Endovascular treatment for Type B dissection in Marfans: is it worthwhile? A systematic review.

Davide Pacini,[a,*] Alessandro Parolari,[b,c,*] Paolo Berretta,[a] Roberto Di Bartolomeo,[a] Francesco Alamanni,[b,c] and Joseph Bavaria.[d]

[a] Department of Cardiac Surgery, S.Orsola-Malpighi Hospital, University of Bologna, Bologna, Italy

[b] Università degli Studi di Milano, Dipartimento di Scienze Cardiovascolari, Milan, Italy

[c] Unit for Clinical Research in Atherothrombosis, Centro Cardiologico Monzino IRCCS, Milan, Italy

[d] Department of Cardiovascular Surgery, Hospital of the University of Pennsylvania, Philadelphia, PA, USA

* =Both these Authors equally contributed to this paper

WORD COUNT: 5463

[*]Address for correspondence:

Alessandro Parolari MD PhD

Unit for Clinical Research in Atherothrombosis

Centro Cardiologico Monzino IRCCS

Via Parea, 4, 20138, MILANO, ITALY

Phone +39-02-580021, Fax +39-02-58011194

e-MAIL: alessandro.parolari@cardiologicomonzino.it

ABSTRACT

Marfan syndrome (MFS) is the most frequent inherited disorder of connective tissue, and is strongly associated to aortic dilatation, dissection and rupture; in these patients Type B dissection occurs substantially. It is not known whether stent grafting which is now frequently used in type B aortic dissection and descending thoracic aneurysms in non-Marfan patients, is a valuable option in Marfans, and reports from the literature are somehow sparse and sporadic. We have performed a systematic review of studies reporting the early and late results of endovascular stent grafting MFS patients with type B dissection in the attempt to quantify possible benefits or potential drawbacks of this approach in these usually very sick patients. Although associated to a low operative risk (1.9%), endovascular stent grafting in MFS patients carries a substantial risk of early and late complications, mainly endoleaks and surgical conversions, and of mortality at mid-term follow-up, being complications relatively more frequent in patients undergoing endovascular stent grafting for chronic dissections; these data suggest caution against the routine use of endovascular stent grafting in these patients.

INTRODUCTION

Marfan syndrome (MFS) is the most common inherited disorder of connective tissue. It involves multiple organ systems; and the incidence of this autosomal-dominant condition is 2-3 per 10,000 individuals. The diagnosis of this syndrome, even if genetic testing is available, is still made using the Ghent criteria. MFS carries an increased risk of aortic dilatation, dissection and rupture, which are responsible for the increased mortality. The success of current medical and surgical treatment of MFS patients has substantially improved the life expectancy of affected patients. Pathological dilatation of the aortic root, namely annuloaortic ectasia, is the typical vascular lesion existing in about 75-85% of patients with MFS [1]. Open surgical treatment for this proximal aortic disease is well established with excellent long-term results [2]. However, in MFS the whole aorta is diseased and patients can experience complications everywhere in the aorta even beyond the primary surgical repair.

Endovascular treatment, which has been demonstrated to be somehow effective in type B aortic dissection and descending thoracic aneurysms in non-Marfan patients, is still under scrutiny in MFS patients [3]. In these patients such as in patients with other connective tissue disorders, the aorta is prone to dilate and, theoretically, endovascular solution may be limited in durability. In addition, the results of stent grafting in these patients are somehow sporadic and not conclusive. The aim of this study is to perform a systematic review of studies reporting endovascular repairs in MFS patients with type B dissection, in order to describe the outcomes and evaluate the practice of endovascular stent grafting in these delicate patients.

MATERIALS AND METHODS

Search Strategy

A systematic search was performed using the PubMed database to identify all studies reporting the results and evaluating the outcome of endovascular treatment of descending thoracic aortic dissections (both acute and chronic in patients with Marfan disease). Original articles, case series, and individual reports published in English language from January 2000 to November 2011 were considered, and we looked for all the studies reporting the outcome of patients who underwent endografting for descending thoracic aorta dissection in MFS. The language of the articles was defined as reported in PubMed. Unpublished data or data reported only in abstract were not included.

Three separate Boolean search strategies were employed; the first one, using the search string "Marfan AND dissection AND (endovascular OR endografting OR stent OR stenting OR graft OR grafting OR TEVAR)" was aimed to identify papers or case reports focused only on Marfans, and yielded 151 papers that were subsequently analyzed by the analysis of the abstract, and then of the full text. The second one, using the search string "Dissection AND (endovascular OR endografting OR stent OR stenting OR graft OR grafting OR TEVAR)" was aimed to identify papers reporting the results of dissections endovascular treatment which could include some Marfans in the case-mix; this search yielded 5421 papers that were assessed by the analysis of the title first, then of the abstract and of the full text (Figure 1); the last one used the search string "Marfan AND (endovascular OR endografting OR stent OR stenting OR graft OR grafting OR TEVAR) **NOT** dissection" in order to identify papers concerning the endovascular treatment of Marfan patients in case of nondissecting aortic aneurysms; this last searched yielded 237 studies which were also assessed by the analysis of the title first, then of the abstract and of the full text.

Tangential electronic exploration of related articles and manual searches of bibliographies, related journals, books and reference lists of reviews was also used, and the ability of our search strategy to identify five relevant studies was tested and found fit for purpose. In the end, 13 articles were selected for further analysis of the results of stent grafting in Marfans [4-16]; of these, four were case series of only Marfan patients [4-7], five were case series reporting stent grafting for descending thoracic aorta dissection in general but also reporting separate data on Marfan patients [8-12], whereas four were case report [13-16].

