

Cite this article as: Sandström C, Roos H, Henrikson O, Fagman E, Johnsson ÅA, Jeppsson A *et al.* Endovascular plugs to occlude proximal entries in chronic aortic dissection. *Interact CardioVasc Thorac Surg* 2022; doi:10.1093/icvts/ivac201.

Endovascular plugs to occlude proximal entries in chronic aortic dissection

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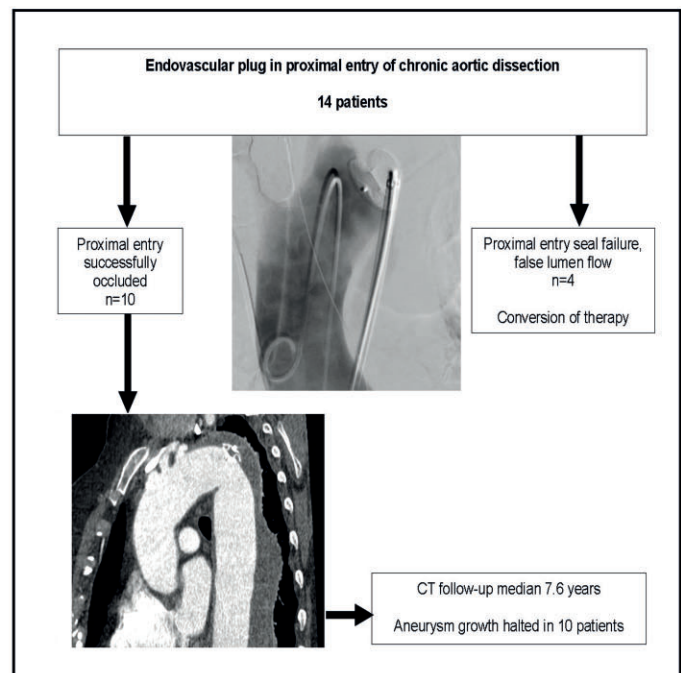
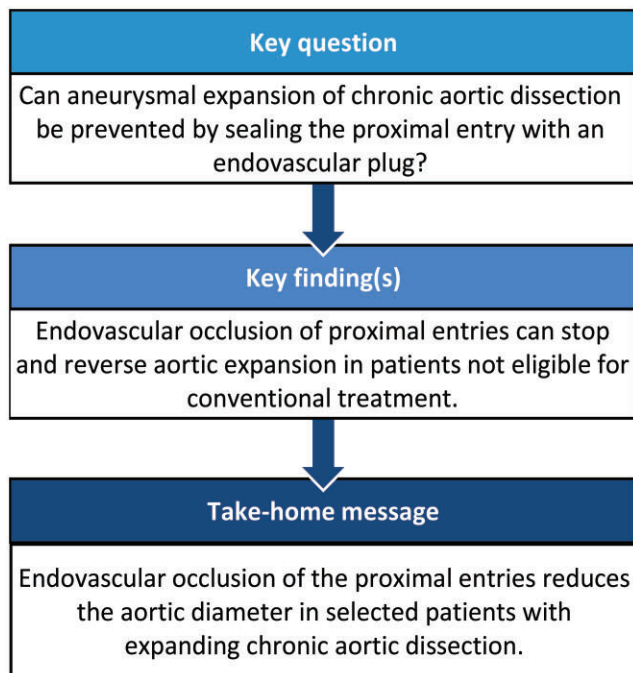
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Received 14 April 2022; received in revised form 16 June 2022; accepted 22 July 2022



Abstract

OBJECTIVES: Patients with expanding chronic aortic dissection and patent proximal entries are sometimes poor candidates for open surgery or TEVAR. Occlusion of proximal entries with endovascular plugs has previously been suggested in selected patients, but clinical results over time are unknown. This study analyses aortic remodelling and clinical outcome after proximal entry occlusion.

METHODS: Between 2007 and 2016, 14 patients, with expanding chronic aortic dissection, considered poor candidates for standard treatment, were treated with endovascular plugs in proximal entries located in the arch ($n=6$) or descending aorta ($n=8$). The Amplatzer™ Vascular Plug II was used for entries ≤ 4 mm and the Amplatzer™ Septal Occluder or Amplatzer™ Muscular VSD Occluder

for entries 5–16 mm. Patients were followed for 0.5–13 years (median 7.3) with clinical visits and computed tomography. Diameters and cross-sectional areas along the aorta were measured.

