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INTERVENTIONAL RADIOLOGY

ORIGINAL ARTICLE

Embolization therapy for type 2 endoleaks after endovascular aortic aneurysm repair: imaging-based predictive factors and clinical outcomes on long-term follow-up

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PURPOSE

To evaluate the technical, radiological, and clinical outcomes after type 2 endoleak (T2EL) embolization in patients with a growing aneurysm sac after endovascular aortic aneurysm repair (EVAR). Additionally, to determine clinical and imaging-based factors for outcome prediction after embolization of a T2EL.

METHODS

A single-institution, retrospective analysis was performed of 60 patients who underwent a T2EL embolization procedure between September 2005 and August 2016 to treat a growing aneurysm sac diameter following EVAR. The patients' electronic medical records and all available pre- and post-embolization imaging were reviewed. Statistical analysis methods included logistic regression models for binary outcomes, proportional odds models for ordinal outcomes, and linear regression models for continuous outcomes. The Kaplan–Meier method was used to estimate the overall survival probability.

RESULTS

Technical, radiological, and clinical success rates after T2EL embolization were 95% (n = 57), 26.7% (n = 16), and 76.7% (n = 46), respectively. Persistent aneurysm sac expansion was found in 31 patients (51.7%). Unsharp or blurred T2EL delineation on pre-interventional computed tomography (CT) was a predictive factor for a post-embolization persistent visible endoleak and persistent growth of the aneurysm sac (P = 0.025). Median survival after T2EL embolization was 5.35 years, with no difference observed between patients with persistent sac expansion compared with patients with stable or decreased sac diameter.

CONCLUSION

Progression of the aneurysm sac diameter was observed in half the study patients, despite technically successful T2EL embolization. Unsharp or blurred T2EL delineation on pre-interventional CT seemed to be an imaging-based predictor for a persistent T2EL and progressive aneurysm sac growth after embolization.

KEYWORDS

Abdominal aortic aneurysm, catheter angiography, CT angiography, embolization, endoleak

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Current international guidelines propose endovascular aortic aneurysm repair (EVAR) as the standard treatment for abdominal aortic aneurysm (AAA) in selected patients with suitable vascular anatomy.[1,2] However, endoleaks, defined as persistent blood circulation in the aneurysm sac, remain the Achilles' heel of EVAR procedures.[3-6] A type 2 endoleak (T2EL), caused by backflow from collateral arteries into the aneurysm sac, has an occurrence rate of approximately 15% after successful EVAR and accounts for approximately half of all endoleaks.[3,7,8] The management of a T2EL remains controversial; some experts propose conservative management as a safe strategy,[9,10] while others have demonstrated T2ELs as a cause of late rupture with a need for reintervention.[4,11] Current guidelines recommend treatment in patients with a T2EL after EVAR associated with aneurysm sac expansion of >10 mm in diameter.[1] Due to the relatively high late-complication rate in patients with a T2EL after EVAR, lifelong radiological surveillance is currently recommended in these patients.[12,13]

Short-term outcome data after T2EL embolization are variable,[3,14-18] and long-term radiological and clinical outcome data are scarce.[19] Additionally, relatively little is known about how predictive pre-embolization imaging factors are for better or worse outcomes.

The aim of this study is to determine the technical and long-term radiological and clinical outcomes after T2EL embolization and to assess clinical and imaging-based factors for outcome prediction after embolization of T2ELs associated with aneurysm sac expansion following EVAR.

Methods

Patients

This retrospective study was approved by the Ethics Committee of the University Hospitals KU Leuven (S62135). All consecutive patients who underwent an elective T2EL embolization procedure between September 2005 and August 2016 were included in the study. Inclusion criteria were a T2EL associated with growth of the aneurysm sac diameter by at least 5 mm compared with the diameter prior to EVAR or growth of the aneurysm sac diameter by less than 5 mm compared with the diameter prior to EVAR but associated with a growth of the largest diameter of the T2EL, as measured in the venous phase, compared with previous follow-up computed tomography (CT) imaging; however, our approach to include patients for T2EL embolization is rather aggressive compared with current society guidelines.[9] Patients with a T2EL associated with other types of endoleaks were excluded from the study. The decision to refer the patient for an embolization procedure was made in consensus during multidisciplinary case discussion meetings, which included vascular surgeons and interventional radiologists. The patients' demographics and clinical follow-up data were gathered from their electronic medical records. Radiological documents, including CT scans prior to and after EVAR, as well as angiographic studies and interventional procedures, were studied on a picture archiving and communication system (PACS, Agfa-Gevaert, Mortsel, Belgium). Measurements of the aortic aneurysm and side branches were performed prior to embolization on a graphical CT workstation (Syngo.via, Siemens Healthcare, Forchheim, Germany). Twenty-five patients (42%) were referred from community hospitals to the authors' institution for interventional management of T2ELs. Referred patients' data were collected after contacting the referring physician, and medical records and all available CT scans were reviewed for each patient.

Initial EVAR was performed using the Excluder device (W. L. Gore & Associates, Flagstaff, AZ, USA) on 28 patients (47%), the Zenith device (Cook, Bloomington, IN, USA) on 17 patients (28%), and the Endurant device (Medtronic, Minneapolis, MN, USA) on 9 patients (15%). Other devices were used on 6 patients [lifepath (n = 1), ovation (n = 1), fortron (n = 2), and talent (n = 2)]. All patients received lifelong aspirin at a dose of 80 mg daily after EVAR.

No prophylactic aortic side branch embolization to prevent T2ELs was performed prior to initial EVAR, despite recent insights suggesting pre-emptive aortic side branch embolization may be associated with lower rates of sac enlargement, incidence of T2ELs, and reinterventions.[20]

Main points

- Progression of aneurysm sac diameter is common after type 2 endoleak (T2EL) embolization.
- Unsharp (blurred) contours are predictive for a persistent T2EL.
- Greater need for surgical conversion is seen with blurred T2ELS.

