Reintervention after endovascular repair for aortic dissection: A systematic review and meta-analysis

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ABSTRACT

Objectives: Thoracic endovascular aortic repair has been chosen as a less-invasive alternative to open surgery for the treatment of aortic dissections; however, the advantages have been challenged by the postoperative reintervention during the follow-up period. This study aimed at evaluating the incidence, reasons, and potential risk factors for reintervention.

Methods: Studies reporting reintervention after endovascular repair were identified by searching PubMed and Embase in accordance with preferred reporting items for systematic reviews and meta-analyses guidelines, and by reviewing the reference lists of retrieved articles. Sensitivity analysis and subgroup analyses were performed to determine the sources of heterogeneity. Funnel plot and Egger's test were used to determine the publication bias.

Results: A total of 27 studies encompassing 2403 patients with aortic dissection were identified. The pooled incidence of reintervention after endovascular repair was 15% (95% confidence interval, 12-19) during 33.7 months of follow-up. The 3 most common reasons for reintervention were endoleak (33.2%), false lumen perfusion and aortic dilation (19.8%), and new dissection (6.9%). The potential factors for reintervention were the mean age of onset and diabetes mellitus determined by performing a single meta-regression analysis ($P < .001$ and $.044$, respectively).

Conclusions: Current data suggest that the incidence of reintervention after endovascular therapy is relatively high during midterm follow-up. Advanced age of onset is a risk factor and diabetes mellitus is a protective factor of reintervention after endovascular therapy. The possible mechanism that diabetes mellitus protects patients from reintervention should be explored further. (J Thorac Cardiovasc Surg 2016;152:1279-88)

The overall incidence of reintervention after TEVAR.

Central Message

The pooled estimated incidence of reintervention after endovascular repair was 15%, and the 3 most common reasons were endoleak, false lumen perfusion and aortic dilation, and new dissection.

Perspective

The incidence of reintervention after endovascular repair was relatively high during midterm follow-up. For patients with aortic dissection with an advanced age of onset, more elaborate operation and close postoperative care are required to lower the reintervention rate and improve the prognosis of aortic dissection.

See Editorial Commentary page 1289.

The estimated annual incidence of aortic dissection is 2 to 6 per 100,000 individuals, and the prevalence appears to be increasing independently of the aging population.¹ The advent of thoracic endovascular aortic repair (TEVAR)

has altered the management algorithm for aortic dissections.² Because TEVAR is associated with lower risks of mortality and morbidity, the procedure has been chosen as a less-invasive alternative to traditional open surgery for the treatment of complicated type B aortic dissections in recent years, especially in elderly patients with greater comorbidities.^{3,4} However, the advantages of TEVAR have been challenged by the postoperative adverse events, such as endoleak, stent-graft migration, retrograde type A aortic dissection (RTAD), and distal redissection. In most

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Abbreviations and Acronyms

CI	= confidence interval
RTAD	= retrograde type A aortic dissection
TEVAR	= thoracic endovascular aortic repair

situations, these events require reintervention to save lives or obtain a better prognosis. It is conceivable that the prognosis of TEVAR could be improved after determining the reasons and potential risk factors of reintervention. To date, nonetheless, no systematic review and meta-analysis of reintervention after TEVAR for aortic dissections have been performed.

In the current study, we systematically reviewed all available published data reporting reintervention after TEVAR in patients with aortic dissection and pooled the data for analyzing the incidence, reasons, and potential risk factors for reintervention.

MATERIALS AND METHODS

This systematic review and meta-analysis were performed in accordance with the standards set forth by the statement from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses.⁵ Because this study was a systematic review and meta-analysis based on published articles, ethical approval was waived by the Institutional Review Board of Changhai Hospital. [Video 1](#) shows the topic selection process of reintervention after endovascular therapy.

Data Sources and Search Results

The PubMed and Embase databases were searched from inception to June 2, 2015, restricted to studies in English and on humans. There were no restrictions on the year or type of publication. The search strategy was amended for each database ([Table E1](#)). A hand search also was performed of all the references in the included studies for potential valuable and relevant publications.