Data collection

Three authors (DP, AP, and PB) searched for the articles potentially dealing with the topic. Two investigators (DP and AP) abstracted data from all eligible studies using a standardized Excel file. Three authors (DP, AP, and PB) retrieved data on study design and size, patient demographics and in-hospital and late outcomes. No attempts have been made to obtain missing data from the authors, who were contacted only in case of possible overlapping of different case series.

Data extraction and study outcomes.

A standardized data retrieval form was created and collected data were tabulated on a spreadsheet. Data on autorship, year of publication, patient population, as well as data concerning immediate and late

outcomes were extracted from the articles. The primary end points included perioperative and late mortality, major complications, endoleaks, surgical conversions, and need of additional endovascular procedures. The outcome definitions, as well as preoperative variables definitions used by the original researchers were accepted.

Case series and case reports reporting only MFS patients were classified as focused only on MFS patients and data from these papers ("papers focused on Marfans") were reported in tables which were separated from data which could be retrieved from papers which reported data concerning stent grafting for descending thoracic aorta dissection in general which contained also some data about Marfans. These papers were classified as "papers not focused on Marfans" but reporting data also on MFS patients. We preferred to discriminate between these two categories of papers as data extracted from papers focused on Marfans were more reliable and complete with respect to data which could be mined by papers not focused on Marfans. In fact sometimes, in these latest papers it was possible to derive some results by the fact that the whole patient population did not show some kind of complication (e.g. paraplegia, endoleaks etc.); but this could have provided some degree of underestimation or the real complication rate. And for this reason, in addition to the results pooled together, the data available from both the two categories of papers, differently focused on Marfans, were reported separately. Summary data were reported as percentages (categorical data) or combined means ± combined s.d. (continuous data).

No formal analysis of study quality was performed. There was no formal funding source for this study. The authors had complete control of the search, data analysis, and writing. No other individuals were involved.

RESULTS

Endovascular stent grafting in Marfans due to aortic dissections. Ultimately 12 papers with 54 patients were identified; one paper was discarded from further analysis because of possible double publication [8]; also, as there was possible overlapping in the reports of some patients between two papers [4, 10], data concerning four patients were removed from one of the two publications [4] (data were available from the Institution of the Authors). Overall, 40 of these patients were identified from papers focused on Marfans, whereas data concerning 14 additional patients could be extracted from papers not necessarily focused on

this pathology. Overall, 11 Marfan patients (20.4%) underwent endovascular stent grafting for acute dissection, whereas 43 (79.6%) were treated for chronic dissection. Preoperative clinical features are reported on Table 1. Marfan patients undergoing stent grafting were young (40.9 ± 14.6 years old), mainly male gender (around three fourths), had previously already undergone a cardiovascular surgical procedure in the vast majority (around 80%) and one third was affected by some degree of renal failure. On average, patients with acute dissection were younger than patients with chronic dissection (31.9 vs 44.2 years, respectively); also, as expected, stent grafting was performed on an urgent/emergency priority in all acute dissection cases, and in 21% of patients with chronic dissection.

Concerning intraoperative and periprocedural clinical features of the patients population (Table 2), the average number of stents implanted was 1.65 ± 0.77, the average size was 33 ± 3.5 mm (31.6 mm in acute and 34.3 mm in chronic dissections, respectively), the proximal landing zone was in 81% of cases the native aorta and in 19% of patients a previously implanted graft; also, in 12% of cases the left subclavian artery was covered by the stent; concerning these technical variables, there were some differences between acute and chronic dissection, being left subclavian artery more frequently covered a previous aortic graft used as landing zone in acute dissections. Post-procedure endoleak rates were substantial (overall 21.6%; 16% type I, 4.4% type II, and 2.2% type III, respectively); as there were no endoleaks when the landing zone was in a previously implanted graft, the endoleak rate occurring not in graft was relatively high (29.0%); interestingly, an early endoleak occurred more frequently in case of chronic aortic dissection, being the overall rate of this complication 9/29 (31%) and 1/11 (9%) in chronic and acute dissections, respectively. As no leak occurred when the endoprosthesis was positioned in previously implanted graft, but only in native aortas, the rate of early endoleaks occurring in native aortas for acute dissections was 1/8 (12.5%) whereas in case of chronic dissection this complication occurred in 9/25 patients (31.0%), a difference that, although non statistically significant, may have some clinical meaning.

Postoperative clinical features are reported in Table 3: overall, thoracic aortic endografting in Marfans with aortic type B dissection was associated with low operative risk (1.9% in the whole patient population and 2.5% in the papers focused on Marfans) and low stroke and paraplegia rates, both between 1.9% (all papers) and 2.5% (focused papers), and relatively low surgical conversion incidences, from 3.7% (all papers)

and 5.0% (papers on Marfans); no major differences were found between acute and chronic dissections, although it has to be noted that patients presenting with acute dissections and a remarkably free of complications early postoperative course; but this, due to the low number of patients needs further confirmations. Finally, the postoperative stay of these patients was, on average, quite protracted (around 13 days).

Finally, at an average follow-up of around 2.5 years, mortality and morbidity (Table 4) were considerable. There were a total of 6 deaths with a rate of 13% in papers focused only on Marfans and 12% in all papers pooled together (it should be noted that the average age of this patient population was 41 years), and no major differences were found between acute and chronic aortic dissections. Four of the deaths were aortic-related. Both the need of new endovascular procedures and of surgical conversion were also quite high, around 16%-18% for both procedures, and also endoleak rates ranged from 18% in papers analyzing only Marfans to 16% in all papers. Interestingly, although the surgical conversion rates were similar in acute and chronic dissections, new dissection, endoleaks, and the need of a new endovascular procedure occurred only in patients presenting with chronic dissections and the rates of these complications were 16.7% for new dissection, 25% for endoleaks and 25% for the need of an additional stent grafting, respectively.

