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ORIGINAL ARTICLE

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Results of a prospective follow-up study after type A aortic dissection repair: a high rate of distal aneurysmal evolution and reinterventions

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Key question

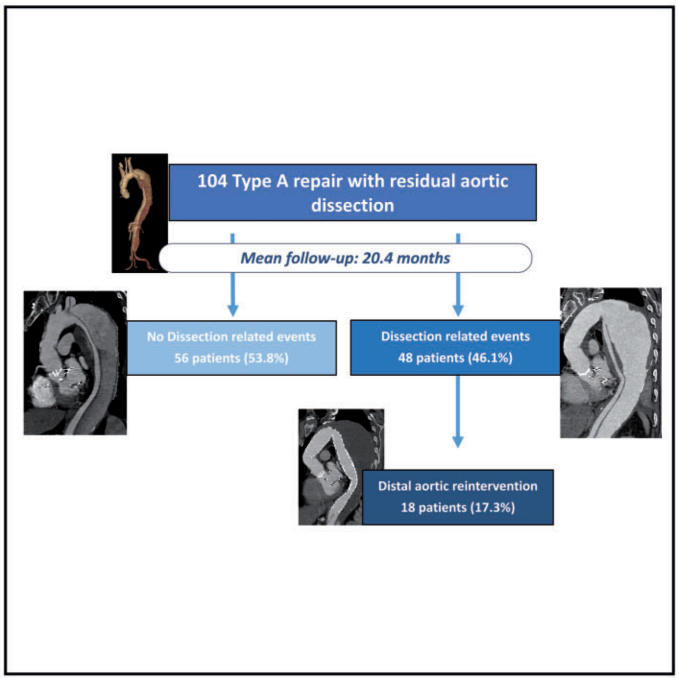
What happens to the distal descending thoracic aorta after type A aortic dissection repair?

Key finding(s)

Residual aortic dissection (RAD) is associated with a high rate of aneurysmal evolution and reintervention.

Take-home message

RAD justifies close follow-up; patients with poor prognostic factors could be treated at an early phase to improve long-term outcomes.



Abstract

OBJECTIVES: We investigated the anatomical evolution of residual aortic dissection after type A repair and factors associated with poor prognosis at a high-volume aortic centre.

METHODS: Between 2017 and 2019, all type A aortic dissections were included for prospective follow-up. Patients without follow-up computed tomography (CT) scan available for radiological analysis and patients without residual aortic dissection were excluded from this study. The primary end point was a composite end point defined as dissection-related events including aneurysmal evolution (increased diameter > 5 mm/year), aortic reintervention for malperfusion syndrome, aortic diameter >55 mm, rapid aortic growth >10 mm/year or aortic rupture and death. The secondary end points were risk factors for dissection-related events and reintervention analysis. All immediate and last postoperative CT scans were analysed.

RESULTS: Among 104 patients, after a mean follow-up of 20.4 months (8–41), the risk of dissection-related events was 46.1% (48/104) and the risk of distal reintervention was 17.3% (18/104). Marfan syndrome ($P < 0.01$), aortic bicuspid valve ($P = 0.038$), innominate artery debranching ($P = 0.025$), short aortic cross-clamp time ($P = 0.011$), initial aortic diameter >40 mm ($P < 0.01$) and absence of resection of the primary entry tear ($P = 0.015$) were associated with an increased risk of dissection-related events or reintervention during follow-up.

CONCLUSIONS: Residual aortic dissection is a serious disease requiring close follow-up at an expert centre. This study shows higher reintervention and aneurysmal development rates than currently published. To improve long-term outcomes, the early demographic and anatomic poor prognostic factors identified may be used for more aggressive treatment at an early phase.

Keywords: Prospective follow-up • Aortic centre • Type A aortic dissection • Residual aortic dissection • Aneurysmal evolution • Reinterventions

ABBREVIATIONS

CI	Confidence interval
CPB	Cardiopulmonary bypass
CT	Computed tomography
FL	False lumen
HR	Hazard ratio
RAD	Residual aortic dissection
SA	Supra-aortic
SD	Standard deviation
TAAD	Type A aortic dissection
TEVAR	Thoracic endovascular aortic repair

INTRODUCTION

A patent false lumen (FL) in the descending aorta is the most common situation encountered after replacement of the ascending aorta for type A aortic dissection (TAAD), ranging from 43% to 77.5%, and is a well-known risk factor for aortic growth, reinterventions and mortality [1–6].