Study Selection

The inclusion criteria were (1) patients with aortic dissection requiring another intervention after TEVAR, (2) at least 10 patients in the study, and (3) at least 6 months of follow-up. On the basis of the guidelines, case reports, conference abstracts, reviews, systematic review, and meta-analyses, other researches and other diseases were excluded. After full-text articles were assessed for eligibility, the mixed pathology including both aortic dissections and aneurysms was excluded.

Data Extraction and Outcome Definitions

Two investigators independently assessed studies for inclusion criteria and extracted data using a standard form. Disagreements were resolved by consensus with internal authors at designated consensus meetings. Data were extracted pertaining to the baseline demographics, comorbidities, follow-up period, study design, years of enrollment, incidence and reasons for reintervention, prior aortic intervention rate, technical success rate, in-hospital/30-day mortality, and oversizing of the stent graft.

The outcomes were the incidence, reasons, and potential factors for reintervention after TEVAR during follow-up. Reintervention was defined as the second intervention for the management of complications after the initial TEVAR, not including the second-stage operation. Potential risk factors were defined as the factors for reintervention determined by single meta-

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VIDEO 1. How did we choose the topic of reintervention after endovascular therapy? Video available at: [http://www.jtcvsonline.org/article/S0022-5223\(16\)30657-2/addons](http://www.jtcvsonline.org/article/S0022-5223(16)30657-2/addons).

regression analyses on the variables of age, male gender, follow-up period, technical success, in-hospital/30-day mortality, prior aortic intervention, Marfan syndrome, and comorbidities. Type I endoleak was defined as a sealing failure at 1 of the attachment sites of the graft to the vessel wall (proximal leak, type Ia; distal, type Ib), whereas type III endoleak was defined as a device failure in the form of dysjunction of the components of a modular graft system (type IIIa) or a defect in the fabric of the graft (type IIIb). New dissection referred to the new-onset and metachronous dissection separate from the initially treated aortic dissection, which precluded the RTAD or stent graft-induced dissection. Persistent perfusion of the false lumen meant the blood flow persistently entered into the false lumen through the distal reentry tears, which resulted in aortic dilation or rupture.

Data Synthesis and Statistical Analysis

The amount of heterogeneity was estimated using I^2 statistics, which indicates the percent of heterogeneity across studies that cannot be explained by chance variation alone. I^2 greater than 50% was considered to indicate high heterogeneity. Sensitivity analysis was performed, and a random-effect model was chosen when heterogeneity was greater than 50%. Publication bias was assessed through a funnel plot, and Egger's regression test was applied.

The values were expressed as numbers, percentages, and median/mean. Potential factors for reintervention were determined by a single meta-regression analysis using STATA version 12.0 (StataCorp LP, College Station, Tex). The pooled estimated incidence of reintervention after TEVAR was performed using R-project (version 3.2.0, <http://www.r-project.org/>). The probability values were 2 tailed, and the null hypothesis was rejected for P values less than .05.

RESULTS**Study Selection and Characteristics**

The literature search identified 293 potentially relevant studies, as shown in the flow diagram in [Figure 1](#). Of these, 29 full-text articles were assessed for eligibility. Finally, 27 studies comprising 2403 patients with aortic dissection (2029 TEVAR, 44 open surgery, and 330 medication cases) between 1995 and April 2013 were included in the meta-analysis.^{3,6-31}

The patients' characteristics and comorbidities are summarized in [Table 1](#). Almost all of the patients were

FIGURE 1. Flow diagram according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.

diagnosed with type B aortic dissections. The average age was 57.6 years, and 75.7% of patients were men. The comorbidities were coronary artery disease (14.0%), chronic obstructive pulmonary disease (12.7%), diabetes mellitus (8.8%), hypertension (80.9%), renal insufficiency (12.3%), and smoking (50.0%). The percentage of patients diagnosed with Marfan syndrome was 2.2%.