Endovascular stent grafting in Marfans due to nondissecting aortic aneurysms. The literature search concerning the results of stent grafting in case of nondissecting aortic aneurysms in Marfans yielded four studies [17-20]; of these, two were case reports [18, 19], one was a case series of 4 patients [20], whereas one was a paper not focused on Marfans but it was reporting the results of endovascular treatment of 11 complicated aortic aneurysms, of which 6 were Marfans [17]. In the end 16 patients could be collected, mainly thoracoabdominal aneurysms. The appendix reports the features of these patients, but a formal analysis of these cases was not done due to the very limited number of cases.

DISCUSSION

The treatment of thoracic aortic disease has changed radically with the advances made in endovascular therapy since the concept of TEVAR was first described 15 years ago. Many studies have demonstrated excellent outcomes of TEVAR for the treatment of TAAs, with reduced reported perioperative morbidity and mortality in comparison with conventional open repair. More recently, similar outcomes have been

demonstrated for the treatment of type B dissections, although some recent papers could not document a survival advantage or reduced complications rates at 1 and 2 years for patients with subacute or chronic type B dissection undergoing endovascular repair with respect to patients treated with optimal medical therapy [3, 10]. Much less information is available concerning the outcomes of MFS patients. Our systematic review shows that, in MFS setting, with the limits of relatively low number of treated patients and of the lack of control group (e.g. optimal medical treatment), the results of endovascular stent grafting are –at the best- suboptimal, especially when the initial presentation is a chronic dissection. Our systematic review has shown that the peri-procedural mortality rate (1.9%) may be similar or even better with respect to previous experiences performed on acute and chronic type B dissections (a recent meta-analysis performed on the results of stent grafting only in chronic Type B dissections shows a 30-day mortality rate of 3.2% [21], whereas the RESTORE patient registry reported an in-hospital mortality rate of 5% and 13% in acute and chronic dissections, respectively, all the deaths occurring in complicated type B dissections [22]). On the other hand, the incidence of periprocedural endoleaks is sensibly higher in MFS patients (21.6% in our systematic review) with respect to dissections, and even in this case this is due to the complications that occur mainly in chronic presentations. A recent meta-analysis [21] documents that, in case of aortic dissections, the incidence of this complication is about half (12%) with respect to MFS patients and in RESTORE patient registry the incidence of this complication is less than one third (7%) [22] than that of Marfans overall.

We may also speculate that, as in the MFS patients reported in our systematic review there is a very high prevalence of previous aortic surgical procedures (around 80%), an almost doubled-tripled endoleak rate is really of major concern, as we might expect that in these patients that the proximal or distal landing area of the stent grafts could be on prosthetic material from previous surgery and not on a diseased aorta, and in fact the incidence of endoleaks occurring not in grafts approached 30% in the whole patient population, being 12.5% and 36% in acute and chronic dissections, respectively. In addition, even if some other experiences report similar early endoleaks rates [3], the issue of previous CV surgery persists as previous vascular surgery that might anyway warrant less diseased landing zones.

Concerning mid-term results, the issue of high endoleak rates persists unchanged, with the addition of not

only remarkably high reoperation rates (similar in acute and chronic dissections), but also with high incidence of endovascular procedures, occurring mainly in chronic dissection patients; taken together, these findings suggest that MFS patients have suboptimal results also at mid term; in fact at an average follow-up of 2.5 years, comparable to previous reports [3, 10, 21, 22], the occurrence of this threaded complication is quite high, between 16% and 18%, and the need of a new aortic surgical procedure is also much higher, between 14% and 18%. And, also in this case, these recurrences occur even if some of the landing zones are expected to occur on prosthetic material that was implanted at previous cardiovascular operations. Finally, also the death rate at follow-up is remarkable (12%) if we consider that the average age of this patient population is of 41 years. Moreover, the large majority of the late deaths (4 out of 6) were aortic-related. Even this finding does not compare favorably at all with the previously reported survival rates of 99% at 2 year of the RESTORE registry [22], as well as with 9% mortality at a median follow-up of 26 months reported in a recent meta-analysis [21] and with 6.5% mortality at 22 months of the Talent registry [8].

Taken together, the data reported in this systematic review of the results of endovascular stent grafting for the treatment of Type B dissection in MFS syndrome, especially in chronic presentations, are the proof of concept that this type of approach needs to be considered with the greatest caution and pros and cons need to be evaluated case by case. On the other hand, open surgery has demonstrated to be effective in the treatment of chronic dissection of the distal thoracic aorta with more stable results even if associated with higher early mortality rate (9.6%). In fact, the need of further aortic repairs is significantly lower after open surgery with a freedom from aortic reoperation of 93% and 83% at 5 years and 10 years, respectively [23]. The fact that there are no comparative studies versus optimal medical therapy or even versus open surgery, together with the relatively low numbers of patients who have been treated and then reported in literature also raises a problem of publication bias and suggest, together with the limits of possible underestimation of the complication rates that this systematic review might have done (please see the methods section) that complication rates in these patients may be even higher than that reported.

Further evidence is needed to help us in determining what are the best strategies in these very complex patients.

Figure legend

Figure 1: Flow diagram of the systematic literature search.