In addition, several risk factors promote aneurysmal evolution of the descending aorta after residual dissection: a ratio of the true and FL diameter <1, young age, male sex, connective tissue diseases, aortic diameter >40 mm, absence of resection of the primary entry tear or new entry tear and technique used for the initial TAAD repair [2–5, 7–9]. Aortic arch repair has been reported to improve the long-term outcomes of acute TAAD, avoid aneurysmal evolution and provide extensive repair [10, 11]. However, ascending aorta or hemiarch replacement remains the most commonly used surgical procedure [12] but is associated with a high risk of patent FL.

Several studies (including randomized controlled trials) have shown the long-term benefit of thoracic endovascular aortic repair (TEVAR) compared to optimal medical treatment in type B aortic dissection to prevent aortic aneurysm progression and mortality [13, 14]. However, there is little knowledge on TEVAR for residual aortic dissection (RAD), and some series have shown that endovascular treatment is associated with good anatomical results and a low rate of morbimortality [15].

Knowing the exact rate of long-term aneurysmal evolution, reoperations and mortality of RAD would justify more aggressive interventional treatment at the subacute phase to prevent dissection-related events.

The aim of this study was to assess the rate of aneurysmal evolution and reintervention of RAD after TAAD repair and factors associated with poor prognosis at a high-volume aortic centre with prospective follow-up.

PATIENTS AND METHODS

Study patients

The institutional review board approved the project (approval number 2019-48). The ethics committee waived the need for individual written informed consent.

Between January 2017 and December 2019, all patients treated surgically for TAAD aortic dissection at our aortic centre were included for prospective follow-up. In our centre, TAAD was surgically treated; we did not perform endovascular treatment and patients were contraindicated to surgery after multidisciplinary discussion taking into account physiological age, neurological status, comorbidities and operative risk (i.e. major stroke, limited life expectancy).

Demographic and preoperative and intraoperative variables were collected, including age, sex, cardiovascular risk factors, past medical and surgical history, cardiorespiratory and renal status, operative risk, symptoms in the acute phase and procedure details.

Inclusion and exclusion criteria

All survivors (discharge alive from intensive care units) with a postoperative computed tomography (CT) scan in our centre were included in this study. Patients without follow-up CT scan available for radiological analysis and patients without RAD were excluded from the study.

End points

The primary end point was a composite end point: dissection-related events including aneurysmal evolution (aortic growth >5 mm) distal reintervention or death.

The secondary end points were demographical and anatomical risk factors (entry tear >10 mm and maximum aortic diameter on the arch and/or descending aorta >40 mm, location and absence of resection of the primary entry tear) for dissection-related events and reinterventions.

Follow-up

All patients had an immediate postoperative CT scan and underwent clinical and radiological follow-up at 3, 6 and 12 months and annually in the case of favourable progress.

In this study, all preoperative, immediate postoperative and last postoperative CT scans were analysed by 1 vascular surgeon, 1 cardiac surgeon and 1 radiologist. For patients with reintervention, we analysed the last CT scan before reintervention.

Computed tomography protocol

All patients underwent postoperative and follow-up examinations with a three-phase CT scan.

Image analysis and measurements were performed using three-dimensional imaging software (OSIRIX software, Geneva, Switzerland). The maximal aortic diameter measurements were performed on the perpendicular axis according to the centreline using a semiautomated centreline algorithm at three different levels of the aorta (ascending aorta aortic arch and descending thoracic aorta). The principal entry tear (new entry tear or non-resected primary entry tear) was measured and located. FL patency was assessed as an FL that was enhanced anywhere in the downstream aorta during arterial- and venous-phase CT and FL disappearance was considered complete FL thrombosis [1].

Surgical procedures

Initial surgery for type A aortic dissection. At our centre, during an emergency, if the entry site was located at the ascending aorta, replacement of the ascending aorta or hemiarch aorta was performed. Hemiarch replacement with open distal anastomosis during moderate hypothermic circulatory arrest with cardiopulmonary bypass (CPB) and selective antegrade cerebral perfusion was preferred when possible. If the entry site was located at the distal part of the aortic arch, partial arch replacement with innominate artery debranching was performed.