Imaging studies

Patients underwent triphasic CT scans and catheter-directed angiography of the endoleak prior to referral for embolization. All CT scans in our institution were obtained using helical multidetector CT scanners; the type of CT scanner used depended on the time period of inclusion. The CT protocol for follow-up imaging after EVAR included a triple-phase technique with unenhanced, arterial, and delayed venous phases. Contrast-enhanced arterial phase images were generated during an injection of 80–120 mL (depending on the renal function of the patient) of non-ionic contrast material at a flow rate of 4 mL/second using bolus tracking with a threshold of 120 Hounsfield units. Delayed venous phase images were obtained 70 seconds after the arterial phase scan. Catheter-directed angiography of the endoleak was performed under local anesthesia through an arterial puncture in the right or left groin. Flush abdominal aortography in anteroposterior and profile views (30 mL of non-ionic iodized contrast medium at a flow rate of 10 mL/second) was performed using a pigtail catheter, followed by selective catheterization of the superior mesenteric artery (SMA) (20 mL of non-ionic iodized contrast medium at a flow rate of 4 mL/second) and the ipsilateral internal iliac artery and contralateral iliac stent-graft limb (10 mL of non-ionic iodized contrast medium at a flow rate of 5 mL/second) using a Simmons 2 catheter.

Patient follow-up after T2EL embolization took place at 1, 6, and 12 months, and yearly thereafter in accordance with the EUROSTAR guidelines for EVAR follow-up,[5] with special attention given to aneurysm sac diameter and persistence or disappearance of the embolized T2EL. Patients were followed up with until the end of the study period (January 2019), the patient's death, or conversion by open surgical repair.

Evaluation of imaging-based risk factors

Measurements performed on the aortic aneurysm and side branches prior to embolization included the maximum diameter of the AAA, maximum axial diameter (perpendicular to the long axis of the abdominal aorta) of the T2EL at the venous phase, patency of the lumbar arteries (LA) and inferior mesenteric artery (IMA). Additionally, the location of the endoleak in the AAA was determined (>75% of the endoleak area located anterior or posterior in the aneurysm sac) to show sharp (Figure 1) or unsharp (blurred) T2EL delineation. Blurred delineation was defined as irregular delineation of at least 75% of the endoleak contour (Figure 2). All measurements were performed after consensus by two interventional radiologists with 5 and 20 years of experience, respectively, in vascular radiology and embolization techniques. Progressive expansion or shrinkage of the aneurysm sac was defined as an increase or decrease, respectively, of 5 mm or more in the maximum aneurysm diameter. An absence of significant change in AAA diameter (<5 mm) was recorded as no change in the aneurysm sac diameter.

Finally, the embolization approach (transarterial versus translumbar/transperitoneal access) was decided at the discretion of the attending interventional radiologist based on the location of the T2EL, the AAA sac, surrounding tissues, and the maximum axial diameter of the endoleak (measured in axial sections in the delayed phase). The translumbar/transperitoneal approach was the first-line choice if percutaneous access to the T2EL was technically feasible and safe.

Figure 1. Venous phase, contrast-enhanced axial computed tomography image in a patient with a growing aneurysm sac and a sharply delineated type 2 endoleak (white arrows) posterior to the endograft limbs.

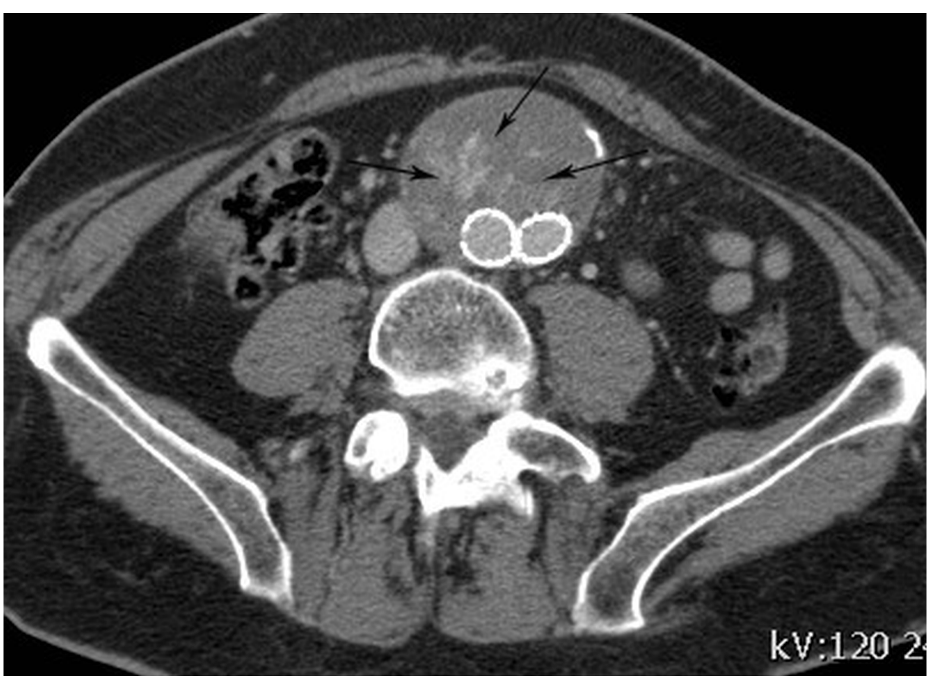


Figure 2. Venous phase, contrast-enhanced axial computed tomography image in a patient with a growing aneurysm sac and an unsharply delineated type 2 endoleak (small black arrows) anterior to the endograft limbs.

T2EL embolization technique

Patients' informed consent was obtained by both the referring vascular surgeon and the attending interventional radiologist prior to the embolization procedure. The anticoagulation regimen, including aspirin at a dose of 80 mg daily, was unchanged after the embolization procedure.

Transcatheter embolization of the T2EL

Under general anesthesia, a 4 or 5 French (F) sheath was inserted in the right or left common femoral artery, and catheterization of the SMA or ipsilateral internal iliac artery was performed using a 4 or 5 F Simmons 1 or Cobra catheter (Cook Medical, Bloomington, IN, USA; or Terumo Europe, Leuven, Belgium), followed by superselective catheterization using a microcatheter (Cantata 2.5, Cook Medical, Bloomington, IN, USA; or Maestro 2.4, Merit Medical, South Jordan, UT, USA) of the arc of Riolan and IMA or the iliolumbar artery and lower LA where the IMA or iliolumbar artery was the feeding artery of the T2EL, respectively. The microcatheter was advanced as close as possible to or into the nidus of the endoleak, and then embolics were injected in order to completely close the nidus of the T2EL. Embolics used included microcoils (Microtornado, Cook Medical, Bloomington, IN, USA; or Target microcoils, Boston Scientific, Natick, MA, USA), ethylene vinyl-alcohol copolymer (Onyx, Medtronic, Minneapolis, MN, USA), or glue as a 3:1 mixture of ethiodized oil (Lipiodol, Guerbet, Aulnay-sous-Bois, France) and n-butyl cyano-acrylate (Histoacryl, B. Braun, Melsungen, Germany).