RESULTS: Occlusion of proximal entries was achieved in 10/14 patients (71%), including 4 patients with an adjunctive reintervention needed for complete seal in the segment. Unchanged or reduced maximum thoracic aortic diameter was observed in all 10 patients with successful occlusion. In 4 patients, proximal occlusion was not achieved and early conversion to FET ($n = 1$), FET/TEVAR ($n = 2$) or TEVAR ($n = 1$) was performed. Two aorta-related deaths occurred during follow-up, both after early conversion.

CONCLUSIONS: Endovascular occlusion of proximal dissection entries of expanding chronic aortic dissections can induce favourable aortic remodelling and may be considered in selected patients with expanding chronic aortic dissection who are poor candidates for open surgery or stent graft repair.

Keywords: Chronic type B aortic dissection • Type A aortic dissection • Vascular plug • Septal occluder • Aortic remodelling • Aneurysm

ABBREVIATIONS

CTA	Computed tomography angiography
FET	Frozen elephant trunk
TEVAR	Thoracic endovascular aortic repair

INTRODUCTION

Expansion of a chronic aortic dissection may lead to lethal rupture. Proximal dissection entries are often located in the arch, between sutures of the distal anastomosis following emergent tube graft repair of the ascending aorta (Stanford type A dissection), or as primary intima tears in the descending aorta (Stanford type B dissection). Treatment strategies in chronic dissections aim to stop antegrade flow from true to false lumen [1, 2]. Optimally, the false lumen will then thrombose and shrink. For chronic type A dissection this can be achieved with an open arch reconstruction and frozen elephant trunk (FET) [3, 4] or with a branched stent graft [1]. For expanding chronic type B aortic dissection, the preferred treatment is thoracic endovascular aortic repair (TEVAR) [2]. When the proximal sealing zone for a stent graft is inadequate, chronic type B dissections may require an open procedure with FET or open vascular by-pass surgery enabling coverage of the arch branches. However, open arch reconstructions with FET, with or without TEVAR extension, are major procedures, with significant risk for morbidity and mortality, particularly in frail patients [5].

For patients with aneurysm expansion and contraindication for open thoracic surgery or TEVAR, an alternative less invasive endovascular off-label technique using endovascular plugs to occlude proximal entries may be considered [6]. Two types of plugs can be used: septal occluders, designed for treatment of atrial or ventricular septal defects [7], and vascular plugs, designed to block high flow peripheral arteries [8]. Shared features for these devices are their nitinol-mesh design with 2 or 3 discs, separated by 1 or 2 thinner connecting waists. For the treatment of dissections entries, 1 disc is deployed in the true lumen and the other(s) in the false lumen, with a connecting waist centred in the entry. The choice of plug is based on the diameter of each entry.

We have previously described our initial experience with off-label endovascular occlusion of proximal entries in 4 patients with chronic dissections [6]. The aim of the present study is to describe a larger cohort of patients with focus on long-term outcome.

PATIENTS AND METHODS

Ethical statement

This retrospective review was approved by the Swedish ethical review authority (Dnr 2020-01250). Patients were preoperatively informed about the off-label use of endovascular plugs, but for this retrospective evaluation, individual consent was waived by the committee.

Patients

Between October 2007 and February 2016, 14 patients (median age 60 years, range 43–78) with expanding chronic aortic dissection were treated with endovascular plugs in the proximal dissection entries (Table 1). Indication for treatment was expanding chronic aortic dissection with a maximum diameter >6 cm or diameter progression >1 cm in 1 year in patients considered to have high risk for open surgery and/or an aortic anatomy precluding TEVAR. The decisions to treat patients with this off-label indication were made by a multi-disciplinary board with cardiothoracic surgeons, vascular surgeons, and interventional radiologists. Patient's preference was also considered in some patients who were possible candidates for open aortic reconstruction, with its inherent risks, as these patients favoured a minimally invasive technique as first choice, with careful postoperative monitoring and option to use other techniques later should the plug treatment prove insufficient. No patient treated with this new method at our institution was excluded from the study.

Planning of procedures

The thinnest slices from the most recent preoperative computed tomography angiography (CTA) were analysed in an image processing workstation (GE, USA) in the multiplanar reconstruction setting. Routes for catheterization of both the true and the false aortic lumen were carefully assessed preoperatively. The size, location and shape of each entry was determined. The smallest entry diameter was used to determine device type and size. A device diameter was chosen to enable coverage of the entry with sufficient margin to enable secure anchorage in the intended position.