REFERENCE LIST

[1] Marsalese DL, Moodie DS, Vacante M, et al. Marfan's syndrome: natural history and long-term follow-up of cardiovascular involvement. J Am Coll Cardiol 1989;14:422-8; discussion 9-31.

[2] Gott VL, Greene PS, Alejo DE, et al. Replacement of the aortic root in patients with Marfan's syndrome. N Engl J Med 1999;340:1307-13.

[3] Nienaber CA, Kische S, Akin I, et al. Strategies for subacute/chronic type B aortic dissection: the Investigation Of Stent Grafts in Patients with type B Aortic Dissection (INSTEAD) trial 1-year outcome. J Thorac Cardiovasc Surg 2010;140:S101-8; discussion S42-S46.

[4] Botta L, Russo V, La Palombara C, Rosati M, Di Bartolomeo R, Fattori R. Stent graft repair of descending aortic dissection in patients with Marfan syndrome: an effective alternative to open reoperation? J Thorac Cardiovasc Surg 2009;138:1108-14.

[5] Ince H, Rehders TC, Petzsch M, Kische S, Nienaber CA. Stent-grafts in patients with marfan syndrome. J Endovasc Ther 2005;12:82-8.

[6] Marcheix B, Rousseau H, Bongard V, et al. Stent grafting of dissected descending aorta in patients with Marfan's syndrome: mid-term results. JACC Cardiovasc Interv 2008;1:673-80.

[7] Nordon IM, Hinchliffe RJ, Holt PJ, et al. Endovascular management of chronic aortic dissection in patients with Marfan syndrome. J Vasc Surg 2009;50:987-91.

[8] Kische S, Ehrlich MP, Nienaber CA, et al. Endovascular treatment of acute and chronic aortic dissection: midterm results from the Talent Thoracic Retrospective Registry. J Thorac Cardiovasc Surg 2009;138:115-24.

[9] Geisbusch P, Kotelis D, von Tengg-Kobligk H, Hyhlik-Durr A, Allenberg JR, Bockler D. Thoracic aortic endografting in patients with connective tissue diseases. J Endovasc Ther 2008;15:144-9.

[10] Nienaber CA, Rousseau H, Eggebrecht H, et al. Randomized comparison of strategies for type B aortic dissection: the INvestigation of STEnt Grafts in Aortic Dissection (INSTEAD) trial. Circulation 2009;120:2519-28.

[11] Thompson M, Ivaz S, Cheshire N, et al. Early results of endovascular treatment of the thoracic aorta using the Valiant endograft. Cardiovasc Intervent Radiol 2007;30:1130-8.

[12] Xu SD, Huang FJ, Yang JF, et al. Early and midterm results of thoracic endovascular aortic repair of chronic type B aortic dissection. J Thorac Cardiovasc Surg 2010;139:1548-53.

[13] Ketelsen D, Kalender G, Heuschmid M, et al. Endovascular aneurysm repair using a reverse chimney technique in a patient with Marfan syndrome and contained ruptured chronic type B dissection. Cardiovasc Intervent Radiol 2011;34:1080-4.

[14] Marzelle J, Kirsch M, Tzvetkov B, Becquemin JP. Paraplegia as a symptom of failure after endovascular therapy of type B aortic dissection in Marfan syndrome. J Vasc Surg 2009;49:478-82.

[15] van Keulen JW, Moll FL, Jahrome AK, van Herwaarden JA. Proximal aortic perforation after endovascular repair of a type B dissection in a patient with Marfan syndrome. J Vasc Surg 2009;50:190-2.

[16] Zaman MJ, Carre V, Parvin S, Shepherd D, Radvan J. Endovascular stent repair for a dissecting thoracoabdominal aneurysm is feasible in the setting of a district general hospital: a multidisciplinary approach. Heart 2002;88:E4.

[17] Baril DT, Carroccio A, Palchik E, et al. Endovascular treatment of complicated aortic aneurysms in patients with underlying arteriopathies. Ann Vasc Surg 2006;20:464-71.

[18] Fleck TM, Hutschala D, Tschernich H, et al. Stent graft placement of the thoracoabdominal aorta in a patient with Marfan syndrome. J Thorac Cardiovasc Surg 2003;125:1541-3.

[19] Kpodonu J, Wheatley GH, 3rd, Diethrich EB. Endovascular reconstruction of a new aortoiliac bifurcation to manage a ruptured thoracoabdominal pseudoaneurysm in a Marfan patient. J Card Surg 2008;23:725-6.

[20] Schwill S, LeMaire SA, Green SY, Bakaeen FG, Coselli JS. Endovascular repair of thoracic aortic pseudoaneurysms and patch aneurysms. J Vasc Surg 2010;52:1034-7.

[21] Thrumurthy SG, Karthikesalingam A, Patterson BO, et al. A Systematic Review of Mid-term Outcomes of Thoracic Endovascular Repair (TEVAR) of Chronic Type B Aortic Dissection. Eur J Vasc Endovasc Surg 2011;42:632-47.

[22] Zipfel B, Czerny M, Funovics M, et al. Endovascular treatment of patients with types A and B thoracic aortic dissection using Relay thoracic stent-grafts: results from the RESTORE Patient Registry. J Endovasc Ther 2011;18:131-43.
[23] Zoli S, Etz CD, Roder F, et al. Long-term survival after open repair of chronic distal aortic dissection. Ann Thorac Surg 2010;89:1458-66.