Translumbar/transperitoneal embolization of the T2EL

With the patient under general anesthesia and in a prone or supine position, an unenhanced cone beam (CB) CT of the AAA was performed (XperCT, Philips Healthcare, Best, the Netherlands) and fused or visually confronted with the pre-interventional contrast-enhanced CT to determine the T2EL in the aneurysm sac. Using CB-CT-based puncture guidance techniques (XperGuide, Philips Healthcare, Best, the Netherlands), the nidus was percutaneously punctured using a sheathed 5 F needle (percutaneous entry thinwall needle, Cook Medical, Bloomington, IN, USA). A microcatheter (Progreat 2.7, Terumo Europe, Leuven, Belgium) was introduced into the nidus through the 5 F sheath, and angiographic imaging of the nidus, afferent arteries, and efferent arteries was performed. These arteries were embolized with microcoils (Microtornado, Cook Medical, Bloomington, IN, USA; or target microcoils, Boston Scientific, Natick, MA, USA), and finally, the nidus was occluded using a 1:1 mixture of ethiodized oil (Lipiodol, Guerbet, Aulnay-sous-Bois, France) and n-butyl cyano-acrylate (histoacryl, B. Braun, Melsungen, Germany).

Definitions for outcome after embolization

The outcome of the T2EL embolization was categorized as a technical, radiological, or clinical success. Technical success was defined as the nidus of the T2EL being fully approachable and completely embolized, with no evidence of residual contrast opacification on completion of angiography. Radiological success was determined by the absence of a persistent endoleak and unchanged or decreased diameter of the aneurysm sac at the latest follow-up CT. Finally, clinical success was defined as the absence of late aortic or endoleak-associated complications such as rupture or the need for surgical conversion on long-term follow-up.

Statistical analysis

Statistical analyses were performed using SAS software (version 9.4 of the SAS System for Windows, Cary, NY, USA). The association between pre-operative characteristics and outcome was analyzed using univariate binary logistic regression models for persistent endoleaks, proportional odds models for ordinal outcomes (decreased/stable/increased aneurysm sac diameter), and linear regression models for continuous outcomes (changes in aneurysm sac diameter). The significance level was established as α: 0.05. The Kaplan–Meier method was used to estimate the overall survival curve. The comparison between groups (e.g., increased versus stable/decreased aneurysm sac diameter) was performed using the Mann–Whitney U test for continuous variables, the chi-square test or Fisher's exact test for categorical variables, or the log-rank test for overall survival. Inter- and intra-observer variability is assessed by Cohen's kappa coefficient. The kappa coefficient takes values between 0 and 1, with higher values indicating better agreement. Interpretation of this statistic suggested by Fleiss characterizes kappa over 0.75 as excellent, 0.40 to 0.75 as fair to good, and below 0.40 as poor.

The univariate Cox proportional-hazards model was fitted to associate persistent T2EL, aneurysm sac diameter increase, or need for reintervention with overall survival.

Results

Sixty patients who presented with aortic aneurysm sac expansion after EVAR underwent an elective T2EL embolization at our institution, with a median time interval of 2.6 years (interquartile range 1.3–4.9 years) in between index EVAR and T2EL embolization procedure. The median follow-up time of our study population after embolization was 6.43 years (Q1–Q3, 4.93–9.00).

Demographics and patient characteristics

The patients' demographics and baseline clinical characteristics prior to embolization of the T2EL are listed in Table 1. The majority of patients in the study population were male (88.3%) with a median age of 79.5 years (range 62–89 years).

Endoleak characterization and embolization technique/approach

Pre-interventional vascular imaging characteristics, including type and diameter of the AAA, delineation, and diameter at the location of the T2EL within the AAA, as well as data on the embolization procedures, are summarized in Table 2. In addition, the kappa-coefficient [95% confidence interval (CI)] for inter- and intra-observer variability was 0.64 (0.42; 0.85) and 0.88 (0.75; 1.00), respectively. In 36 patients (60%), the indication for T2EL embolization was a mean sac expansion between pre-EVAR and pre-embolization (9.2 mm; 5–27 mm); a minimum increase of the maximum AAA sac diameter (<5 mm) associated with an increase in the diameter of the nidus of the T2EL (>5 mm) was an indication for embolization in 6 patients (10%). Finally, in 18 patients (30%), it was unclear whether the increase in the diameter of the T2EL or of the AAA was the main indication for embolization of the T2EL.

The afferent artery of the T2EL was the LA in 42 patients (70%), the IMA in 10 patients (16.7%), and a combination of the LA and IMA in 8 patients (13.3%).

Technical, radiological, and clinical success

Technical success

In 57 patients (95%), it was possible to embolize the nidus of the T2EL completely, as demonstrated on completion angiography. In 3 patients (5%), incomplete embolization of the nidus of the T2EL was demonstrated on completion angiography; two of these three patients were embolized in a translumbar approach using glue, which resulted in a partial filling of the nidus of the T2EL. However, follow-up CT scans were not able to demonstrate either a persistent T2EL or progressive expansion of the aneurysm sac. The remaining patient was treated using a transcatheter approach for a T2EL fed by a left iliolumbar artery. Superselective embolization was performed using glue and resulted in the partial filling of the endoleak. A follow-up unenhanced CT scan revealed a persistent increase in AAA diameter from 86