Procedures

All procedures were elective and performed under general anaesthesia. Vascular access was obtained bilaterally in the

Table 1: Demographics of 14 patients with chronic dissection treated with occlusion of proximal entries with endovascular plugs

Pt	Age (years)	Sex	Dissection Stanford type (A/B)	Duration since debut (years)	Previous surgery	Proximal entry(ies) (location from LSA in mm)	Maximal diameter (location)
1	57	F	B	0.8		60	PDA
2	70	F	B	2.2		34	PDA
3	63	M	B	2.6		207	PDA
4	70	M	B	0.7		37	PDA
5	69	F	B	7.5	Asc, prothesis	44	PDA
6	78	M	B	2.0		25	PDA
7	43	M	B	3.0		30, 59	PDA
8	62	F	B	4.0		15	MDA
9	63	M	A	5.4		0, 237	PDA
10	50	F	A	0.4	Asc	-17	Arch (PDA)
11	57	M	A	3.1	Asc	0, -39	PDA
12	52	F	A	1.6	Asc	-20	PDA
13	51	M	A	10.8	Asc, prothesis × 2	-43	PDA
14	57	M	A	3.2	Asc	-20, -28	PDA

Asc: ascending aorta; F: female; LSA: left subclavian artery; M: male; mm: millimetre; MDA: mid descending aorta; PDA: proximal descending aorta; Pt: patient.

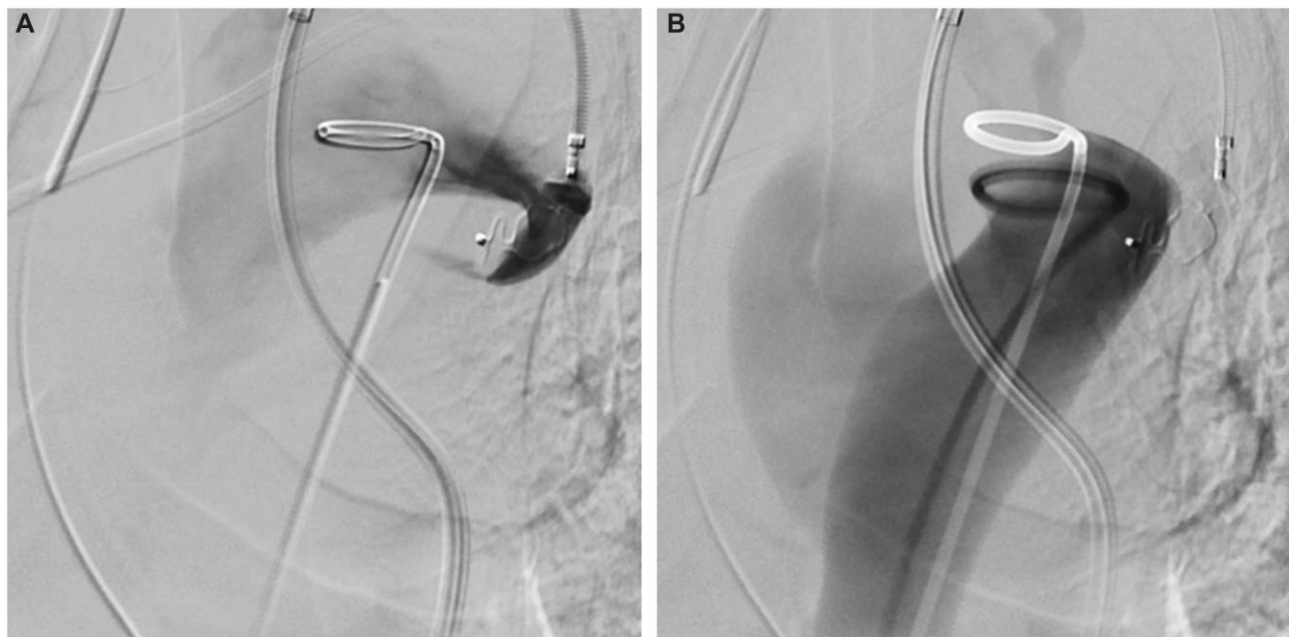


Figure 1: Positioning of a vascular plug, angiography from the (A) false lumen and (B) true lumen.

common femoral arteries. One catheter was manoeuvred through the true lumen to the ascending aorta, proximal to the dissection entry. Another catheter was placed in the false lumen, in close proximity to the entry, as evaluated with the preoperative computed tomography (CT). When needed, transoesophageal ultrasound was used to confirm catheter positions. The entry was traversed with a guidewire, directed from either the false or the true lumen, as described below.

Endovascular plugs

Two different types of endovascular plugs were used depending on the size of the entry. Both types are made of self-expanding nitinol mesh. The Amplatzer™ vascular plug II was used for entries with a diameter of ≤ 4 mm. The plug has 3 discs, separated by 2 waists. The size of the plug is defined by the diameter of the discs when released. The 2 waists are narrow, ~ 2 mm, and same

for all sizes. Choice of size for sealing dissection devices was determined by the configuration of the intima surrounding the entry. The plug was positioned in the entry with the delivery catheter by the false lumen and the tip in the true lumen. The first disc, closest to the tip of the catheter, was deployed in the true lumen. The catheter was then retracted until the expanded first disc rested on the intima, as confirmed by angiography. Thereafter, the 2 remaining discs were deployed in the false lumen, anchoring the plug in the entry hole (Fig. 1A and B). This technique has previously been described [6].