After systemic heparinization, CPB was established by direct cannulation of the right axillary artery.

Retrograde cold blood cardioplegia was infused every 15 min. Circulatory arrest was instituted when the vesical temperature was 25°C. We preferred moderate hypothermia with antegrade cerebral perfusion for cerebral protection during circulatory arrest.

Aortic root replacement with a composite prosthesis was performed according to the modified Bentall procedure in patients with dilation of the aortic root or an aortic root damaged by the entry tear.

Distal reintervention. Indications for reinterventions were aortic diameter >55 mm, rapid aortic growth (10 mm/year), malperfusion syndrome or aortic rupture.

Hybrid treatment with TEVAR and open supra-aortic (SA) debranching in at least two steps remain the first-line therapy at our centre when the RAD involves the aortic arch, as detailed regarding hybrid repair [16]. The decision to extend the proximal landing zone was based on the location of the main new entry tear (on distal anastomosis of the ascending aortic repair, on the aortic arch or in the descending thoracic aorta). In the absence of RAD in the aortic arch and when the entry tear was in the descending thoracic aorta, we performed TEVAR on the descending thoracic aorta.

The distal extension of the stent graft was based on the distal extension of the dissected aortic aneurysm. Since 2017, we have added bare stent deployment in the thoraco-abdominal aorta to induce remodelling of the distal dissected aorta [the Stent-Assisted Balloon-Induced Intimal Disruption and Relamination in Aortic Dissection Repair (STABILISE) technique].

Table 1: Baseline characteristics

Variables	Total (*N* = 104)	Dissection-related events (*N* = 48)	No dissection-related events (*N* = 56)
Male gender, *n* (%)	75 (72.1)	32 (66.7)	43 (76.8)
Age (years), mean (SD)	62.1 (11.1)	63.5 (10.7)	60.7 (11.3)
Hypertension, *n* (%)	62 (59.6)	33 (68.8)	29 (51.8)
Dyslipidaemia, *n* (%)	17 (16.3)	6 (12.5)	11 (19.6)
Smoking, *n* (%)	24 (23.1)	13 (27.1)	11 (19.6)
Diabetes, *n* (%)	2 (1.9)	0 (0.0)	2 (3.6)
COPD, *n* (%)	8 (7.7)	5 (10.4)	3 (5.4)
Atrial fibrillation, *n* (%)	11 (10.6)	8 (16.7)	3 (5.4)
CAD, *n* (%)	11 (10.6)	4 (8.3)	7 (12.5)
Renal failure, *n* (%)	2 (1.9)	0 (0.0)	2 (3.6)
Marfan syndrome, *n* (%)	10 (9.6)	6 (12.5)	4 (7.1)
Bicuspid aortic valve, *n* (%)	8 (7.7)	6 (12.5)	2 (3.6)

CAD: coronary artery disease; COPD: chronic obstructive pulmonary disease; SD: standard deviation.

Statistical analysis

All analyses were performed using R software, version 3.6.0 (R Foundation for Statistical Computing, Vienna, Austria). Means and standard deviations (SDs) were used to describe continuous variables; categorical variables were described as numbers and frequencies.

Risk factors for dissection-related events and distal reinterventions were assessed using time-to-event analysis. The survival rate without events was estimated using the Kaplan–Meier method. Univariable Cox models were built to estimate hazard ratios (HRs) with their 95% confidence intervals to quantify the association between baseline characteristics and event risk over time. A multivariable analysis was then performed to estimate adjusted HRs with their 95% confidence intervals. All variables whose *P*-value was <0.20 in the univariable analysis were considered candidates for the multivariable Cox model. Backward stepwise selection was applied to keep only variables that were statistically associated with the end point in the multivariable analysis. Primary entry tears >10 and primary entry tears on distal anastomosis were forced in the multivariable model when analysing distal reintervention. Firth's penalized maximum likelihood bias reduction was applied to limit the width of the 95% confidence intervals. The log minus log survival plot was graphed to assess whether the Cox proportional hazards assumption was met.