Incidence, Reasons, and Potential Risk Factors for Reintervention

The perioperative characteristics and incidence of reintervention of included studies are presented in Table 2. The pooled estimates of prior aortic intervention rate, technical success, and in-hospital/30-day mortality were 15.0%, 98.3%, and 4.3%, respectively. Mean follow-up period was 33.7 months.

The incidence of reintervention after TEVAR is depicted in Figure 2. The pooled overall incidence of reintervention was 15% (95% confidence interval [CI], 12-19) with a large degree of heterogeneity ($I^2 = 84.8\%$). A funnel plot is presented in Figure E1 (Egger's regression test, $P < .001$).

To determine the potential sources of heterogeneity, a sensitivity analysis of included studies using a random effect model was performed (Table E2). However, the heterogeneity was still high after omitting each one of the studies. Then, the subgroup analyses of reported acute,^{3,9,10,12,13,19,23-25} chronic,^{7,8,14,18,20,22,26,27,31} complicated,^{3,6,13,14,16,18,21-26,28-30} and prior aortic intervention^{3,6,7,11,13,15,16,18,20,21,26,28} dissections were performed. The pooled incidences of reintervention in acute and chronic dissection subgroups were 14% (95%

TABLE 1. Baseline characteristics of included study subjects

Study reference and year	Time span	Design	Disease	Patients, n	Mean age, y
Wilkinson and colleagues ⁶ 2013	1995-2012	Retrospective, single center	Complicated TBAD	49	70.1
Nozdrzykowski and colleagues ⁷ 2013	1/2000-5/2010	Retrospective, single center	CTBAD	32	62.0
Jia and colleagues ⁸ 2013	1/2007-12/2010	Prospective, multicenter	Uncomplicated CTBAD	208	52.1
Garbade and colleagues ⁹ 2010	2000-2008	Retrospective, single center	ATBAD	46	65.0
Chemelli-Steingrubler and colleagues ¹⁰ 2010	7/1996-4/2008	Retrospective, single center	ATBAD	38	64.0
Jánosi and colleagues ¹¹ 2015	7/1999-5/2010	Retrospective, single center	TBAD	142	62.2
Huang and colleagues ¹² 2015	1/2012-6/2012	Retrospective, single center	ATBAD	81	53.0
Faure and colleagues ¹³ 2015	2000-2013	Retrospective, 2 centers	Complicated ATBAD	24	68.0
Song and colleagues ¹⁴ 2014	5/2012-4/2013	Retrospective, single center	Complicated CTBAD	20	50.0
Kitamura and colleagues ¹⁵ 2014	1998-2012	Retrospective, single center	TBAD	45	55.5
Hanna and colleagues ³ 2014	7/2005-9/2012	Retrospective, single center	Complicated ATBAD	50	59.0*
Faure and colleagues ¹⁶ 2014	10/2000-12/2011	Retrospective, single center	Complicated AD	41	66.0
Weng and colleagues ¹⁷ 2013	11/2006-5/2011	Retrospective, single center	AD	99	60.0
Lee and colleagues ¹⁸ 2013	4/1997-6/2010	Retrospective, single center	Complicated CTBAD	71	55.1
Shu and colleagues ¹⁹ 2013	7/2003-5/2012	Retrospective, single center	ATBAD	127	46.1
Mani and colleagues ²⁰ 2012	8/2000-8/2010	Retrospective, single center	CTBAD	58	66.0
Lombardi and colleagues ²¹ 2012	12/2007-8/2009	Prospective, multicenter	Complicated TBAD	40	58.0
Andacheh and colleagues ²² 2012	2002-2010	Retrospective, single center	Complicated CTBAD	73	58.0
Steuer and colleagues ²³ 2011	12/1999-12/2009	Retrospective, single center	Complicated ATBAD	60	67.0
Shu and colleagues ²⁴ 2011	7/2002-1/2009	Retrospective, single center	Complicated ATBAD	45	42.6
Kim and colleagues ²⁵ 2011	9/2002-8/2009	Retrospective, single center	Complicated ATBAD	41	67.6*
Kang and colleagues ²⁶ 2011	2000-2007	Retrospective, single center	Complicated CTBAD	76	61.5
Xu and colleagues ²⁷ 2010	6/2001-9/2007	Retrospective, single center	CTBAD	84	53.3
Parsa and colleagues ²⁸ 2010	6/2005-11/2008	Retrospective, single center	Complicated TBAD	55	59.0
Zhang and colleagues ²⁹ 2015	9/1998-7/2012	Retrospective, single center	TBAD	252	54.1
VIRTUE ³⁰ 2014	12/2006-8/2009	Prospective, multicenter	Complicated TBAD	100	60.7
Nienaber and colleagues ³¹ 2009	11/2003-11/2005	Prospective, multicenter	Complicated TBAD	72	60.3
Total, n (%)	NA	NA	NA	2029	57.6