Table 1A

Preoperative clinical features (papers focused only on Marfan patients)

Author	Journal	Year	Patients (n)	Marfans (n)	Pathology		Age (yrs)	Male gender	Previous CV surgery	Priority-urgent/emergent	Diabetes	Renal failure	Aortic diameter (mm)
Botta	J Thorac Cardiovasc Surg	2009	8	8	Dissection	Acute 4 Chronic 4	28.2 ± 6.7 56.8 ± 9.0	3 4	4 4	4 0	0 1	0 3	48 ± 4 53.0 ± 0.5
Ince	J Endovasc Ther	2005	6	6	Acute dissection		33 ± 15	4	5	n.a	n.a.	n.a.	33 ± 5
Ketelsen	Cardiovasc Intervent Radiol	2011	1	1	Complicated chronic dissection		69	1	1	1	n.a.	n.a.	77
Marcheix	JACC Cardiovasc Interv	2008	15	15	Chronic dissection		38.7 ± 12.8	9	11	0	1	5	61 ± 25
Marzelle	J Vasc Surg	2009	1	1	Chronic dissection		29	1	1	1	n.a.	n.a.	85
Nordon	J Vasc Surg	2009	7	7	Chronic dissection		45.9 ± 10	6	7	3	n.a.	n.a.	64 ± 11
Van Keulen	J Vasc Surg	2009	1	1	Complicated chronic dissection		55	1	0	1	n.a.	n.a.	40
Zaman	Heart	2002	1	1	Acute dissection		42	1	0	1	n.a.	n.a.	n.a.
Subtotal, acute dissections			**11**	**11**			**31.9 ± 12.3**	**8/11 (72.7%)**	**9/11 (81.8%)**	**5/5 (100%)**	**0/5**	**0/5**	
Subtotal, chronic dissections			**29**	**29**			**44.2 ± 14.3**	**22/29 (75.9%)**	**24/29 (82.8%)**	**6/29 (20.7%)**	**2/18 (11.1%)**	**8/18 (44.4%)**	
Total (%)			**40**	**40**			**40.9 ± 14.6**	**30/40 (75.0%)**	**33/40 (82.5%)**	**11/34 (32.4%)**	**2/23 (8.7%)**	**8/23 (34.8%)**	

Table 1B

Preoperative clinical features (papers not focused on but reporting data also on Marfan patients)

Author	Journal	Year	Patients (n)	Marfans (n)	Pathology		Age (yrs)	Male gender	Previous CV surgery	Priority-urgent/emergent	Diabetes	Renal failure	Aortic diameter (mm)
Nienaber	Circulation	2009	72	2	Dissection	Chronic 1 Subacute 1	n.a. n.a.	n.a. n.a.	n.a. n.a.	0 0	n.a. n.a.	n.a. n.a.	n.a. n.a.
Geisbush	J Endovasc Ther	2008	7	6	Chronic dissection		49.5	4	3	n.a.	n.a.	n.a.	n.a.
Xu	J Thorac Cardiovasc Surg	2010	84	1	Cronic dissection		n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Thompson	Cardiovasc Intervent Radiol	2007	52	5	Chronic dissection		n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Total (%)			**215**	**14**				**4/6 (66.7%)**	**3/6 (50.0%)**	**0/2**	**n.a.**	**n.a.**	**n.a.**

Table 1C

Summary of the preoperative clinical features (combined means ± s.d. or percentages of Tables 1A and 1B)

Marfans (n)	Age (yrs) (n=40)	Male gender	Previous CV surgery	Priority-urgent/emergent	Diabetes	Renal failure	Aortic diameter (mm) (n=39)
54	**40.9 ± 14.61**	**34/46 (73.9%)**	**36/46 (78.3%)**	**11/36 (30.6%)**	**2/23 (8.7%)**	**8/23 (34.8%)**	**54 ± 20.3**

Table 2A

Intraoperative and periprocedural clinical features (papers focused only on Marfan patients)

Author	Patients (n)	Marfans	Endoprosthesis type	Stent-graft/ pt	Stent size (mm)	Proximal landing zone	LSA closure	Overall endoleak	Type I endoleak	Type II endoleak	Type III endoleak	Endoleak in graft	Endoleak not in graft
Botta	8	8	n.a.	Acute (n=4) 2 ± 0.2	31.6 ± 2.5	Graft=3, aorta=1	1	1	0	1	0	0	1
				Chronic (n=4) 2.5 ± 0.6	35.0 ± 1.1	Graft=0, aorta=4	0	1	1	0	0	0	1
Ince	6	6	Talent	1	n.a.	Aorta	0	0	0	0	0	n.a	0
Ketelsen	1	1	Valiant, Viabhan, Endurant	3	38	Aorta	0	0	0	0	0	n.a	0
Marcheix	15	15	Talent	1.5 ± 0.7	n.a.	Aorta	2	5	4	1	0	n.a	5
Marzelle	1	1	Valiant	3	33.0 ± 4.6	Graft	0	1	1	0	0	0	1
Nordon	7	7	Talent, Valiant	3 (2-6)	n.a.	Graft=3, aorta=4	n.a.	2	1	0	1	0	2
Van Keulen	1	1	Valiant	2	35 ± 1.4	Aorta	0	0	0	0	0	n.a	0
Zaman	1	1	Gore	1	n.a.	Aorta	1	0	0	0	0	n.a	0
Subtotal Acute dissections	**11**	**11**			**31.6 ± 2.5**	**graft=3/11 (27.2%) aorta=8/11 (72.7%)**	**2/11 (18.2%)**	**1/11 (9.1%)**	**0/11**	**1/11 (9.1%)**	**0/11**	**0/3**	**1/8 (12.5%)**
Subtotal Chronic dissections	**29**	**29**			**34.3 ± 2.99**	**graft=4/29 (13.8%) aorta=25/29 (86.2%)**	**2/22 (9.1%)**	**9/29 (31.0%)**	**7/29 (24.1%)**	**1/29 (3.4%)**	**1/29 (3.4%)**	**0/4**	**9/25 (36.0%)**
Total	**40**	**40**			**33.8 ± 3.11**	**graft=7 (17.5%) aorta=33 (82.5%)**	**4/33 (12.1%)**	**10/40 (25.0%)**	**7/40 (17.5%)**	**2/40 (5.0%)**	**1/40 (2.5%)**	**0/7**	**10/33 (30.3%)**