All statistical tests were two-sided, and for all analyses, a *P*-value of <0.05 was considered statistically significant.

Table 2: Perioperative characteristics

Variables	Total (*N* = 104)	Dissection-related events (*N* = 48)	No dissection-related events (*N* = 56)
Primary entry tear, *n* (%)			
Ascending aorta	89 (85.6)	36 (75.0)	53 (94.6)
Aortic arch	19 (18.3)	14 (29.2)	5 (8.9)
Descending aorta	6 (5.8)	5 (10.4)	1 (1.8)
Resection	95 (91.3)	40 (83.3)	55 (98.2)
Distal replacement, *n* (%)			
Ascending aorta	102 (98.1)	47 (97.9)	55 (98.2)
Ascending aorta + hemiarch	79 (76.0)	36 (75.0)	43 (76.8)
Partial arch + IA debranching	23 (22.1)	11 (22.9)	12 (21.4)
Aortic root management, *n* (%)			
Bentall intervention	22 (21.2)	7 (14.6)	15 (26.8)
Supracoronary aortic replacement	82 (78.8)	41 (85.4)	41 (73.2)
Operative timing (min), mean (SD)			
CPB time	168 (58.2)	160.9 (51.7)	174.1 (62.1)
Aortic cross-clamp time	98.4 (47.9)	88.3 (41.5)	110.1 (53.7)
CA time	25.6 (10.8)	24.8 (11.3)	25.7 (10.8)
Arterial cannulation, *n* (%)			
Axillary cannulation alone	79 (76.0)	39 (81.3)	40 (71.4)
Femoral cannulation alone	19 (18.3)	8 (16.7)	11 (19.6)
Axillary and femoral cannulation	6 (5.8)	1 (2.1)	5 (8.9)

CA: circulatory arrest; CPB: cardiopulmonary bypass; IA: innominate artery; SD: standard deviation.

RESULTS

Population characteristics

Between January 2017 and December 2019, 202 patients were admitted for TAAD at our aortic centre: 14 patients were contraindicated to open surgery and 188 patients were treated and included for prospective follow-up. The mean age was 63.7 years (25–83 years), and 70.2% were men (132/188). The in-hospital mortality rate was 13.8% (26/188), 44 patients (23.4%) did not have RAD (41 type II De Bakey aortic dissections, and in 3 type I De Bakey aortic dissections, the dissected aorta disappeared after the initial aortic repair) and 17 patients (9.0%) did not have a follow-up CT scan available for radiological analysis because follow-up was carried out in their city or country. These patients were excluded from radiological analysis.

In total, 104 survivors of RAD with at least a 1-year follow-up comprised the study group.

Demographic data are presented in Table 1.

Perioperative data

Perioperative characteristics are summarized in Table 2.

We performed 31 concomitant procedures: 5 coronary artery bypass grafts, 23 innominate artery debranching (entry tears in the distal aortic arch), 1 superior mesenteric artery stenting, 1 left common carotid artery stenting and 1 right carotid artery stenting for neurological deficits prior to cardiac surgery due to carotid dissection.

On the postoperative CT scan, there was a patent FL in 94.2% of cases (98/104), a new entry tear on distal anastomosis in 49.0% of cases (51/104), and a residual entry tear in the aortic arch or the distal aorta in 23.1% (24/104) and 31.7% (33/104) of cases, respectively.

Follow-up results

Dissection-related events of the descending aorta. After a mean follow-up of 20.4 months (range 8–41), the incidence of dissection-related events of the descending aorta was 46.1% (48/104) and the mean aortic diameter of the descending thoracic aorta in this group was 52.1 mm (SD 5.5) (Fig. 1). There were 18 reinterventions (17.3%) among which 1 aortic-related death (0.9%) and 30 aneurysmal evolution >5 mm/year (28.8%).

The Kaplan–Meier estimated dissection-related events-free survival rates at 12, 24 and 36 months were 80.4%, 57.3% and 22.0%, respectively (Fig. 2).

