd, IVth grade or when patient is before pregnancy. In other recommendations the aortic root size, diameter of annulus and Valsalvae sinus, sinotubular junction and their ratios play a role in setting up the indication for surgery [9,2].

Dilatation exceeding the person's normal aortic section twice is regarded as pathologic ascendent aortic dilatation. Prophylactic surgery is suggested in the case as well, when the dilatation reaches or passes in the sinotubular junction value of 45 mm or in case of positive family anamnesis for AD or when the growth rate of the dilatation in the last half-one year is – confirmed with imaging methods – reached or passed 5 mm.

Evaluating the „best bet" methods for preventive aortic operation in Marfan patients is approximated on the basis of general experience and the use of own material besides the guidance of other authors comments articles but the final decision remains always offered to the person being operated. Mechanical valve with vascular graft or composit conduit implantation is suitable for most of the patients while if possible, anticoagulation is avoided by keeping original valve structure when left untouched by the underlying condition. For young female or female still in the fertility period or in case of known planned pregnancy it is advisable to implant biological valve or biological valve bearing conduit [10]. Coronary artery reimplantation if done with the button technique, decreases later local complications [8].

As for operation technique, aortic cannulation is preferable to femoral if possible, because the duration of the operation and extracorporeal perfusion is shorter, there is no need for recannulating the arterial access point and systemic normorthermic operations can be performed. Myocardial protection is locally done with permanent or fractioned cooling.

Complications of the basis disease and surgical intervention on the thoracic aorta necessitates post-operative monitoring and life-long follow-up in Marfan-syndrome. Short term complications include acute surgery induced general (eg. infections) and specific problems (eg. methodical, technical consequences, surgical bleeding, impact of cardiac surgery on the central nervous and other organ sys-

tems). Secondary vascular complications should be monitored life-long after the succesful treatment of the diseased thoracic aorta of Marfan patients due to the systemic property of the extant syndrome [8].

Preventive operations have zero 30 days mortality and still the best results in approaching normal population life extent compared to the survival of other indication groups [8].

Watching for secondary late vascular complications at preventive operations, echocardiographic control is recommended every 3 months in the first year then yearly. Spiral-CT and magnetic resonance imaging (MR) control is advised every 2–3 years. Screening and follow-ups were conducted by the National Marfan Foundation (leader: Z. Szabolcs) [11].

Conclusions

Identifying the condition and registering people with MFS in a national database, the regular check-ups, preventive operations are important. First of all health preservation, the change of lifestyle (quit smoking, avoiding straining movements, managing hypertension), certain medications (beta blockers, certain types of angiotensin receptor blocking anti-hypertensive drugs) can help to restrain the progression of the disease regarding the aorta.

Timing is crucial for the preventive operation, because the underlying disease (MFS) exposes the aorta to be a "ticking" bomb that can lead to serious consequences like aortic dissection or rupture with possible fatal outcome. When to apply surgery is signaled according to indication criteria.

Preventive aortic operations at MFS patients enjoy the benefitial outcomes and nature of the management compared to other acute type, emergency or urgent operations done on the aorta in patients affected by the syndrome.

The effective prevention of monitored patients lay on carrying out the prophylactic surgery together with the continuous check-up of the predisposed and operated patients by the help of a professional nationwide register for people with MFS that, if not created yet, should be established as well.

References

1. Judge DP, Dietz HC – Marfan's syndrome. Lancet 2005, 366: 1965-1976.
2. Judge DP, Dietz HC – Therapy of Marfan syndrome. Annu Rev Med 2008, 59: 43–59.
3. Deac R – Chirurgie cardiovasculară bazata de probe, in: Deac R (ed): Chirurguie Cardiovasculară. Ed. Acad. Bucureşti, 2009, vol VII: 41–61.
4. Aburawi EH, O'Sullivan J – Relation of aortic root dilatation and age in Marfan's syndrome. Eur Heart J 2007, 28: 376–379.
5. Gaşpar M – Aneurizmele si disectiile aortei ascendente şi ale arcului aortic. Tratament chirurgical. Ed. Mirton, Timişoara, 2001.
6. Bentall H, de Bono A – A technique for complete replacement of the ascending aorta. Thorax 1968, 23: 338–339.
7. David TE, Armstrong S, Maganti M, et al. – Long-term results of aortic valve-sparing operations in patients with Marfan syndrome. J Thorac Cardiovasc Surg 2009, 138: 859–864.
8. Szabolcs Z – A Marfan-syndroma szívsebészeti vonatkozásai. Habilitációs Tézis. Semmelweis Egyetem, Budapest, 2010
9. Ates M – When should we replace the ascending aorta in Marfan syndrome? Eur J Cardiothorac Surg 2007, 31: 331–332.
10. Cameron DE, Alejo DE, Patel ND, et al. – Aortic root replacement in 372 Marfan patients: evolution of operative repair over 30 years. Ann Thorac Surg 2009, 87: 1344–1349.
11. Szabolcs Z, Bíró G, Hüttl K, et al. – Secunder late vascular complications after aortic root reconstruction in Marfan patients, Cardiologia Hungarica 2008, Suppl H: 16.