Septal occluders, the Amplatzer™ Atrial Septal Occluder or Amplatzer™ Muscular VSD Occluder was used for larger entries, 5–16 mm in diameter. Septal occluders features in addition a polyester material in the discs, intended to shorten occlusion time and facilitate tissue in-growth after implantation. Both the diameter of the discs and the diameter of the waist vary with different sizes and the choice of size is primarily based on the



Figure 2: Positioning of a septal occluder. Vascular plug in entry in the greater curvature.

diameter of the waist, matching the size of the hole to be sealed. The occluder was deployed with the delivery catheter from either the true or the false lumen, depending on anatomical features in each case. One disc was positioned in each lumen, with the waist centred in the entry hole (Fig. 2).

Follow-up

Perioperative complications, reinterventions and deaths were retrieved from medical records. The first postoperative CTA (arterial phase) was performed within 1 month after the index endovascular occlusion procedure to confirm seal of treated entries. Seal of entries was defined as the absence of false lumen contrast enhancement near the entry. If complete seal was achieved, follow-up CTA was performed at 6 months, at 1 year and then annually, unless results mandated for shorter intervals. For morphometric analysis of aortic remodelling during follow-up, aortic diameters and transection areas were measured and compared between the first postoperative CTA and the last follow-up CTA. The last follow-up CTA used in the study was the last one obtained before April 2021, or before open conversion, TEVAR or death occurred. Image analysis was performed by 1 expert vascular radiologist (Charlotte Sandström) and were not blinded. The thinnest slice acquisitions (0.5–1.25 mm) available were transferred to an image post-processing workstation (Aquarius, version 4.4.11, TeraRecon, Inc., Durham, NC, USA) and viewed in the multiplanar reconstruction setting.

A standardized measurement protocol was used. The maximum diameter of the aorta was the main outcome variable. To numerically describe remodelling along the aorta, a structured protocol was used with predetermined measurement positions. Diameter and cross-sectional area of the whole aorta, the true lumen and the false lumen were measured at each position. Areas were determined using a multiple-click semiautomatic area

measurement tool (Fig. 3). The most proximal measuring position was in the ascending aorta at the site of its maximal diameter (zone 0) and 2 positions were in the aortic arch immediately distal of the brachiocephalic trunk (zone 1) and the common left carotid (zone 2), respectively. The aortic wall immediately distal to the left subclavian artery origin was used as reference point for the remaining downstream positions, separated by 5-cm intervals along the aorta (Fig. 4). All measurements were done perpendicular to the centreline using biplanar adjustments at each position. Snapshots of the four-part pictures were saved, facilitating robustness in achieving paired measurements (Fig. 3). Stable diameter was defined as ≤ 5 -mm change during the entire follow-up.

Statistical analyses

The data were analysed using Excel [Microsoft® Excel for Mac version 16.16.27 (201012)] and SPSS 26 (IBM Corp., Armonk, NY, USA). Continuous variables are presented as median and range, while categorical variables are presented as the total number of events and percentages in parentheses. Change in the total aortic diameter and change in percentage of false to total lumen areas at each position were calculated using measurements at baseline (first postoperative acquisition) and paired measurements from the latest available scan: $(f - b)$ where f is the latest follow-up measure and b is the baseline measure.

RESULTS

Six patients had a Stanford type A dissection; 5 of them were previously treated with a supracoronary ascending aortic graft but had a persisting entry in the arch. One patient with type A dissection was initially treated conservatively due to initially missed intramural haematoma. The remaining 8 patients had a Stanford type B dissection initially treated conservatively.

Dissection entries and endovascular plugs

Three patients with initial type A dissection had entries in the suture line of the distal anastomosis of the tube graft in the ascending aorta (patients 11, 13 and 14). Of the 3 remaining patients with initial type A-dissection, 2 had entries in the aortic arch and 1 had an entry at the origin of the left subclavian artery. All 8 patients with type B dissection had proximal entries through primary intima tears in the descending aorta. Twelve patients were treated for a singular proximal entry during the index occlusion procedure. Two patients were treated for 2 separate proximal entries in close proximity to each other. Localizations of entries in relation to the origin of the left subclavian artery are shown in Table 1.