Table 1. Patients' demographics and baseline clinical characteristics

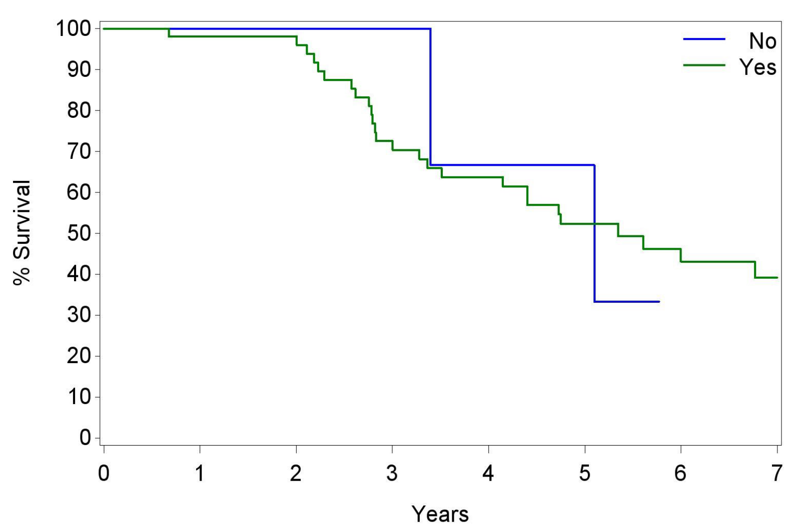
Demographic parameter	Statistic	All
Age	n	60
	Median	79.5
	Q1, Q3Q1, Q3	(72.0; 83.0)
Sex		
Male	n (%)	53 (88.33%)
Female	n (%)	7 (11.67%)
Smoking	n (%)	28 (46.67%)
Diabetes	n (%)	4 (6.67%)
Coronary artery disease	n (%)	15 (25%)
Chronic renal insufficiency	n (%)	4 (6.67%)
Arterial hypertension	n (%)	42 (70%)
COPD	n (%)	7 (11.67%)
Hyperlipidemia/hypercholesterolemia	n (%)	28 (46.67%)
Peripheral vascular disease	n (%)	4 (6.67%)

Q1, Q3, first and third quartile; COPD, chronic obstructive pulmonary disease.

Table 2. Pre-interventional vascular imaging characteristics and data on the embolization procedures

Pre-interventional vascular imaging characteristics	Statistic	All
Type of abdominal aortic aneurysm		
Infrarenal, aorto-bi-iliac AAA	n (%)	1 (1.67%)
Infrarenal, aorto-left-iliac AAA	n (%)	2 (3.33%)
Infrarenal, aorto-right-iliac AAA	n (%)	6 (10%)
Infrarenal AAA	n (%)	51 (85%)
AAA diameter (mm) prior to type 2 endoleak embolization	n	60
	Median	70.5
	Q1, Q3Q1, Q3	(63.0; 78.0)
Type 2 endoleak diameter (mm) prior to embolization	n	60
	Median	25.0
	Q1, Q3Q1, Q3	(18.0; 35.0)
Type of endoleak type 2 delineation		
Blurred (patchy)	n (%)	17 (28.33%)
Sharp	n (%)	43 (71.67%)
Location of type 2 endoleak in AAA		
Anterior	n (%)	12 (20%)
Posterior	n (%)	48 (80%)
Approach to type 2 endoleak		
Transarterial	n (%)	12 (20%)
Translumbar	n (%)	48 (80%)
Embolization material to occlude type 2 endoleak		
Glue (lipiodol and enbucrylate)	n (%)	29 (48.33%)
Glue (lipiodol and enbucrylate) and microcoils	n (%)	26 (43.33%)
Microcoils	n (%)	3 (5%)
Onyx	n (%)	2 (3.33%)

AAA, abdominal aortic aneurysm; Q1, Q3, first and third quartile.



Number at risk								
No	3	3	3	3	2	2	0	0
Yes	56	52	46	33	28	20	14	10

Figure 3. No significant difference in overall survival was observed in patients with or without technically successful type 2 endoleak embolization procedure ($P = 0.9158$).

mm prior to embolization to 99 mm at the latest follow-up CT. Long-term clinical follow-up did not reveal any AAA rupture up to the time of patient death due to cardiac decompensation. Kaplan–Meier analysis could not demonstrate a difference in survival between patients with and without technically successful T2EL embolization ($P = 0.916$), as shown in Figure 3. A serious post-embolization complication was observed in 2 patients at 10 and 12 months, respectively, after initially successful translumbar and transcatheter embolization; this was due to infection of the endograft and bilateral psoas abscesses (Figure 4a-c). The responsible microorganisms in the translumbar case were *Staphylococcus hominis* and *Staphylococcus capitis*. Both of these are human skin commensals, suggesting that the infection was inoculated through the percutaneous puncture. These serious infection complications were definitively and successfully resolved with stent-graft resection and surgical aorto-bi-iliac reconstruction with autologous deep vein.

In 4 patients (6.7%), a second embolization procedure was performed 11, 20, 21, and 34 months, respectively, after the initial translumbar T2EL, due to a persistent T2EL in combination with progressive growth of the AAA sac, identified on follow-up CT scan at 6 months, 1 year, 1 year, and 2 years, respectively, after initial T2EL embolization.

Radiological success

Follow-up with multiphase CT scans was performed in 59 patients (98.3%). In one patient (1.7%), follow-up was performed with duplex ultrasound and an unenhanced CT scan at the referring hospital due to chronic renal insufficiency. Median radiological follow-up after T2EL embolization was 5.3 years (3.5–7.0 years). On follow-up CT scans, a persistent post-embolization T2EL was noted in 35 patients (58.3%). This was associated with an increase in maximum aneurysm sac diameter in 31 patients (51.7%) with a mean increase in maximum sac diameter of 8.3 mm, as summarized in Table 3. Twenty-two patients (36.7%) showed stable aortic diameter, and 7 patients (11.7%) showed a decrease in AAA diameter. Overall, radiological success was observed in 16 patients (26.7%).

Pre-interventional unsharp or blurred T2EL delineation was statistically significant as a predictive factor for a persistent endoleak at follow-up ($P = 0.025$). Other imaging or embolization variables showed no statistically significant difference in radiological or clinical success (Table 4).

