Presentation and outcome of Marfan’s syndrome patients with dissection and thoraco-abdominal aortic aneurysm

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Abstract

Background: In Marfan’s syndrome, there is a paucity of data regarding intervention criteria for surgery of the dissected thoraco-abdominal aorta. Methods: A retrospective analysis of 22 Marfan’s patients with distal aortic dissection managed between September 1999 and April 2006 was performed. Serial diameters and linear expansion rates were calculated from imaging studies and the outcome of intervention was analysed. Results: There were 14/22 male patients (median age 38 years), and 18 had prior aortic surgery. Surgery was recommended in 20 patients and undertaken in 19 (1 died prior to operation). Of the operated patients, 2 presented with rupture, 2 with airway obstruction, 1 with intermittent paraplegia and 14 underwent planned surgery for increased expansion rate or pain. All patients had residual type A or chronic type B dissection. The median aortic dimension at surgery was 6.7 cm (interquartile range (IQR) 5.5—8.2). The preoperative mean expansion rate increased from 0.5 cm/year to 1.7 cm/year (*p < 0.001), prior to operation. Fifteen patients underwent Crawford Extent II, two underwent Extent I and two underwent Extent III repair. Profound hypothermia and CSF drainage was used in 16 and 18 patients, respectively. There was no early mortality, paraplegia or renal failure. At a median postoperative follow-up of 56 months (range 6—86), the survival of the operated cohort was 90%. Conclusions: Thoraco-abdominal aortic aneurysm repair in Marfan’s syndrome can be performed with good outcomes. Intervention should be based on size or accelerated expansion. Any role of endovascular management needs careful consideration.

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Keywords: Aorta; Aneurysm; Surgery; Imaging

1. Introduction

In Marfan’s syndrome (MFS), the dominant vascular pathology affects the ascending aorta [1]. Although β-receptor antagonists may slow expansion of the ascending aorta [2], the majority with aortic root dilatation ultimately require surgery [3]. This proximal aortic surgery comprises composite valve-graft or valve-sparing aortic root replacement, and both have produced excellent long-term outcomes with approximately 80% 10-year survival [1,4,5]. The life expectancy of MFS patients has consequently improved dramatically. Between 1972 and 1995, the median (50%) cumulative probability of survival was extended from 48 years to 72 years [6]. However, a fraction of patients experience continuing distal aortic enlargement and aneurysm formation, which may progress to rupture and death [7], (Fig. 1). While there is abundant literature regarding proximal aortic procedures in MFS, there are little data on the progression and management of distal aortic complications [4,5,8—10]. In this study, we report a consecutive series of MFS patients with distal dissection.

2. Patients and methods

We retrospectively reviewed the prospectively collected data of 22 consecutive MFS patients with residual type A or type B dissection managed between September 1999 and April 2006 at a single institution. All patients satisfied the criteria of the current Ghent nosology for MFS diagnosis [11]. Demographic and clinical data were retrieved, and all available serial imaging studies (computerised tomography and magnetic resonance imaging) were analysed. The short axis aortic diameter of the maximally dilated aortic segment was measured with a previously validated calliper method [12]. This allowed calculation of a linear expansion rate per
In order to describe the relative contribution of false and true luminae-to-aneurysm growth, we measured the diameter of the true and false luminal channels in a varying plane perpendicular to the central site of the intimal flap at four levels (Level 1, the upper descending aorta; Level 2, the bifurcation of trachea; Level 3, the lower edge of left atrium and Level 4, origin of coeliac artery).