The Amplatzer™ vascular plug II was used in 8 patients (Table 2) with a plug size ranging between 8 and 20 mm (median 12 mm). The Amplatzer™ septal occluder was used in 7 patients. Waist diameters of the occluder ranged between 6 and 16 mm (median 10 mm). One patient received both a vascular plug and a septal occluder during the index procedure due to 2 differently sized entries (patient 7).

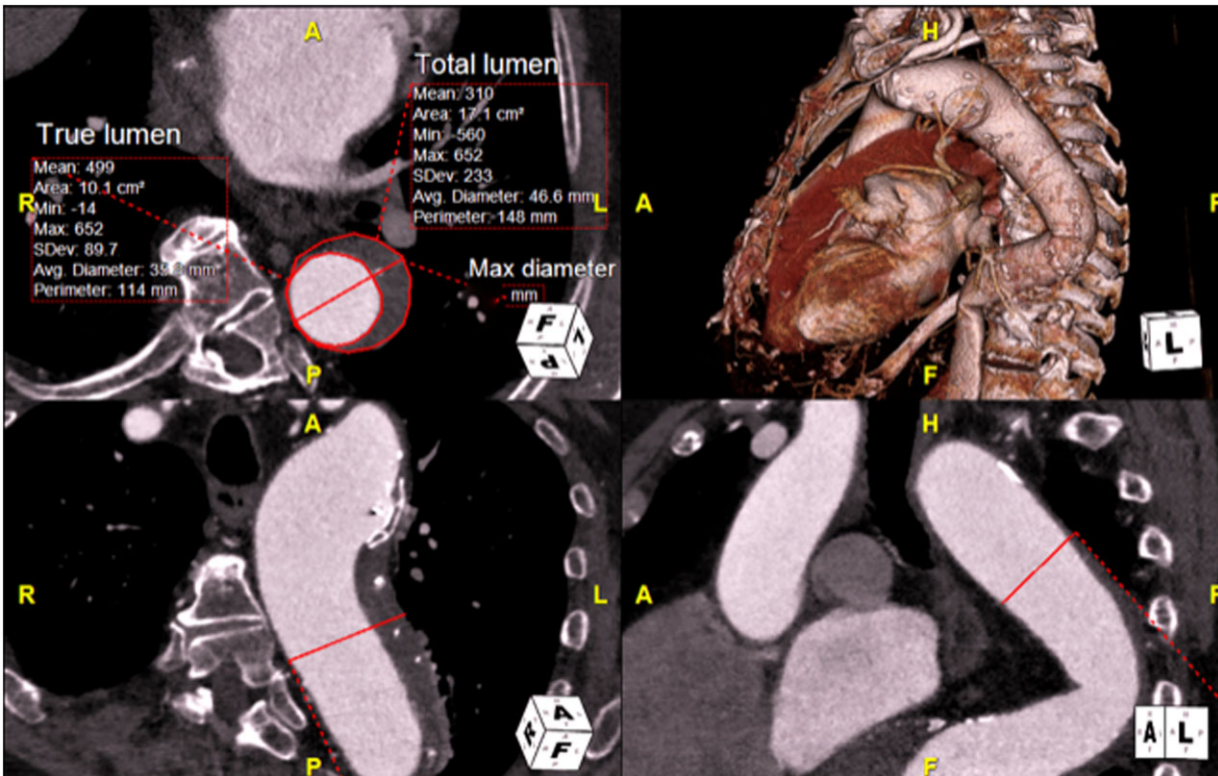


Figure 3: Diameter measurements were done in planes orthogonal to the true lumen centreline of the aorta at intervals of 5 cm. This example demonstrates measurements downstream of a septal occluder.

Periprocedural events

There were no adverse events such as deaths, neurological complications, paraplegia, renal failure or major bleeding related to the primary occlusion of entries. There was no 90-day mortality.

Early adjunctive reinterventions

Postoperative CTA showed that complete occlusion of proximal inflow to the false lumen was not achieved in 8/14 patients during the index procedure. Three of these patients were assessed as without further treatment options with this technique and were assigned to closer follow-up. In 5 patients, additional entries were identified in the postoperative CTA and these patients received early adjunctive reinterventions (Table 2). These reinterventions included additional plugs in entries that had been missed during the first procedure in 3 patients whereas 1 was in the distal descending aorta. One patient had both an additional plug and coil embolization of an intercostal artery. Coil embolization of retrograde flow from the left subclavian artery was performed in 1 patient. After these adjunctive reinterventions, complete seal was achieved in 4/5 patients while 1 still had persistent flow.

Aortic remodelling during follow-up

Including adjunctive reinterventions described above, successful seal of the proximal inflow to the false lumen was thus achieved in 10/14 (71%) patients as confirmed by subsequent CTA.