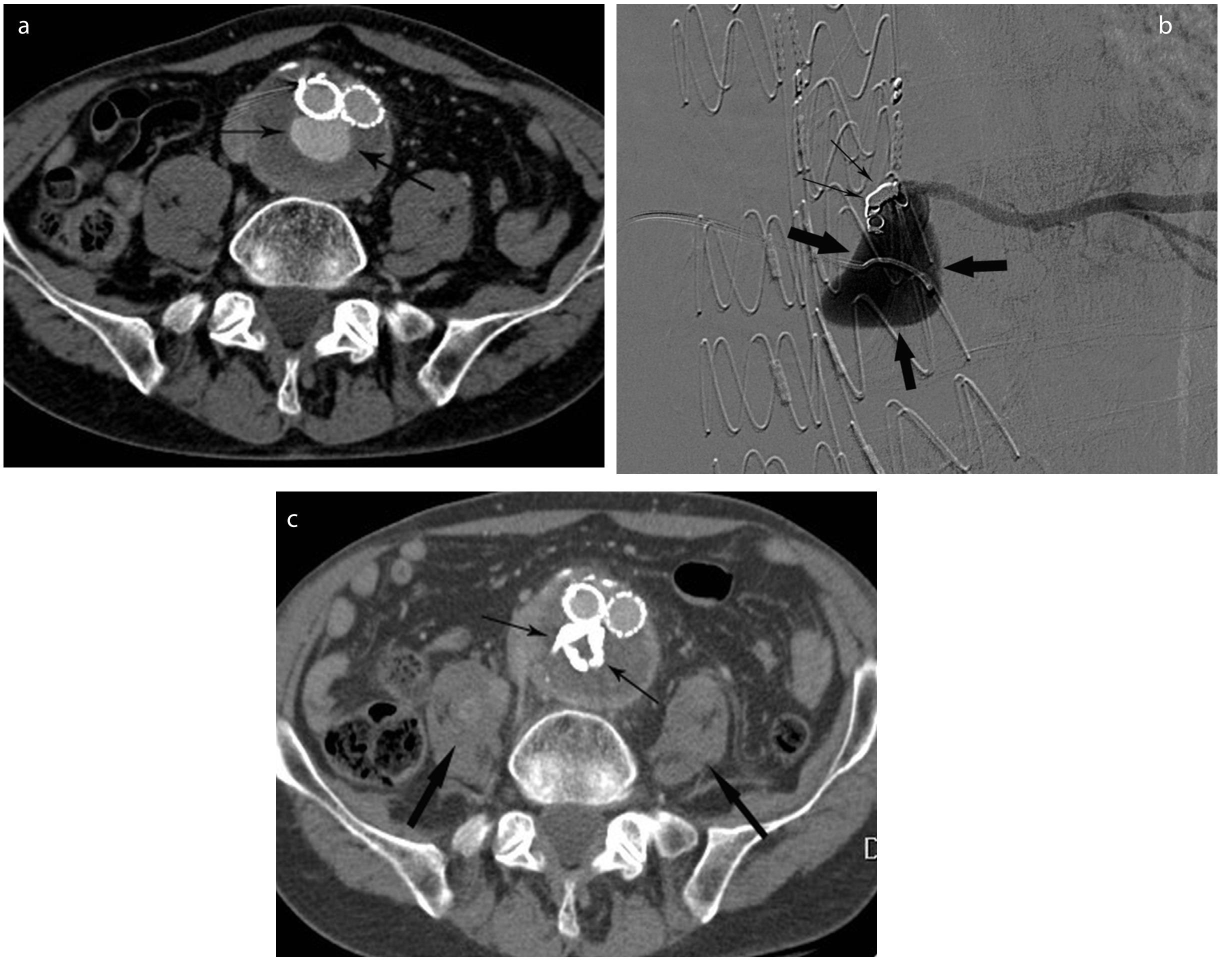


Figure 4. **(a)** Venous phase, contrast-enhanced axial computed tomography (CT) image in a patient with a growing aneurysm sac and a sharply delineated type 2 endoleak (small black arrows) posterior to the endograft limbs; the patient was referred for translumbar direct puncture and embolization of the type 2 endoleak. **(b)** Digital subtraction angiography of the nidus (large black arrows) of the type 2 endoleak after direct translumbar puncture. Also, note the coils (small black arrows) deployed in the proximal left fourth lumbar artery. **(c)** Follow-up contrast-enhanced CT scan nine months after translumbar endoleak embolization demonstrating the cast of glue (mixture of enbucrylate and ethiodized oil) (small black arrows) completely filling the type 2 endoleak. Also note the contrast-enhancing foci in both psoas muscles (large black arrows), suggestive of psoas abscesses.

Blurred T2EL delineation at the pre-embolization CT scan was observed in 17 patients (28.3%), with a mean aneurysm sac diameter increase of 10.9 mm (median 10.0, Q1–Q3, 0.0–15.0, range –6.0–38.0 mm). Of the 17 patients (64.7%) with blurred T2EL delineation, 11 showed an increase in AAA diameter, 5 (29.4%) had a stable AAA diameter, and only 1 patient (5.9%) showed a decrease in AAA diameter after T2EL embolization.

Smoking and hyperlipidemia were associated with radiological success (P = 0.010 and P = 0.047, respectively), as summarized in Table 4. Kaplan–Meier analysis could not demonstrate a difference in survival between patients with and without radiological success after T2EL embolization (P = 0.813), as shown in Figure 5.

Table 3. Radiological outcome after type 2 endoleak embolization

Variable	Statistic	All
Technical success		
Yes	n (%)	57 (95.00%)
Persistent endoleak after T2EL embolization		
Yes	n (%)	35 (58.33%)
Change in AAA diameter after T2EL embolization		
Decreased	n (%)	7 (11.67%)
Stable	n (%)	22 (36.67%)
Increased	n (%)	31 (51.67%)
Absolute change in AAA diameter after T2EL embolization	n	60
	Median	4.5
	Q1, Q3	(0.0; 14.0)
Radiological success after T2EL embolization		
Increased AAA diameter and/or persistent endoleak	n (%)	44 (73.33%)
Stable or decreased AAA diameter and no persistent endoleak	n (%)	16 (26.67%)
Clinical success after T2EL embolization		
Yes	n (%)	46 (76.67%)