2.1. Operative technique

In operated patients, the technique, in brief, comprised full haemodynamic monitoring, single lung ventilation and cerebrospinal fluid (CSF) drainage. Cardiopulmonary bypass (CPB) was instituted via using left common femoral arterial return and vacuum-assisted left femoral venous drainage using a 28–32F cannula advanced to the right atrium by an open Seldinger technique. In non-ruptured patients, full preparatory dissection preceded CPB. The aneurysm was exposed through a left thoraco-laparotomy with chest entry via the fourth and seventh interspaces. The lower interspace incision was extended trans-costally and advanced distally along the linea alba. Patients were cooled to a nasopharyngeal temperature nadir of 15°C. Proximal open arch anastomoses were constructed in a 15° Trendelenberg position during a period of hypothermic circulatory arrest (HCA) with head packing in ice. Following distal arch transection at the appropriate level and proximal fenestration if necessary, a gelatine-impregnated polyester graft (Gelweave Vascutek Anteflo; Sulzer Vascutek, Renfrewshire, UK) was anastomosed using Teflon buttressing. Proximal perfusion was recommenced via a graft side arm. Where possible, a distal clamp was moved sequentially down the aorta to maintain lower body flow, but in most cases distal corporeal arrest was necessary. The anastomosis of a T7-11 intercostal aortic patch was followed by sequential reperfusion. A distal anastomosis (aortic bifurcation or bi-iliac) using a separate graft preceded visceral anastomoses to restore hypogastric flow. Following intercostal and hypogastric reperfusion re-warming was initiated. The visceral and renal vessels were then sequentially attached to the graft either as patches or more recently using a specific multi-branched graft (Gelweave Coselli, Sulzer Vascutek, Renfrewshire, UK). The bypass was discontinued at 36°C. One Extent I and two Extent III repairs were accomplished using CPB without HCA. Cell salvage was used throughout and CSF drainage maintaining CSF pressure ≤10 mmHg continued for 48 h.

2.2. Data presentation and statistics

Descriptive data are presented numerically or as percentages. Continuous data were assessed for normality and presented as mean (95% confidence limits (95% CL)) or median (interquartile range (IQR)). Comparisons were undertaken using non-parametric analysis (Mann–Whitney U-test). Graphical data are presented as mean ± standard error (SEM). Data were analysed using SPSSv12.0 (SPSS; Chicago, IL). The authors had full access to the data and take responsibility for their integrity. All authors have read and agreed to the manuscript as written.

3. Results

3.1. Presentation

There were 22 patients (14 male) with a median age of 38.5 years (range 23–61). All patients had residual type A (n = 3) or type B dissection (n = 19) with a prior presentation of acute type B dissection in seven patients. Eighteen had undergone prior surgery (10/18 performed in other institutions) (Table 1). No type A dissection patients had undergone arch replacement at initial repair, although two had undergone subsequent arch replacement prior to TAA surgery. One patient had stent aortoplasty of distal arch and proximal descending aorta for acute type B dissection in another institution and presented with a pain due to a type I endoleak with marked expansion and imminent rupture, and required concomitant total arch replacement. One patient underwent emergency partial gastric resection for gastric necrosis due to coeliac axis malperfusion and remains under surveillance for a 4.5 cm aneurysm. Twenty patients were under surveillance follow-up and surgery was recommended in all for new symptoms of pain (n = 5), airway obstruction (n = 2), intermittent paraparesis (n = 1) or accelerated expansion (n = 9). Three patients ruptured following a recommendation for surgery, of which one died out of hospital and two underwent emergency repair (Fig. 2). Thus, surgery was undertaken in 19 patients of whom 15 patients underwent Crawford Extent II, 2 underwent Extent I and two Extent III repair.

3.2. Operative details and outcomes

All Extent I and II patients (17/19) underwent surgery utilising profound hypothermia and circulatory arrest. Two
Extent III patients underwent repair utilising partial cardiopulmonary bypass and aortic clamping. The mean CPB and HCA were 246 min (95% CL 217—278) and 21 min (95% CL 16—24), respectively. The mean intercostals, hypogastric, visceral and renal ischaemic times (°C) were 40 min (95% CL 34—46), 51 min (95% CL 34—69), 92 min (95% CL 38—167) and 86 min (95% CL 32—139), respectively. There was no 30-day mortality, paraplegia or paraparesis. No patients required renal support, but the maximum creatinine (days 1—7) was 154 μmol l⁻¹ (95% CL 132—176) compared to a preoperative value of 95 μmol l⁻¹ (95% CL 88—103) (p < 0.001). Two patients required re-exploration for bleeding and one patient required revision of the superior mesenteric artery anastomosis for thrombosis. Inotropic support (>48 h) was required in four, and five patients were ventilated for greater than 48 h, two of whom required tracheotomy. One patient suffered a small frontal lobe infarct manifest as status epilepticus but recovered to full employment at 6 months. Two patients had transient confusion postoperatively. The median intensive care stay was 8 (IQR 7—9) days and median hospital stay was 19 (IQR 17.5—25.2) days.