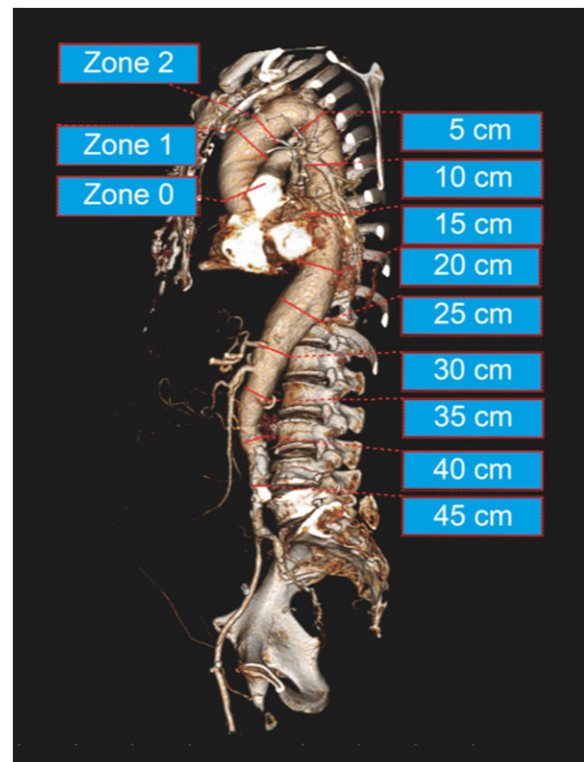


Figure 4: Model of positions of measures.

The 10 patients who had successful seal of the proximal entries had a median CT follow-up of 7.6 years (range 1.3–11.7). Using reversed Kaplan–Meier estimate, the median CT follow-up time

Table 2: Follow-up of 14 patients with chronic dissection that underwent endovascular occlusion of proximal entries with endovascular plugs

Pt	Clinical follow-up (years from index)	Indication maximum diameter (mm)	Last maximum diameter (mm)	Index intervention	Adjunctive re-intervention	Secondary reinterventions	Deaths (causes)
1	2	67	61	so			Yes/unknown
2	13	66	47	so			No
3	6.1	80	60	so	so, CE		Yes/COPD, sepsis
4	10.3	53	50	so			No
5	0.5	59	82	so		TEVAR	Yes/assumed Aortic rupture
6	7.6	73	72	so		^a Supracoronary tube graft	No
7	5.1	52	52	so, vp		FET and TAAAR	No
8	9.3	51	35	vp			No
9	7.8	71	73	vp	vp	FET, TEVAR and TAAAR	No
10	9.6	38	33	vp			Yes/Covid infection
11	8.4	72	71	vp	vp		No
12	7	57	49	vp	CE		No
13	1.3	65	82	vp		FET, TEVAR	Yes/assumed Aortic rupture
14	6.9	68	72	vp, vp	vp	FET, TEVAR	No

^aNon-dissection induced aneurysm of ascending aorta.

CE: coil embolization; COPD: chronic obstructive pulmonary disease; FET: frozen elephant trunk; Pt: patient; so: septal occluder; TAAAR: thoraco-abdominal aortic replacement; TEVAR: thoracic endovascular aortic repair; vp: vascular plug.

Table 3: Diameter changes (mm) along the aorta relatively to left subclavian artery at last follow-up compared to first CT after index treatment in 10 patients with successful seal of proximal entry

Pt	Zone 0	Zone 1	Zone 2	5 cm	10 cm	15 cm	20 cm	25 cm	30 cm	35 cm	40 cm	45 cm	Follow-up years (from index to last CT)
1	-1	-1	1	-17	-17	-2	4	9	-2	1			1.3
2	0	4	2	-26	-10	-17	-6	9	1	2	4	-3	11.7
3	1	1	0	-13	-7	-1	-2	-1	5	3			5.2
4	0	1	-2	-5	-7	-6	-2	4	8	8	4	6	9.8
6	^a	-7	-1	0	-2	1	#	1	1	3	1	3	7.3
8	-1	-1	2	-5	-3	-4	-3	-2	-1	0			9.2
9	-1	-4	1	1	-2	-1	1	1	-1	0	6	9	4.0
10	-2	-4	-3	-7	-9	-2	-2	-1	7	3			9.1
11	-3	-5	-5	-5	-4	-8	-5	4	3	3	4		7.9
12	0	-2	-6	-7	-13	-9	2	6	3	4	1		6.6

Plug-associated favourable results are highlighted.

^aSupracoronary graft.

#: missing value due to total aorta not in field of view. Pt: patient.