Table 2B

Intraoperative and periprocedural clinical features (papers not focused on but reporting data also on Marfan patients)

Author	Patients (n)	Marfans	Endoprosthesis type	Stent-graft/ pt	Stent size (mm)	Proximal landing zone	LSA closure	Overall endoleak	Type I endoleak	Type II endoleak	Type III endoleak	Endoleak in graft	Endoleak not in graft
Nienaber	72	2	Chronic (n=1): Talent Subacute (n=1): Talent	n.a n.a.	n.a. n.a.	n.a. n.a.	n.a. n.a.	n.a. n.a.	n.a. n.a.	n.a. n.a.	n.a. n.a.	n.a. n.a.	n.a. n.a.
Geisbush	7	6	Talent, Valiant, Tag	1.67	32.5 ± 4.2	Graft=2, aorta=4	n.a.	1	1	n.a.	n.a.	0	1
Xu	84	1	Talent, Endofit, Hercules, Vasoflow, Grikin	n.a.	n.a.	Aorta	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Thompson	52	5	Valiant	n.a.	n.a.	n.a.	n.a.	0	0	0	0	n.a	n.a.
Total	**215**	**14**			32.5 ± 4.2	**Graft=2 (28.6%) Aorta=5 (71.4%)**	**n.a.**	**1/11 (9.1%)**	**1/11 (9.1%)**	**0/5**	**0/5**	**0/2**	**1/4 (25.0%)**

Table 2C

Summary of the intraoperative and periprocedural clinical features (combined means ± s.d. or percentages of Tables 2A and 2B)

Stent-graft/pt (n=33)	Stent size (mm)	Proximal landing zone	LSA closure	Overall endoleak	Type I endoleak	Type II endoleak	Type III endoleak	Endoleak in graft	Endoleak not in graft
1.65 ± 0.77	**33.4 ± 3.54**	**Graft = 9 (19.1%) Aorta = 38 (80.9%)**	**4/33 (12.1%)**	**11/51 (21.6%)**	**8/51 (15.7%)**	**2/45 (4.4%)**	**1/45 (2.2%)**	**0/9**	**11/38 (28.9%)**

Table 3A

Early postoperative clinical features (papers focused only on Marfan patients)

Author	Patients (n)	Marfans	In-hospital mortality	Aortic-related death	Surgical conversion	Paraplegia/ paraparesis	Stroke	ARF	Postop. stay (days)
Botta	8	8	Acute (n=4) 0 Chronic (n=4) 0	0 0	0 1	0 0	0 0	0 0	9.8 (9-12) 7.5 (6-8)
Ince	6	6	0	0	0	0	0	n.a.	8±2
Ketelsen	1	1	0	0	0	0	0	0	6
Marcheix	15	15	0	0	0	0	1	n.a	14 ± 13
Marzelle	1	1	0	0	1	1	0	0	42
Nordon	7	7	1	0	0	0	0	n.a.	n.a.
Van Keulen	1	1	0	0	0	0	0	0	n.a.
Zaman	1	1	0	0	0	0	0	0	10
Subtotal, acute diss.	**11**	**11**	**0/11**	**0/11**	**0/11**	**0/11**	**0/11**	**0/6**	
Subtotal, chronic diss.	**29**	**29**	**1/29 (3.4%)**	**0/29**	**2/29 (6.9%)**	**1/29 (3.4%)**	**1/29 (3.4%)**	**0/6**	
Total	**40**	**40**	**1/40 (2.5%)**	**0/40**	**2/40 (5%)**	**1/40 (2.5%)**	**1/40 (2.5%)**	**0/12**	

Table 3B

Early postoperative clinical features (papers not focused on but reporting data also on Marfan patients)

Author	Patients (n)	Marfans	In-hospital mortality (Marfans)	Aortic-related death	Surgical conversion	Paraplegia/ paraparesis	Stroke	ARF	Postop. stay (days)
Nienaber	72	2	Chronic (n=1) n.a Subacute (n=1) n.a.	n.a. n.a.	0 0	n.a. n.a.	n.a. n.a.	n.a. n.a.	n.a. n.a.
Geisbush	7	6	0	0	0	0	0	n.a.	n.a.
Xu	84	1	0	0	0	0	0	n.a.	n.a.
Thompson	52	5	0	0	0	0	0	n.a.	n.a.
Total	**215**	**14**	**0/12**	**0/12**	**0/14**	**0/12**	**0/12**	**n.a.**	

Table 3C

Summary of the early postoperative clinical features (combined means ± s.d. or percentages of Tables 3A and 3B)

Stent-graft/pt (n=33)	In-hospital mortality (Marfans)	Aortic-related death	Surgical conversion	Paraplegia/ paraparesis	Stroke	ARF	**Postop. stay (days)** (n=24)
1.65 ± 0.77	**1/52 (1.9%)**	**0/52**	**2/54 (3.7%)**	**1/52 (1.9%)**	**1/52 (1.9%)**	**0/12**	**13.2 ± 12.93**

Table 4A

Follow-up clinical features (papers focused only on Marfan patients)