One patient with severe kyphoscoliosis died at 7 months postoperatively with bronchopneumonia and a further patient died at 5 years following repeat aortic and mitral valve replacement for xenograft failure. There have been five late interventions, two aortic arch replacement for asymptomatic expansion, one redo AVR and MVR, one internal iliac artery aneurysm coiling and two incisional hernia repairs. At a median postoperative follow-up of 56 months (range 6—86), the survival of the operated cohort is 90%. All previously employed patients have returned to work.

### 3.3. Aneurysm size and expansion

Twenty patients were under surveillance with a median follow-up of 50 months (IQR 17—145). The mean short axis diameter at the time of surveillance initiation was 3.60 cm (95% CL 3.27—3.93), increasing to 5.86 cm (95% CL 5.24—6.49) (p = 0.055) after a median interval of 2.35 (IQR 2.3—5.0) years. At the time of recommendation for surgery the mean diameter had risen to 6.78 cm (95% CL 6.30—7.65) (p < 0.001) (Fig. 3).

Three asymptomatic patients aged 35, 61 and 30 years ruptured in the interval between recommendation and operation with aortic dimensions of 7.65, 8.0 and 9.1 cm, respectively. The preoperative mean linear expansion rate increased from 0.5 cm/year (95% CL 0.4—0.6) to 1.7 cm/year (95% CL 1.1—2.2) (p < 0.001), in the last interval (0.8 years) prior to operation (Fig. 4). The increase in expansion rate in the penultimate interval prior to this was not significant (p = 0.407). The accelerated rate of expansion prompted the

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**Table 1**

<table>
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<th>Age (years)</th>
<th>Sex</th>
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<th>Indication</th>
<th>Maximum size (cm)</th>
<th>Extent</th>
<th>CPB time (min)</th>
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**Fig. 2.** Chest X-ray of a patient with ruptured TAAA showing large aortic contour, left haemothorax and rightwards mediastinal shift.
recommendation for surgery. The false-to-true lumen ratio increased abruptly in the interval prior to intervention ($p < 0.001$), but had not changed in the penultimate or previous intervals (Fig. 4). The expansion rate of the maximally dilated and dissected segment of the aorta also increased according to size. The expansion rate at a dimension of 40 mm was 0.36 cm/year (95% CL 0.22–0.47), rising to 0.64 cm/year (95% CL 0.20–1.07) for dimension 40–50 mm and 0.66 cm/year (95% CL 0.28–1.04) for dimension 51–60 mm. The expansion rate increased abruptly for dimension >60 mm, 1.42 cm/year (95% CL 1.07–1.77) ($p < 0.001$).

4. Discussion

This report demonstrates that patients with MFS and distal aortic dissection experience exponential expansion of their aorta and false lumen over time. Although aortic size per se may be an indication for operation, a change in expansion rate accompanied by an increased fractional size of the false lumen appear to be additional tools of assessment to facilitate a decision to recommend surgery in otherwise asymptomatic patients. Once surgery is undertaken, excellent outcomes can be achieved. Although the exact aortic size or expansion rate at which surgery should be recommended cannot be determined from this study, rupture occurred in 50% of asymptomatic patients with dimensions >7.0 cm but not in those with aneurysms <7.0 cm, suggesting that the current recommended criteria for intervention at 6.0–6.5 cm are satisfactory and prudent [13]. Provided such patients are subject to careful and frequent surveillance follow-up, an increase of expansion rate to $\geq 1$ cm/year, albeit assessed over a shorter time interval, can also be used as a guide to intervention. The size criteria for intervention on the distal aorta in MFS have been based largely on a consensus that the MFS aorta may rupture at a lower dimension than the non-MFS aorta. This report now adds direct evidence which supports the recommended approach [13,14].