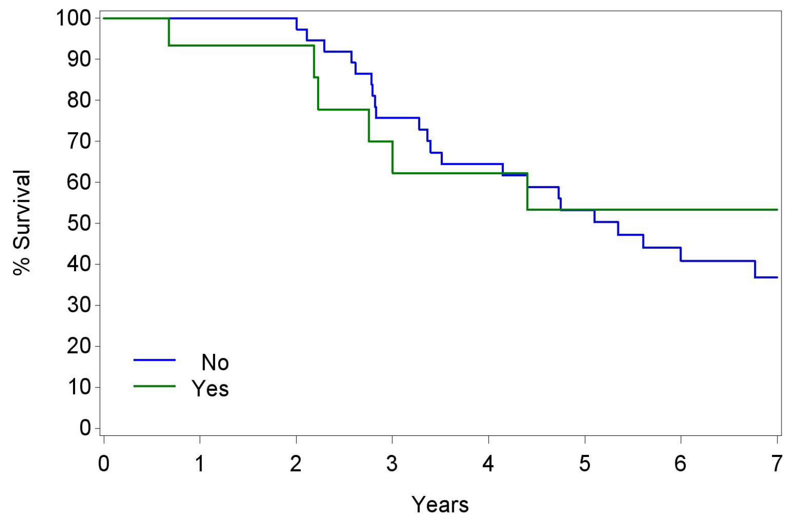
T2EL, type 2 endoleak; AAA, abdominal aortic aneurysm; Q1, Q3, first and third quartile.

Table 4. Relation between patients' demographics, imaging characteristics, and radiological/clinical outcome

Patients' demographics			Radiological success			Clinical success		
		Statistic	No	Yes	*P* value	No	Yes	*P* value
Sex	**Male**	n (%)	38 (71.7%)	15 (28.3%)	0.663	12 (22.6%)	41 (77.4%)	0.660
	Female	n (%)	6 (85.7%)	1 (14.3%)		2 (28.6%)	5 (71.4%)	
Smoking	**No**	n (%)	28 (87.5%)	4 (12.5%)	0.008	11 (34.4%)	21 (65.6%)	0.031
	Yes	n (%)	16 (57.1%)	12(42.9%)		3 (10.7%)	25 (89.3%)	
Diabetes	**No**	n (%)	37 (69.8%)	16 (30.2%)	0.173	12 (22.6%)	41 (77.4%)	0.660
	Yes	n (%)	7 (100.0%)	0 (0.0%)		2 (28.6%)	5 (71.4%)	
Chronic renal failure	**No**	n (%)	42 (75.0%)	14 (25.0%)	0.287	14 (25.0%)	42 (75.0%)	0.564
	Yes	n (%)	2 (50.0%)	2 (50.0%)		0 (0.0%)	4 (100.0%)	
Coronary artery disease	**No**	n (%)	33 (73.3%)	12 (26.7%)	1.000	12 (26.7%)	33 (73.3%)	0.483
	Yes	n (%)	11 (73.3%)	4 (26.7%)		2 (13.3%)	13 (86.7%)	
Hypertension	**No**	n (%)	14 (77.8%)	4 (22.2%)	0.755	4 (22.2%)	14 (77.8%)	1.000
	Yes	n (%)	30 (71.4%)	12 (28.6%)		10 (23.8%)	32 (76.2%)	
COPD	**No**	n (%)	40 (75.5%)	13 (24.5%)	0.370	13 (24.5%)	40 (75.5%)	1.000
	Yes	n (%)	4 (57.1%)	3 (42.9%)		1 (14.3%)	6 (85.7%)	
Hyperlipidemia	**No**	n (%)	27 (84.4%)	5 (15.6%)	0.039	8 (25.0%)	24 (75.0%)	0.744
	Yes	n (%)	17 (60.7%)	11 (39.3%)		6 (21.4%)	22 (78.6%)	
Peripheral vascular disease	**No**	n (%)	42 (75.0%)	14 (25.0%)	0.287	13 (23.2%)	43 (76.8%)	1.000
	Yes	n (%)	2 (50.0%)	2 (50.0%)		1 (25.0%)	3 (75.0%)	
Age (at embolization)		n	44	16	0.834	14	46	0.506
		Median	79.0	80.0		77.5	80.0	
		Q1, Q3	(71.5; 83.0)	(72.0; 84.5)		(74.0; 82.0)	(71.0; 84.0)	

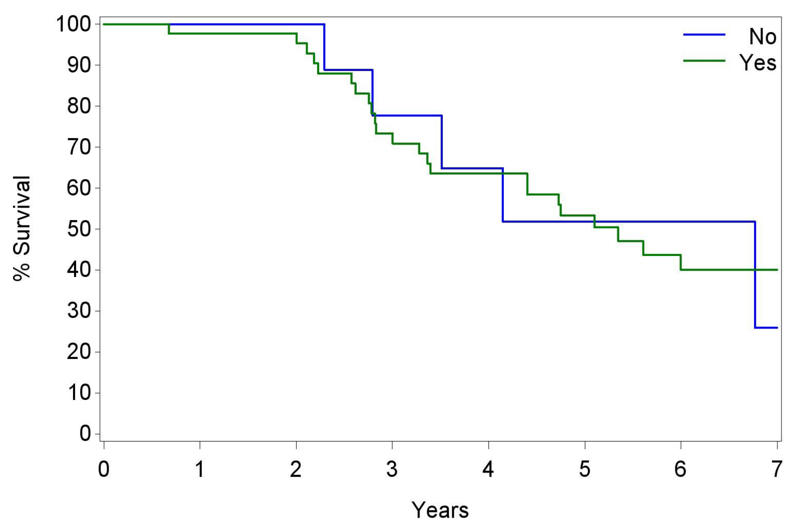
Post-embolization persistent endoleak on follow-up CT examination				
Imaging characteristic		**Odds ratio (95% CI)**	***P* value**	**n patients**
Approach	Transarterial vs. direct puncture	0.655 (0.184; 2.335)	0.514	60
Embolization technique	Global test		0.049	60
Type 2 endoleak origin	Global test		0.955	60
Maximal endoleak diameter		0.970 (0.921; 1.023)	0.260	60
Endoleak contour	Blurred vs. sharp	4.889 (1.226; 19.488)	0.025	60
Endoleak location in the AAA	Anterior vs. posterior location	2.538 (0.611; 10.551)	0.200	60
Change in aneurysm sac diameter (increased vs. stable/decreased)				
Imaging characteristic		**Odds ratio (95% CI)**	***P* value**	**n patients**
Approach	Transarterial vs. direct puncture	0.598 (0.180; 1.988)	0.402	60
Embolization technique	Global test		0.152	60
Type 2 endoleak origin	Global test		0.127	60
Maximal endoleak diameter		0.970 (0.923; 1.019)	0.228	60
Endoleak contour	Blurred vs. sharp	2.159 (0.691; 6.743)	0.186	60
Endoleak location in the AAA	Anterior vs. posterior location	0.438 (0.131; 1.461)	0.179	60
Clinical success				
Imaging characteristic		**Odds ratio (95% CI)**	***P* value**	**n patients**
Approach	Transarterial vs. direct puncture	1.667 (0.319; 8.703)	0.545	60
Embolization technique	Global test		0.882	60
Type 2 endoleak origin	Global test		0.578	60
Maximal endoleak diameter		0.992 (0.935; 1.053)	0.801	60
Endoleak contour	Blurred vs. sharp	0.419 (0.119; 1.473)	0.175	60
Endoleak location in the AAA	Anterior vs. posterior location	1.667 (0.319; 8.703)	0.545	60