CAD, Coronary artery disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; HTN, hypertension; RI, renal insufficiency; TBAD, type B aortic dissection; CTBAD, chronic type B aortic dissection; NR, not reported; ATBAD, acute type B aortic dissection; AD, aortic dissection; NA, not applicable. *Data presented as median.

CI, 8-20) (Figure 3, A) and 17% (95% CI, 10-23) (Figure 3, B), respectively. The heterogeneities were still high in the acute and chronic dissection subgroups (86.4% and 86.7%, respectively). The phase of dissection was not a source of heterogeneity, because there was an overlap of 95% CI between the acute and chronic subgroups. The pooled reintervention incidences in the complicated and prior aortic intervention dissection subgroups were 19% (95% CI, 14-25) (Figure 4, A) and 22% (95% CI, 17-26) (Figure 4, B), respectively. The heterogeneities were 83.2% and 57.1%, respectively.

The reasons for reintervention after TEVAR are summarized in Table E3. The 3 most common reasons for reintervention were endoleak (82/247, 33.2%), false lumen perfusion and aortic dilation (49/247, 19.8%), and new dissection (17/247, 6.9%).

The individual effects of several covariates on reintervention are shown in Table 3. We found that the mean age of onset and diabetes mellitus were potential influential factors for reintervention after TEVAR ($P < .001$ and $.044$, respectively). The results indicated that advanced age of onset and

diabetes mellitus were potential risk and protective factors for reintervention, respectively.

DISCUSSION

TEVAR has been recognized as a novel and less-invasive alternative to open surgery for treating aortic dissections with a better prognosis.³² However, postoperative adverse events such as endoleak, stent-graft migration, and RTAD have undermined the superiorities of TEVAR. In most situations, these life-threatening adverse events must be addressed after evaluating the overall condition of patients. Increasing attention has been paid to reintervention in recent years.

In the present meta-analysis, the pooled overall incidence of reintervention was 15.0%, which was higher than the previously reported rate of 8.1%.⁴ Several factors that resulted in the discrepancy must be considered in this study. First, approximately 15% of patients underwent prior aortic intervention before endovascular therapy. TEVAR was the secondary intervention for these patients. They were more likely to experience complications and undergo the third

TABLE 1. Continued

Male, n	CAD, n	COPD, n	DM, n	HTN, n	RI, n	Smoking, n	Marfan, n
28	18	10	6	41	7	49	0
23	6	7	9	32	13	NR	4
154	25	23	NR	187	16	NR	0
32	NR	9	9	40	NR	NR	0
29	11	9	3	33	5	2	0
96	19	NR	NR	114	NR	NR	0
70	9	NR	4	60	NR	42	1
14	2	NR	1	20	3	9	0
17	1	NR	1	18	NR	14	1
NR	NR	NR	NR	NR	NR	NR	0
36	9	7	6	46	17	28	4
34	6	9	2	31	2	18	1
82	NR	NR	NR	NR	NR	NR	5
50	2	NR	4	58	3	28	5
101	32	NR	17	103	26	99	16
48	NR	NR	NR	NR	NR	NR	0
28	3/38	1/39	3	37	2	21/36	0
52	NR	NR	NR	NR	NR	NR	1
40	12	NR	1	33	NR	25	0
33	6	6	8	10	7	NR	0
31	11	7	3	38	6	30	1
49	29	17	8	75	14	32	2
69	NR	NR	9	67	NR	26	1
41	8	9	8	53	21	37	0
206	9	10	16	193	16	117	0
76	14	14	1	69	5	NR	0
62	NR	7	5	61	NR	14	2
1501 (75.7)	232 (14.0)	145 (12.7)	124 (8.8)	1419 (80.9)	163 (12.3)	591 (50.0)	44 (2.2)