Table 4: Changes in ratio false/total lumen area × 100(%) along the aorta relatively to left subclavian artery at last follow-up compared to first postoperative CT in 10 patients with successful seal of proximal entry

Pt	Zone 0	Zone 1	Zone 2	5 cm	10 cm	15 cm	20 cm	25 cm	30 cm	35 cm	40 cm	45 cm
1	0	0	0	-67	-48	-45	-37	-7	-8			
2	0	0	0	-62	-48	-77	-44	-4	-8	+28	-13	-8
3	0	0	0	-14	-11	-3	-10	-2	0	0		
4	0	0	0	-36	-31	-34	+25	-22	-3	+16	-8	+8
6	0	0	0	-9	-7	-9	#	-3	-6	+3		
8	0	0	0	-23	-41	-33	-29	-32	-51	0		
9	0	0	0	-2	-3	-1	+9	-3	+12	+5	+13	+15
10	0	-14	-18	-26	-68	-18	-27	-13	+5	#		
11	0	-17	-26	-9	-21	-7	-6	-1	-4	+3	+6	
12	0	-19	-40	-62	-38	-25	-3	+6	+39	+2		

Negative values indicate remodelling in true lumens' favour. #: missing value due to total aorta not in field of view.

Pt: patient.

was 9.2 years. All these patients had an unchanged or reduced maximal diameter in the descending thoracic aorta or thoracic arch at the last CT, compared to baseline CT (Table 3). Remodelling varied along the aorta and was related to the distance from the vascular plugs. Diameter reduction was most often observed in the proximal descending aorta, downstream of the plugs. The length of beneficial remodelling (unchanged or reduced diameter) along the aorta is shown in Table 3. A corresponding favourable remodelling was not seen in the abdominal aorta. Changes in ratio between the false and total lumen area coincided with changes in total aortic diameter. Hence, total diameter reductions appeared to be associated with shrinking of the false lumen (Table 4). Correspondingly, increased false lumen area was observed in those patients who had an increasing total diameter in the abdominal aorta. When analysed separately based on the Stanford classification, 4/6 cases with type A and 6/8 cases with type B dissections had a favourable morphometric outcome in the descending aorta during follow-up with either reduction or stabilization of the maximum diameter.

Reinterventions and clinical events during follow-up

Follow-up from index intervention until death or end of follow-up April 2021 was median 7.3 years (range 0.5–13 years) (Table 2).

Patients where successful occlusion of the proximal entry was achieved. Two patients with successful initial occlusion were reintervened during follow-up despite satisfactory remodelling in the descending aorta after the plug treatment. In 1 patient with type B dissection (patient 6), the diameter of the ascending aorta increased despite absence of dissection in the arch or the ascending aorta. This patient received a supracoronary graft in the ascending aorta and had persistent stable diameter of the descending thoracic aorta during follow-up, had no further complications during follow-up and has not needed any further reintervention. In the patient with a previously conservatively treated type A dissection (patient 9), expansion progressed in the abdominal aorta distal to the plug-treated segment of the descending aorta, where an unchanged aortic diameter was observed. This patient was reintervened twice, first with FET and TEVAR and later with thoraco-abdominal aortic replacement with good clinical outcome.

Patients where successful seal of the proximal entry was not achieved. The 4 patients with persistent false lumen flow in the treated aortic segment were reintervened (Table 2). Three of them had further increase of maximum aortic diameter (patients 5, 13 and 14) and 1 had a stable diameter (patient 7). The median time between the index plug procedure and the decision to reintervene was 6 months (range 5–7). One patient received treatment with TEVAR despite suboptimal anatomy (patient 5). The patient died 8 days after TEVAR due to aortic rupture. Three patients were converted to FET (patient 7) or FET with TEVAR (patients 13 and 14). One patient died 3 months after completed reintervention due to aortic rupture (patient 13). Patient 7 had an open thoraco-abdominal repair 1 year after FET.

In total, 5 patients died during follow-up. Two from aortic rupture, both after conversion performed due to persistent flow after primary plug placement (patients 5 and 13) detailed above, and 3 from other causes (Table 2).

DISCUSSION

In this study, we investigated an off-label technique for targeted closure of proximal entries in 14 patients with expanding chronic aortic dissection and high risk for conventional treatment, using vascular plugs or septal occluders. With a median CT follow-up of 7.6 years, successful occlusion of proximal entries was achieved in 10/14 patients (71%). In this group, plug treatment stopped further aneurysmal expansion in the arch and the descending thoracic aorta but not in the abdominal aortic segment. There were no periprocedural complications but 5 patients needed an adjunctive reintervention.