Distal reintervention details and results. Twenty-six patients (25.0%) had an indication for reintervention, and the mean aortic diameter in this group was 55.7 mm (SD 4.6). Among them, 8 did not undergo reintervention: 6 patients were followed up until 60 mm because of a high risk of reoperation and 2 patients had a contraindication for reintervention [1 patient with a previous stroke and sequala after type A repair and 1 contraindication in an elderly patient (82 y/o patient)].

Among 18 reinterventions, 13 patients were treated before the end of the first year of follow-up, 4 during the second year (1 at 14 months, 1 at 16 months, 2 at 18 months) and 1 at 32 months; the mean delay between TAAD repair and distal reintervention was 11.2 months (range 1–36).

One patient was treated for malperfusion syndrome and aneurysmal evolution >5 mm and 17 patients were treated for aneurysmal evolution >55 mm or 10 mm/year.

We performed 2 TEVAR and 16 hybrid repairs with SA debranching and TEVAR. Among 16 hybrid repairs, we performed complete SA debranching in 15 patients: left subclavian artery debranching alone in 1 case (Figs 3 and 4). One patient died due to aortic rupture during the delay between SA debranching and TEVAR after discharge.

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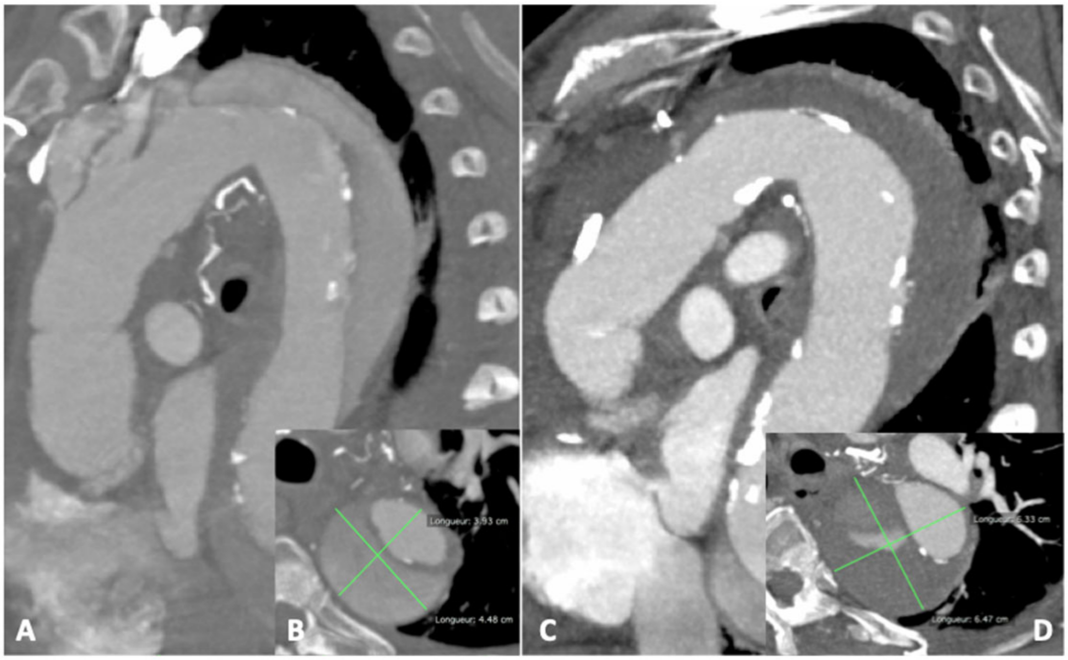

Figure 1: Aneurysmal evolution of the distal descending thoracic aorta. (**A**) Immediate postoperative CT scan with a sagittal view. (**B**) Immediate postoperative CT scan with an axial view in the centerline. (**C**) 1-year postoperative CT scan with a sagittal view. (**D**) 1-year postoperative CT scan with an axial view in the centerline.

In 1 patient with Marfan syndrome, there was also aneurysmal evolution of the abdominal aorta and iliac arteries treated by aorto-bi-iliac graft through median laparotomy.

After TEVAR, the technical success rate was 100% (17/17), and no perioperative death was observed. FL thrombosis of the thoracic aorta was obtained in 100% of patients. There was no stroke or spinal cord ischaemia.

Risk factors for dissection-related events and distal reinterventions

Univariable analysis is summarized in Table 3.