TABLE 2. Perioperative characteristics and crossover/reintervention rate of included studies

Study reference and year	Patients, n	Prior aortic intervention, n (%)	In-hospital/30-d mortality, %	Mean follow-up, mo	Reintervention, n (%)	Technical success, %	Proximal oversizing, %
Wilkinson and colleagues ⁶ 2013	49	13 (26.5)	10.2	27.7	5 (10.2)	100	NR
Nozdrzykowski and colleagues ⁷ 2013	32	6 (18.8)	6.3	42	9 (28.1)	NR	NR
Jia and colleagues ⁸ 2013	208	NR	0	28.5	9 (4.3)	100	10-20
Garbade and colleagues ⁹ 2010	46	NR	20.0	36.9	8 (17.4)	NR	NR
Chemelli-Steingruber and colleagues ¹⁰ 2010	38	NR	13.1	33	5 (13.2)	NR	NR
Jánosi and colleagues ¹¹ 2015	142	17 (12.0)	4.2	47.2	29 (20.4)	NR	9
Huang and colleagues ¹² 2015	81	NR	6.5	12	2 (2.5)	100	NR
Faure and colleagues ¹³ 2015	24	1 (4.2)	17.0	28	8 (33.3)	100	13.3
Song and colleagues ¹⁴ 2014	20	NR	0	10.3	2 (10.0)	100	NR
Kitamura and colleagues ¹⁵ 2014	45	11 (24.4)	0	90	1y: 6 (13.3)	100	NR
Hanna and colleagues ³ 2014	50	11 (22.0)	0	33.8*	13 (26.0)	98	NR
Faure and colleagues ¹⁶ 2014	41	16 (39.0)	5.0	12.2*	13 (31.7)	100	14.71
Weng and colleagues ¹⁷ 2013	99	NR	NR	25*	8 (8.1)	NR	23 ± 8
Lee and colleagues ¹⁸ 2013	71	17 (23.9)	1.4	49.1*	25 (35.2)	97.2	10
Shu and colleagues ¹⁹ 2013	127	NR	1.6	19.1	4 (3.1)	100	10-15
Mani and colleagues ²⁰ 2012	58	12 (20.7)	5.2	38	12/47 (25.5)	NR	5-15
Lombardi and colleagues ²¹ 2012	40	2 (5.0)	5.0	12	4 (10.0)	NR	0-10
Andacheh and colleagues ²² 2012	73	NR	14.0	18	11/72 (15.3)	99	NR

(Continued)

TABLE 2. Continued

Study reference and year	Patients, n	Prior aortic intervention, n (%)	In-hospital/30-d mortality, %	Mean follow-up, mo	Reintervention, n (%)	Technical success, %	Proximal oversizing, %
Steuer and colleagues ²³ 2011	60	NR	3.3	44.4	19 (31.7)	NR	NR
Shu and colleagues ²⁴ 2011	45	NR	4.4	13*	1 (2.2)	100	10-20
Kim and colleagues ²⁵ 2011	41	NR	9.8	12.4*	9/40 (22.5)	92.5	NR
Kang and colleagues ²⁶ 2011	76	29 (38.2)	5.0	34	17 (22.4)	96	10-15
Xu and colleagues ²⁷ 2010	84	NR	1.2	33.2	4 (4.8)	91.7	10-20
Parsa and colleagues ²⁸ 2010	55	16 (29.1)	2.0	7.1*	13 (23.6)	100	NR
Zhang and colleagues ²⁹ 2015	252	0	2.4	58.4	24 (9.5)	NR	14 ± 2.5
VIRTUE 2014 ³⁰	100	NR	4.0	36	22 (22.0)	98	NR
Nienaber and colleagues ³¹ 2009	72	0	2.8	24	13 (18.1)	95.7	NR
Total, n (%)	2029	151 (15.0)	4.3	33.7	295 (14.6)	98.3	NA