COPD, chronic obstructive pulmonary disease; Q1, Q3, first and third quartile; CI, confidence interval; CT, computed tomography; AAA, abdominal aortic aneurysm.



Number at risk								
No	43	42	37	27	23	19	13	9
Yes	16	13	12	9	7	3	1	1

Figure 5. No significant difference in overall survival was observed in patients with or without radiological success after type 2 endoleak embolization procedure (*P* = 0.8125).



Number at risk								
No	13	12	9	6	5	4	3	1
Yes	46	43	40	30	25	18	11	9

Figure 6. No significant difference in overall survival was observed in patients with or without clinical success after type 2 endoleak embolization procedure (*P* = 0.8045).

Clinical success

Clinical success was achieved in 46 patients (76.7%). Overall, 11 patients (18.3%) were referred for surgical conversion after T2EL embolization. In 3 patients (5%), late rupture of the AAA occurred post-T2EL embolization. All 3 patients showed an increase in AAA diameter and had a persistent T2EL at their follow-up CT scans. In two of these three patients, an additional type 1 endoleak, which was not visible on the CT scan, was identified during surgery. Two patients who presented with stable or decreased AAA diameter underwent open surgery 12 and 10 months, respectively, after T2EL embolization, in connection with an infected endograft. However, no difference in overall survival was found between patients with and without clinical success after T2EL embolization (*P* = 0.805), as summarized in Figure 6.

Patients showing an increase in AAA diameter after T2EL embolization had a greater need for surgical conversion (*P* = 0.043); this applied to 9 patients in this subgroup, compared with only 2 conversions in patients with a stable or decreased AAA diameter. Patients with the combination of blurred pre-embolization T2EL delineation and a persistent post-embolization AAA diameter increase also had a greater need for surgical conversion (*P* = 0.022); this was the case in 5 patients (45.5%), compared with 6 out of 49 patients (12.2%) without this combination of imaging characteristics (the residual group) who required surgical conversion.

Median survival after T2EL embolization in our study population was 5.35 years (3.51–7.07, +/−95% CI). The 2-year survival rate was 98.25% (88.19%-99.75%), the 5-year survival rate was 53.23% (38.38%–66.03%), and the 10-year survival rate was 21.24% (8.67%–37.48%) (Figure 7). There was no mortality related to the embolization procedure or to persistent aneurysm growth late after embolization or to secondary aortic interventions. Smoking was the only clinical parameter associated with clinical success after T2EL embolization (*P* = 0.037). No statistical difference in overall success could be demonstrated between patients with (n = 29) and without (n = 31) a persistent increase in maximum sac diameter after T2EL embolization (*P* = 0.561). Last, univariate analyses for overall survival could not demonstrate any parameter associated with a higher risk for increased mortality, as summarized in Table 5.

Discussion

This study confirms that embolization therapy for a T2EL in patients with a progressive expansion of the AAA sac after EVAR is feasible and relatively safe. In 95% of included patients, the nidus of the T2EL could be accessed with catheters or needles and completely embolized. This is in line with other studies showing a primary technical success rate between 58% and 100%.[18,21,22] In addition, these high technical success rates are found irrespective of the access route to the T2EL, including transcatheter or translumbar/transperitoneal access,[14,18,21,23-26] or the type of embolic agent used.[26-28] Complications related to the embolization procedure are uncommon, with an incidence ranging from 0% to 10%, and may include septic, ischemic, and neurological events.[19] In the presented case studies, two (3.2%) stent-graft infections occurred, most probably related to contamination during direct percutaneous puncture.[29,30] Curative surgical intervention with stent-graft resection and aorto-bi-iliac reconstruction with autologous deep vein,

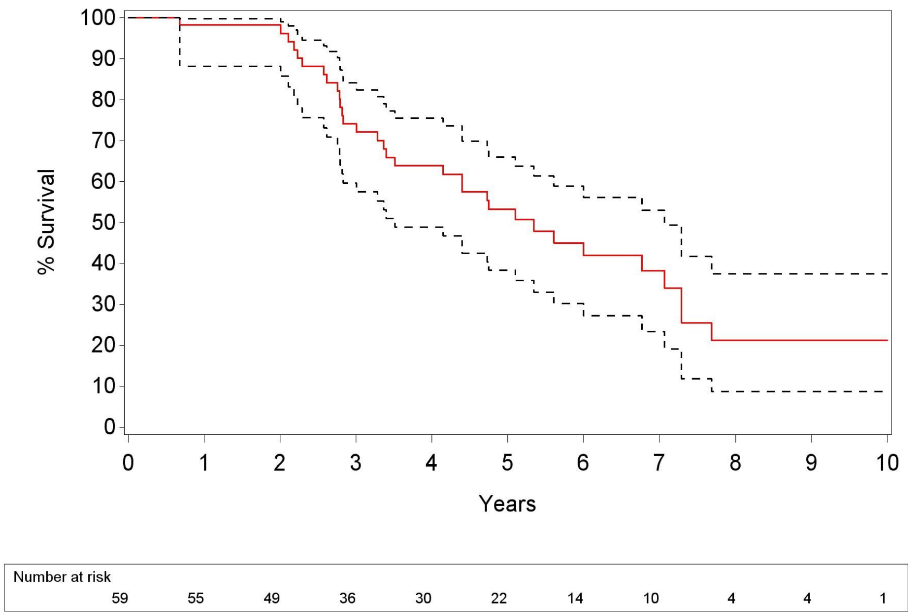


Figure 7. Kaplan–Meier analysis shows estimated 2-year survival in 98.25% (88.19%–99.75%) of patients, 5-year survival in 53.23% (38.38%–66.03%), and 7-year survival in 38.24% (23.35%–52.97%) after type 2 endoleak embolization.