Independent risk factors identified in the multivariable analysis are described in Table 4.

An initial aortic diameter >40 mm was an independent risk factor for dissection-related events and distal reintervention [HR 9.00, 95% confidence interval (CI) 4.17–22.89; $P < 0.01$ and HR 28.54, 95% CI 3.63–224.18; $P < 0.01$, respectively].

A short clamping time (HR 0.99, 95% CI 0.98–1.00; $P = 0.011$) and Marfan syndrome (HR 9.06, 95% CI 2.74–29.99; $P < 0.01$) were independent risk factors for dissection-related events and distal reintervention, respectively.

DISCUSSION

The rate of aneurysmal evolution after acute TAAD repair was estimated to be between 40% and 50% at 5 years in a few studies with long-term CT scan analysis [2, 7, 17]. Despite this high rate of aneurysmal evolution, the risk of reintervention was low between 5% and 20% at 5 years, probably due to a large number of patients lost to follow-up [1–5, 7, 17, 18]. Indeed, with multidisciplinary prospective follow-up at an aortic centre, the natural course of RAD appears to be poor, with a higher rate of

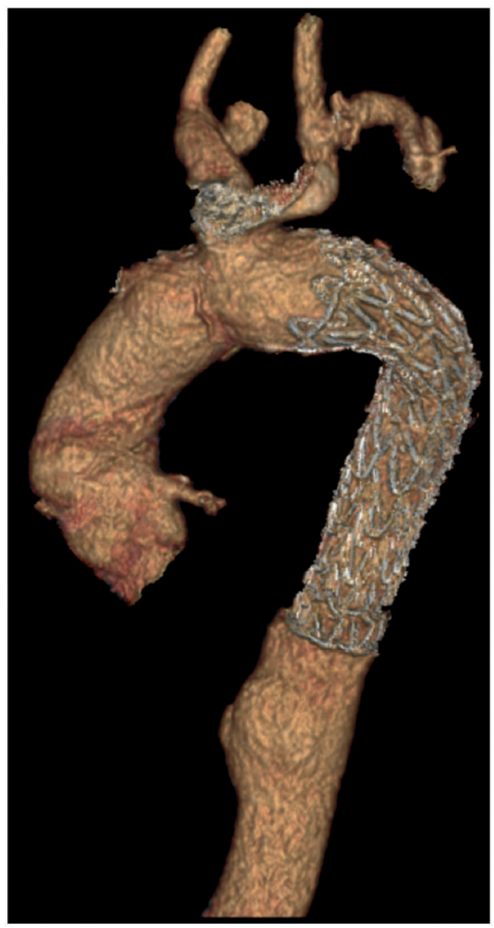

Figure 2: Distal reintervention for aneurysmal evolution of residual aortic dissection: hybrid repair with LSA debranching and endoprosthesis implantation in zone 2.

dissection-related events (46.1%) and reinterventions (17.3%) than previously published. This finding highlights the need for close follow-up with CT scans for these patients starting in the first few months. Indeed, most patients need reinterventions for aneurysmal evolution in the first year, and early follow-up could avoid fatal issues at mid-term. Moreover, a multidisciplinary approach with vascular surgeons, cardiac surgeons and radiologists allows a better analysis of CT scans with different views and improves the management of this complex pathology.

Figure 3: Hybrid repair for aneurysmal evolution of residual aortic dissection. (**A**) CT scan after TAAD repair with IA debranching; (**B**) intrathoracic complete supra-aortic trunk debranching and endoprosthesis implantation in zone 0.

In the present study, Marfan syndrome was associated with the risk of distal reinterventions. This finding has already been described in several studies [1, 3, 4, 8, 18]. Marfan disease causes fragility of the aortic wall, which is responsible for rapid aortic dilation in a large number of cases, more aortic reinterventions and more aortic-related death [19].

We showed new and major results, with bicuspid aortic valves associated with a risk of distal aortic reintervention. Bicuspid aortic valves patients have an increased incidence of aortic dilation, noted in ∼40% of patients at referral centres [20] and we believe that aortopathy is in fact not limited to the ascending aorta but extends to the whole aorta. The risk of unfavourable long-term evolution could be linked to aortic fragility and to a larger initial diameter. Despite its importance, to our knowledge, this association has not been previously published. Kreibich *et al.* [21] reported a significantly larger diameter in the ascending aorta in TAAD between bicuspid aortic valves patients and tricuspid aortic valve patients without long-term different results, but the authors did not measure the descending aortic diameter during follow-up and did not report the distal reintervention rate.