Author	Patients (n)	Marfans (n)	F-up duration (months)	Surgical conversion	Death	Aortic-related death	New endovascular procedure	New disssection	Overall endoleaks	Type I Endoleak	Type II Endoleak	Type III Endoleak
Botta	8	8	Acute (n=4) n.a. Chronic (n=4) n.a.	0 0	0 0	0 0	0 1	0 1	0 0	0 0	0 0	0 0
Ince	6	6	51 ± 22	2	1	0	0	0	0	0	0	0
Ketelsen	1	1	6	0	0	0	0	0	0	0	0	0
Marcheix	15	15	25.2 ± 16.8	5	3	3	3	n.a.	5	4	0	1
Marzelle	1	1	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Nordon	7	7	16 (3-54)	0	1	0	2	n.a.	2	1	0	1
Van Keulen	1	1	4,4	0	0	0	1	0	0	0	0	0
Zaman	1	1	24	0	0	0	0	0	0	0	0	0
Subtotal, acute diss.	**11**	**11**		**2/11 (18.2%)**	**1/11 (9.1%)**	**0/11**	**0/11**	**0/11**	**0/11**	**0/11**	**0/11**	**0/11**
Subtotal, chronic diss.	**29**	**29**		**5/28 (17.9%)**	**4/28 (14.3%)**	**3/28 (10.7%)**	**7/28 (25.0%)**	**1/6 (16.7%)**	**7/28 (25.0%)**	**5/28 (17.9%)**	**0/28**	**2/28 (7.1%)**
Total	**40**	**40**		**7/39 (17.9%)**	**5/39 (12.8%)**	**3/39 (7.7%)**	**7/39 (17.9%)**	**1/17 (5.9%)**	**7/39 (17.9%)**	**5/39 (12.8%)**	**0/39**	**2/39 (5.1%)**

Table 4B

Follow-up clinical features (papers not focused on but reporting data also on Marfan patients)

Author	Patients (n)	Marfans (n)	F-up duration (months)	Surgical conversion	Death	Aortic-related death	New endovascular procedure	New disssection	Overall endoleaks	Type I Endoleak	Type II Endoleak	Type III Endoleak
Nienaber	72	2	Chronic (n=1) n.a. Subacute (n=1) n.a.	n.a. n.a.	n.a. n.a.	n.a. n.a.	n.a. n.a.	n.a. n.a.	n.a. n.a.	n.a. n.a.	n.a. n.a.	n.a. n.a.
Geisbush	7	6	32,8	0	0	0	1	n.a.	1	0	1	n.a.
Xu	84	1	n.a.	n.a.	1	1	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Thompson	52	5	n.a.	0	0	0	0	0	0	0	0	0
Total	**215**	**14**		**0/11**	**1/12 (8.3%)**	**1/12 (8,3%)**	**1/11 (9.1%)**	**0/5**	**1/11 (9.1%)**	**0/11**	**1/11 (9.1%)**	**0/5**

Table 4C

Summary of the follow-up clinical features (combined means ± s.d. or percentages of Tables 4A and 4B)

F-up duration (months) (n=24)	Death	Aortic-related death	Surgical conversion	New endovascular procedure	New disssection	Overall endoleaks	Type I Endoleak	Type II Endoleak	Type III Endoleak
29.9 ± 21.9	**6/51 (11.8%)**	**4/51 (7.8%)**	**7/50 (14.0%)**	**8/50 (16.0%)**	**1/22 (4.5%)**	**8/50 (16.0%)**	**5/50 (10.0%)**	**1/50 (2.0%)**	**2/44 (4.5%)**

APPENDIX 1 - *Endovascular stent grafting in Marfans due to nondissecting aortic aneurysms.*

Table Appendix 1

Preoperative clinical features

Author	Journal	Year	Patients (n)	Marfans (n)	Pathology	Age (yrs)	Male gender	Previous CV surgery	Priority-urgent/emergent	Diabetes	Renal failure	Aortic diameter (mm)
Baril	Ann Vasc Surg	2006	11	6	Complicated aortic aneurysm	48.2 ± 18.5	6	6	n.a	0	0	60.8 ± 18.7
Fleck	J Thorac Cardiovasc Surg	2003	1	1	Thoracoabdominal aneurysm	31	0	1	0	n.a.	n.a.	77
Schwill	J Vasc Surg	2010	4	4	False aneurysm	50.5 ± 7.9	4	4	n.a.	0	1	n.a.
Kpodonu	J Card Surg	2008	1	1	False aneurysm	35	n.a.	1	1	n.a	n.a	

Table Appendix 2

Intraoperative and periprocedural clinical features

Author	Patients (n)	Marfans	Endoprosthesis type	Stent-graft/ pt	Stent size (mm)	Proximal landing zone	LSA closure	Overall endoleak	Type I endoleak	Type II endoleak	Type III endoleak	Endoleak in graft	Endoleak not in graft
Baril	11	6	Talent, Gore, AneuRX	n.a.	32.2 ± 10.7	n.a	n.a.	0	0	0	0	0	0
Fleck	1	1	Gore	2	40	n.a	0	0	0	0	0	0	0
Schwill	4	4	Talent, Gore, AneuRX	2.3 ± 1.3	30.3 ± 4.2	graft	0	1	0	1	0	1	0
Kpodonu	1	1	PowerLink	1	28	graft	0	0	0	0	0	0	0