Table 5. Univariate analysis for overall survival

Parameter	Hazard ratio	*P* value
Persistent type 2 endoleak	0.849 (0.421; 1.710)	0.646
Aneurysm sac diameter increase	1.234 (0.602; 2.529)	0.566
Need for reintervention	0.886 (0.341; 2.306)	0.805

as performed in the two reported cases, provided by far the best outcome.[31] Sella et al.[32] described another infectious complication related to translumbar direct T2EL percutaneous puncture, namely osteomyelitis and discitis of L3-L4 vertebral bodies.

Despite the high technical success rate, the long-term radiological and clinical success rates are moderate. In half the embolized patients in this study, persistent expansion of the aneurysm sac was observed after embolization therapy. Combined complete disappearance of the T2EL and stable or decreased AAA diameter was observed in about a quarter of embolized patients. These results are rather disappointing, as the failure of the aneurysm sac to regress after EVAR is associated with higher long-term mortality;[33] however, the presented results match with those found by Arenas Azofra et al.[14] Therefore, long-term follow-up after T2EL embolization seems mandatory.[34]

Both pre-interventional imaging and clinical parameters for a higher risk of persistent aneurysm sac expansion after T2EL embolization were analyzed, showing unsharp or blurred delineation of the nidus of the T2EL to be predictive of a persistent T2EL after embolization ($P = 0.025$). Potentially, the nidus in these T2ELs might have been much larger than identified on CT scans or angiography, and embolization with liquids might not have covered the whole volume of the leak, resulting in high recurrence rates of the T2ELs. Dudeck et al.[23] found the volume of the nidus to be a predictor for late T2EL recurrence; however, in this study, the maximum diameter of the nidus as visualized by CT scan was not predictive of late recurrence ($P = 0.801$); Mursalin et al.[21] reported the endoleak appearance time on the final operative angiogram and attenuation of the endoleak cavity on the first postoperative CT scan as strong image-based predictors of a persistent T2EL after embolization. In addition, two pre-interventional clinical parameters were identified as predictors for a better outcome. Smoking was found to be a protective factor against a persistent T2EL, aneurysm sac expansion, and the need for late surgical conversion, while hyperlipidemia was associated with better radiological success. These findings are in line with the data presented by Koole et al.[35], showing fewer late T2ELs during post-embolization follow-up in smokers. These findings might be related to the decreased endoleak perfusion associated with atherosclerotic injury of small- and medium-sized afferent and efferent arteries of the T2EL and an increased tendency of coagulation, which might further narrow or occlude afferent and efferent arteries. However, in a univariate analysis, Sarac et al.[19] found continued tobacco use and hyperlipidemia to be associated with continued sac expansion and more secondary embolization procedures, respectively.

Clinical success, defined as the absence of late aortic or endoleak-associated complications, such as rupture or need for surgical conversion, was 76%, which is in line with the results of Sarac et al.[19], who found freedom from second embolization in 76% of patients. The main indication for late surgical conversion was persistent AAA sac expansion despite embolization therapy in patients potentially considered fit for surgery, which was performed in nearly 20% of the study population. In addition, 3 patients (5%) underwent urgent surgical conversion due to AAA rupture. In two of these three patients, a concomitant type 1 endoleak was identified perioperatively. These observations may confirm the findings of Madigan et al.[36] and Aziz et al.[37], revealing an unexpected type 1 or 3 endoleak in association with a known T2EL in 20% of patients converted to surgical repair for the T2EL. Funaki et al.[22] found that type 3 endoleaks were believed to be T2ELs in 7 out of 25 patients (28%). Finally, in 1 patient (1.6%), rupture was associated with an isolated T2EL and expanding AAA sac, which is in line with a 1% to 2% rate of rupture for AAA after EVAR with a persistent T2EL.[7,9,15]

The present study reveals an estimated overall survival rate of 53% and 21% at 5 and 10 years of follow-up, respectively. Additionally, no difference in survival was found between patients with or without AAA sac expansion after T2EL embolization. These findings are in line with the outcomes found by Walker et al.[10] based on a multicenter EVAR registry, concluding that overall all-cause mortality and aneurysm-related mortality are unaffected by the presence of a T2EL. It should be noted that we did not encounter 30-day mortality in the 11 patients treated by surgical conversion for sac expansion associated with a persistent T2EL after embolization therapy.

We also analyzed a subgroup of patients presenting with blurred T2EL delineation prior to embolization that was associated with persistent aneurysm sac expansion after embolization. This subgroup had a significantly higher risk for late surgical conversion compared with other included patients without these two imaging characteristics ($P = 0.022$). Potentially, patients in this specific subgroup might be selected as good candidates for early conversion to surgery if no response to embolization therapy is identified on the first follow-up CT scan.

Finally, this study also has some limitations. First, this is a retrospective, single-center study with a limited number of included patients treated over a period of more than 10 years. However, the inclusion and exclusion criteria for referral to embolization therapy did not change over that time. Second, several clinical and radiological parameters for better or worse outcomes were analyzed; however, these parameters were based on the authors' interests, not on predefined lists. Third, the radiological techniques used to access the nidus of the T2EL and the embolics used for endoleak occlusion were at the discretion of the attending interventional radiologist, without any randomization. Fourth, the evaluation of the endoleak's configuration in sharp or unsharp delineation needs to be proven in future studies and might be dependent on the experience of the reading physicians, as the interobserver agreement for endoleak configuration was rather fair. Lastly, no comparison was made with a control group.

In conclusion, this retrospective study demonstrates a high technical success rate of T2EL embolization, with moderate long-term radiological and clinical outcomes. Blurred delineation of the T2EL is associated with a significantly higher risk of persistent post-embolization T2EL. Although no difference in overall survival was observed between patients with or without persistent AAA sac expansion after T2EL embolization, patients with blurred T2EL delineation prior to embolization, associated with persistent aneurysm sac expansion after embolization, were at a significantly higher risk of requiring late surgical conversion as a definitive treatment for the T2EL and persistent sac expansion.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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