Aortic cross-clamp time was associated with an increased risk of dissection-related events. The risk of aortic events is directly related to the permeability of the FL [1, 2, 7, 18, 22]; the causes of patent FL are related to distal new entry tears or entry tears on the distal aorta. In the present study, 49% of distal anastomosis new entry tears were found, but all patients included had an RAD with a patent FL in most cases, which could explain this finding. Tamura *et al.* [5] reported distal new entry tears in 19 patients (41% of cases) with patent FL. In cases of short aortic cross-clamp time, aortic resection is more limited, and re-entry or unresected tears located in the distal arch are probably more frequent. However, perioperative mortality increases with longer operative times [12, 23], which are balanced with the risk of long-term complications.

Partial aortic arch repair associated with innominate artery debranching was also associated with the risk of reintervention, probably because this was performed in cases of distal entry tears in the aortic arch or descending thoracic aorta, which were identified as risk factors for dissection-related events and

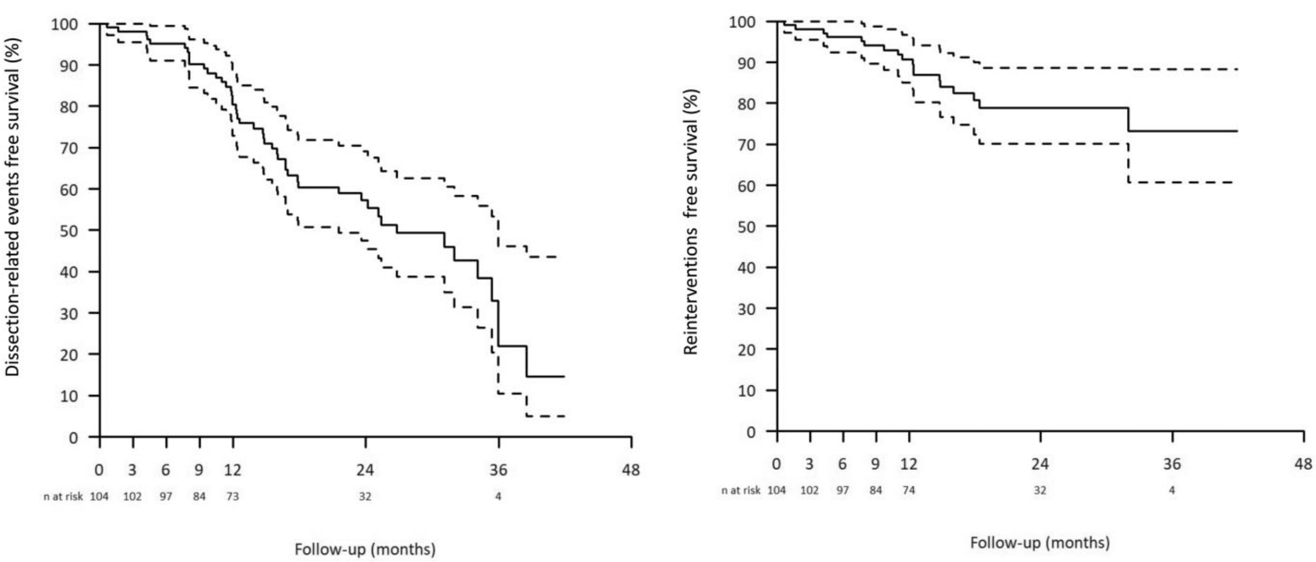

Figure 4: Kaplan-Meier event-free survival curves for dissection-related events and reintervention or death (+: censored data).