Table Appendix 3

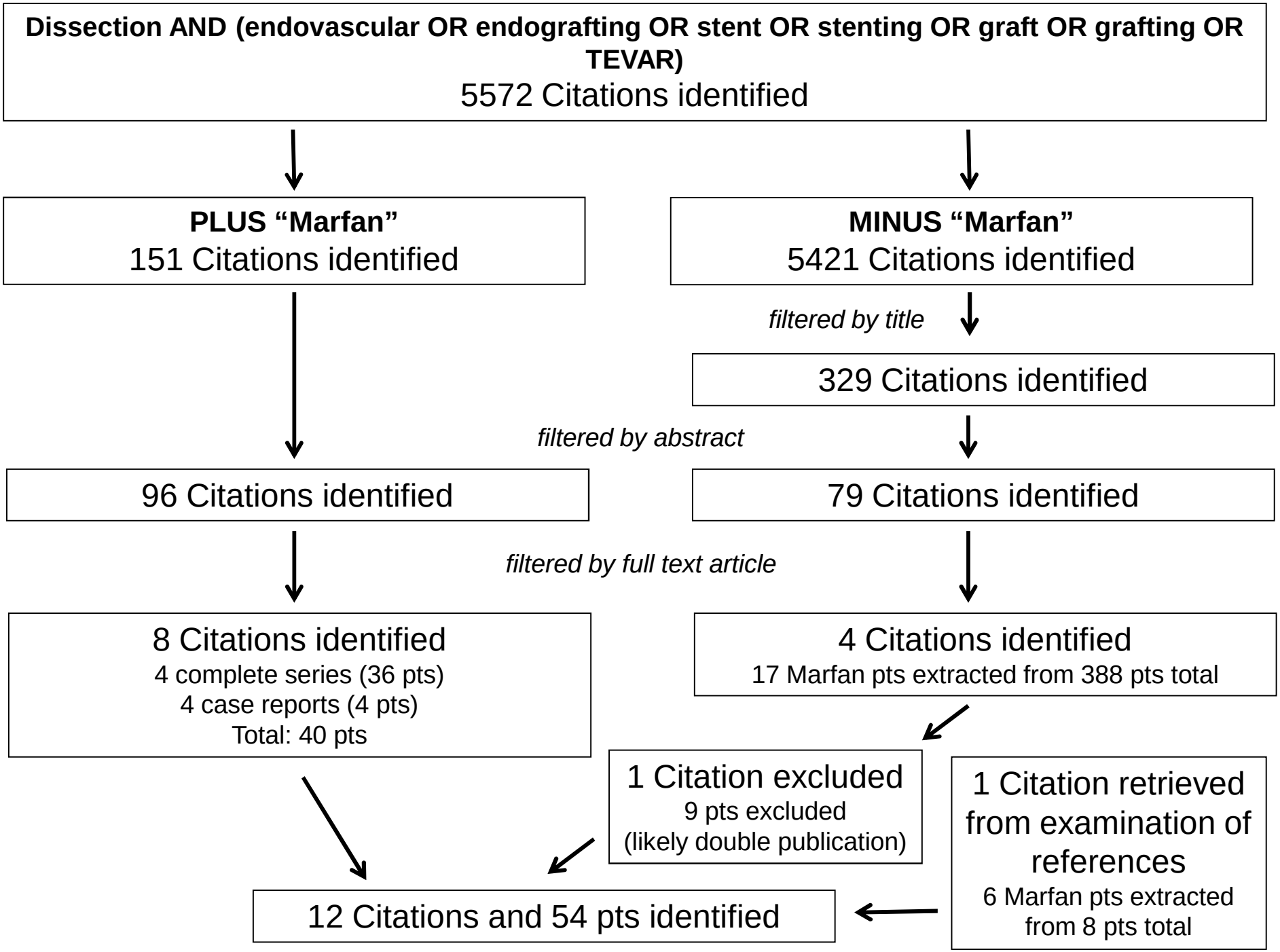
Early postoperative clinical features

Author	Patients (n)	Marfans	In-hospital mortality	Aortic-related death	Surgical conversion	Paraplegia/ paraparesis	Stroke	ARF	Postop. stay (days)
Baril	11	6	0	0	0	0	0	0	n.a.
Fleck	1	1	0	0	0	n.a.	n.a	n.a.	n.a.
Schwill	4	4	0	0	0	0	0	0	10 ± 7.8
Kpodonu	1	1	0	0	0	0	0	0	n.a.

Table Appendix 4

Follow-up clinical features

Author	Patients (n)	Marfans (n)	F-up duration (months)	Surgical conversion	Death	Aortic-related death	New endovascular procedure	New disssection	Overall endoleaks	Type I Endoleak	Type II Endoleak	Type III Endoleak
Baril	11	6	n.a.	0	0	0	1	0	1	0	0	1
Fleck	1	1	32.1	0	0	0	0	0	0	0	0	0
Schwill	4	4	51.5 ± 19.7	0	0	0	0	0	0	0	0	0
Kpodonu	1	1	2	0	0	0	0	0	0	0	0	0


Dissection AND (endovascular OR endografting OR stent OR stenting OR graft OR grafting OR TEVAR)
5572 Citations identified
PLUS "Marfan"
151 Citations identified
MINUS "Marfan"
5421 Citations identified
filtered by title
329 Citations identified
filtered by abstract
96 Citations identified
79 Citations identified
filtered by full text article
8 Citations identified
4 complete series (36 pts)
4 case reports (4 pts)
Total: 40 pts
4 Citations identified
17 Marfan pts extracted from 388 pts total
1 Citation excluded
9 pts excluded
(likely double publication)
1 Citation retrieved from examination of references
6 Marfan pts extracted from 8 pts total
12 Citations and 54 pts identified