Treatment of expanding chronic aortic dissection to prevent lethal rupture is challenging. Most patients are elderly and frail, often with multiple comorbidities. Anatomy and extent of dissection vary considerably between patients. Aortic endografting is the treatment of choice in patients with entries in the descending aorta when a sufficient proximal landing zone is available, but in many patients, a major open procedure, FET, is required to secure proximal seal. Branched TEVAR with extensions to supra-aortic arteries is an evolving option, but technically demanding, not always possible due to anatomy and it is a major procedure in itself, and burdened by a significant risk of cerebral embolization [9]. Therefore, an alternative minimally invasive strategy without the need for a circumferential aortic sealing zone may be an attractive option in selected patients.

Beneficial remodelling of the proximal half of the descending aorta with stabilization or reduction of maximum diameter was observed in patients after successful entry occlusive plug treatment. The maximum diameter decreased and the false lumen area fraction decreased along ~20 cm of the aorta distal of the left subclavian artery. The segment and the length of beneficial aortic remodelling mimic what has been observed after TEVAR for chronic dissection [10–12].

Vigilant follow-up with high-quality imaging is imperative after endovascular occlusion of proximal entries. This is demonstrated in the present study by the need for adjunctive reinterventions after the first postoperative CT in 5/14 patients in whom the proximal entries were not completely occluded by the first procedure. The need for late reinterventions appeared to be in line with outcomes after TEVAR for chronic dissection [11] likely reflecting the underlying disease.

The minimal invasiveness and the procedural safety are the main advantages of endovascular occlusion of proximal entries compared to other invasive treatment options in patients with expanding chronic aortic dissections. There were no periprocedural complications in the present series. Possible disadvantages include the challenge to accurately locate proximal entries, particularly when they are small and/or multiple, and to achieve seal of some entries, particularly when they are very asymmetric. This was indicated by the need for early adjunctive reinterventions in some of our patients. Another likely limitation with the technique may be the size of treatable entries. The largest entry treated in our series had a diameter of 16 mm, and we do not know if septal occluders in even larger entries is possible or safe.

Treating uncomplicated dissection with TEVAR in the subacute phase, is suggested by several investigators [13, 14]. However, since the plugs are anchored on the intima adjacent to the entry hole, while a TEVAR stent graft is anchored to intact aortic wall, proximal of the dissection, plug treatment likely requires an older and more stable dissection membrane compared to TEVAR. We

have not used plug treatment in any patient with a shorter interval from dissection onset than 5 months. The aortic maximum diameter as such, at the time of treatment, did not affect the rate of favourable remodelling in our series.

In this series, all procedures were done in general anaesthesia. This was partly due to local tradition and partly to allow the control of breathing motions during device deployments. However, since blood loss and physiological strain are minimal, the technique should also be feasible in local anaesthesia in cooperating patients.

Limitations

Limitations of this study are the small sample size at a single institution and the retrospective design with the inherent risk of selection bias and non-registered confounders. Only patients who were assessed as poor candidates for open surgery and/or TEVAR were included, except when patient's preference influenced the choice of therapy. Consequently, results are not directly comparable between techniques, and therefore, generalization of the results may be problematic. Since this is a new application of the devices, outcomes may be affected by a learning curve.

CONCLUSION

This study indicates that occluding proximal entries with endovascular plugs is a minimally invasive and safe option in selected patients with expanding chronic aortic dissection who are poor candidates for open repair or TEVAR. Endovascular plug occlusion of chronic dissection entry tears can induce favourable thoracic aorta remodelling in highly anatomical selected candidates. Larger cohorts are needed to confirm our findings and ascertain the durability of this alternative approach.

Funding

This work was supported by Region Västra Götaland (ALFGBG 77190) and Futurum—the academy of healthcare, Region Jönköping County (FUTURUM-963529).

Conflict of interest: None declared.

Data availability

Data available on reasonable request.

Author contributions

Charlotte Sandström: Conceptualization; Data curation; Formal analysis; Validation; Visualization; Writing—original draft. **Håkan Roos:** Conceptualization; Data curation; Formal analysis; Writing—review & editing.

Olof Henrikson: Methodology; Writing—review & editing. **Erika Fagman:** Formal analysis; Writing—review & editing. **Åse A. Johnsson:** Conceptualization; Writing—review & editing. **Anders Jeppsson:** Formal analysis; Writing—review & editing. **Mårten Falkenberg:** Conceptualization; Methodology; Project administration; Writing—review & editing.

Reviewer information

Interactive CardioVascular and Thoracic Surgery thanks Luca Bertoglio, Mario Lescan, Stoyan Kondov and the other, anonymous reviewer(s) for their contribution to the peer review process of this article.

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