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Table 3: Summary and details of significant results of univariable analysis for risk factors for dissection-related events and reintervention

Univariable analysis for risk of dissection-related event	HR (95% CI)	*P*-value
Initial aortic diameter >40 mm	8.59 (4.03–21.69)	<0.01
Bicuspid aortic valve	2.70 (1.06–5.83)	0.038
Aortic cross-clamping time (min)	0.99 (0.98–1.00)	0.048
Primary entry tear		
Ascending aorta	0.42 (0.22–0.84)	0.015
Aortic arch	2.36 (1.22–4.34)	0.012
Descending aorta	2.83 (1.02–6.37)	0.045
Resection	0.36 (0.18–0.81)	0.015
Univariable analysis for risk of reintervention		
Initial aortic diameter >40 mm	14.33 (3.61–129.83)	<0.01
Marfan syndrome	6.54 (2.35–16.57)	<0.01
Bicuspid aortic valve	6.48 (2.17–16.80)	<0.01
Partial arch replacement + IA debranching	2.68 (1.05–6.62)	0.025
Primary entry tear		
Descending thoracic aorta	4.45 (1.16–12.80)	0.032
Resection	0.30 (0.11–0.98)	0.047

CI: confidence interval; HR: hazard ratio; IA: innominate artery.

Table 4: Results of multivariable analysis for risk factors for dissection-related events and reintervention

Variables	HR (95% CI)	*P*-value
Dissection-related events		
Initial aortic diameter >40 mm	9.00 (4.17–22.89)	<0.01
Aortic cross-clamping time (min)	0.99 (0.98–1.00)	0.011
Distal reintervention		
Initial aortic diameter >40 mm	28.54 (3.63–224.18)	<0.01
Marfan syndrome	9.06 (2.74–29.99)	<0.01

CI: confidence interval; HR: hazard ratio.

reintervention. A more aggressive primary operation with total aortic arch repair or frozen elephant trunk would be beneficial with respect to long-term results, allowing more extensive repair without residual entry tears [24, 25]. However, ascending aorta or hemiarch replacement remains the most commonly used surgical procedure in most centres because of a lower perioperative mortality risk [12].

The most relevant anatomical criteria found in the literature were the initial aortic diameter [1, 2, 4, 5, 7, 8, 17, 18] and the presence of a new entry tear on distal anastomosis [5] or the absence of resection of the primary entry tear [1–4, 26]. Our study confirmed these results: an initial aortic diameter >40 mm, absence of primary entry tear resection and distal entry tears in the aortic arch or descending thoracic aorta were risk factors for dissection-related events and reintervention.

The early demographic and anatomic poor prognostic factors identified in this study could be used to propose early endovascular treatment with better anatomical results and a low rate of perioperative complications. Indeed, TEVAR of acute or subacute dissection was associated with rapid expansion of the true lumen and collapse of the FL, whereas TEVAR for chronic dissection failed to induce positive aortic remodelling in most cases [27].

Limitations

This was a monocentric study, which could limit the external validity of this study. The absence of long-term follow-up limited the definitive interpretation of the 'real' rate of aneurysmal evolution and reintervention.

CONCLUSION

Patient inclusion in a prospective cohort improves the quality of the surveillance and could reduce the long-term mortality linked to the risk of late aortic rupture after TAAD repair.

In this study, the rate of aneurysmal evolution and reintervention confirms that RAD is a serious pathology that justifies close follow-up at an aortic centre as soon as the first months after the procedure.

Anatomical criteria coupled with demographic factors associated with poor prognosis could be used in the future to propose more aggressive treatment in the acute or subacute phase to reduce long-term reinterventions and death rates.

Conflict of interest: none declared.

Author contributions

Marine Gaudry: Conceptualization; Data curation; Funding acquisition; Investigation; Methodology; Validation; Writing—original draft. **Alizée Porto:** Data curation; Writing—original draft. **Carine Guivier-Curien:** Software; Validation; Writing—original draft. **Arnaud Blanchard:** Formal analysis; Methodology; Writing—original draft. **Laurence Bal:** Conceptualization. **Noemie Resseguier:** Formal analysis; Methodology; Writing—review & editing. **Virgile Omnes:** Writing—review & editing. **Mariangela De Masi:** Visualization. **Meghann Ejargue:** Data curation; Writing—original draft. **Alexis Jacquier:** Data curation; Visualization. **Vlad Gariboldi:** Data curation. **Valérie Deplano:** Data curation; Writing—original draft. **Philippe Piquet:** Validation; Writing—original draft.

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