It could be argued that our satisfactory surgical outcomes should prompt a further reduction in the dimensional criteria for operation below the recommended dimension of 6–6.5 cm or LER $\geq 1$ cm/year. Large North American aortic surgery centres recommend elective intervention in chronic MFS dissections when the diameter exceeds 4.5–5.5 cm [10]. The outstanding outcomes from such centres may justify this approach. However, such outcomes may not be generalisable to the whole cardiovascular surgical community [13] and it is axiomatic that the institutional risk of surgery remains less than the risk of rupture. LeMaire et al. reported a 2% 30-day mortality, a 1% stroke incidence and a 5% paraplegia/paraparesis incidence in 81 confirmed MFS thoraco-abdominal repairs [10], and the outcomes in the current series are comparable. However, despite this, with a small denominator, subsequent repeatability and quality control can be less assured. Outside of the larger centres, the historical reported mortality for repair of thoraco-abdominal aortic aneurysm has ranged from 10% to 42%. Paraplegia occurs in 4–32% and renal failure in 4–37% of the patients [15–18]. Thus, on this basis, our patients were counselled for a 15% mortality risk and a 10–15% paraplegia risk for Extent II repair, and several asymptomatic patients (including those who ruptured) wished for a considerable period of reflection before submitting themselves to such risk at a young age.

The life expectancy of MFS patients has improved with current medical and surgical treatment [1,6]. However, following proximal aortic surgery, particularly in the presence of chronic dissection, the risk of aneurysmal dilatation of the distal aorta is substantial. Distal aortic complications are a primary cause of late death following root surgery [3,7], and 5–35% of MFS patients require further surgery depending upon the extent of previous surgery and the rigor of follow-up [8,19]. Risk factors for late reoperations are acute or chronic dissection at the time of initial surgery, aneurysms involving major peripheral arteries, hypertension and a smoking history [20].

In patients who have previously undergone elective aortic root surgery, the aortic dimension and the rate of events in the distal aorta are increased [21].

Graft replacement of the thoraco-abdominal aorta in MFS can now be followed by excellent mid- and long-term survival.
(3,8,10,22). This survival is achieved despite the challenge of fragile aortic tissue and the operative extent of repair. If a full repair is undertaken, the 5-year freedom from repair failure is over 95% [10]. As the majority (80—90%) of such patients have chronic dissection and extensive aneurysms, limited intervention would seem likely to prejudice long-term outcomes [3,8].

Various operative techniques and spinal cord protection adjuncts have been used to repair the thoraco-abdominal aorta and excellent outcomes have been achieved using a left heart bypass technique [15,23]. We selected profound hypothermia and HCA primarily because of a perceived greater margin of safety and an unfamiliarity with left heart bypass techniques in our unit [16]. Deep hypothermia may reduce cord injury per se but was supplemented, in this series, by continuous CSF drainage as a putative adjunct. CSF drainage has been shown to enhance cord protection during left heart bypass and aortic clamping, but any additive effect in deep hypothermia remains unproven [23]. However, as perturbations of spinal cord perfusion may be responsible for early or delayed paraparesis, we have added CSF drainage (which was not associated with any complications in this series) to our practice. Future studies are necessary to define any protective role.

One of the patients in this series presented with persistent chest pain, endoleak and marked expansion of the false lumen shortly after endovascular stent aortoplasty. The use of endovascular stent grafts in patients with MFS has clear limitations. Because the entire aorta is affected by MFS, landing zones for endografts are invariably diseased and restricted to situations in which previously placed prosthetic bypass techniques in our unit [16]. Deep hypothermia may reduce cord injury per se but was supplemented, in this series, by continuous CSF drainage as a putative adjunct. CSF drainage has been shown to enhance cord protection during left heart bypass and aortic clamping, but any additive effect in deep hypothermia remains unproven [23]. However, as perturbations of spinal cord perfusion may be responsible for early or delayed paraparesis, we have added CSF drainage (which was not associated with any complications in this series) to our practice. Future studies are necessary to define any protective role.

The improved operative results and prolonged survival in patients with MFS support an aggressive surveillance and treatment approach [10]. Surgery should be undertaken prior to rupture to avoid the substantially higher risk involved. Appropriate surveillance intervals adjusted according to aneurysm size are essential to detect increased expansion rates that may signal the threshold for pre-emptive surgery. Expansion rate increases, and changes in the fractional size of the false lumen should be vigilantly assessed, as they are indicators of potential rupture. Surveillance intervals should be increased in the presence of distal dissection and perhaps a short axis dimension >5 cm. Even after total replacement of the aorta, regular surveillance should be continued to detect late aneurysm formation at anastomotic sites. It remains prudent to recommend elective graft replacement of the involved aortic segment, if the expansion rate accelerates to ≥1 cm/year, if symptoms occur or when the aorta reaches 6.0—6.5 cm in diameter [11,13], provided that the institutional risk of death and paraplegia is lower than the perceived annual risk of rupture.

References