NR, Not reported; NA, not applicable. *Data presented as median.

intervention, because the overall condition was inferior to that of patients without prior aortic intervention. The pooled incidence of reintervention in this subgroup was 22%,

providing convincing evidence. On the other hand, the incidence of in-hospital/30-day mortality in our study was approximately 4.4%, which was lower than the previous

FIGURE 2. Overall incidence of reintervention after TEVAR for aortic dissections. The pooled overall estimate of reintervention incidence after endovascular repair for aortic dissections is shown. CI, Confidence interval.

FIGURE 3. Reintervention incidence in acute and chronic dissection subgroups after endovascular repair for aortic dissections. A, Pooled estimate of reintervention incidence in acute dissection subgroup. B, Pooled estimate of reintervention incidence in chronic dissection subgroup. *CI*, Confidence interval.

rate of 5.8%.⁴ It was reasonable that the higher rate of in-hospital/30-day mortality, the lower rate of reintervention after TEVAR.

The heterogeneity in the meta-analysis was high, even after sensitivity analysis and subgroup analyses were performed. The results indicated that the heterogeneity might be not relevant to the phase of dissection. This systematic review and meta-analysis included all available studies and evaluated the incidence of reintervention after endovascular repair for aortic dissections. Some confounding factors must be taken into consideration. The time span was from 1995 to April 2013, an approximately 18-year period. Thus, the materials, designs, types, and generations of stent graft might be different. Second, the procedures of TEVAR were performed in different countries, hospitals, and races. Third, the management of the patients was performed by different surgical teams, surgeons, and anesthesiologists, and using different brands of prosthetics.

These confounding factors were inevitable to the nature of the meta-analysis. We still believe our results can be helpful to guide readers to further understand the complex clinical problem.

The rate of technical success was 98.3%. Technical success, defined as a sealing of the primary entry tear without residual endoleak at the end of the procedure,¹³ was an indicator of operator skill and experience. However, technical success was unable to predict the long-term prognosis. It was unsuitable and difficult to determine the relationship between technical success and reintervention during the follow-up period.

The 3 most common reasons for reintervention were endoleak, false lumen perfusion and aortic dilation, and new dissection, which were consistent with the results of a previous retrospective study in our center.²⁹ Endoleak, most commonly type I, continues to be a challenge in the endovascular approach for aortic dissections,² especially in

FIGURE 4. Reintervention incidence in complicated and prior aortic intervention dissection subgroups after endovascular repair for aortic dissections. A, Pooled estimate of reintervention in the complicated dissection subgroup. B, Pooled estimate of reintervention in the prior aortic intervention dissection subgroup. *CI*, Confidence interval.

patients receiving scallop, fenestration, and chimney techniques. In this study, 82 endoleaks required reintervention. Endoleak would be affected by many factors, such as anatomy of vascular segment, stent-graft design, and short

proximal landing zone.³³ It was mandatory to correct type I endoleak whenever possible because of its association with mean pressure indexes of 93% in the liquid areas and 62% in the thrombus.³⁴

TABLE 3. Individual effect of 13 covariates on reintervention: Results of random effects meta-regression analyses

Covariates	Included studies	Coefficient	P value
Mean age of onset, y	27	0.0090	<.001
Male, n	26	−0.0008	.057
Coronary artery disease, n	20	−0.0037	.198
Chronic obstructive pulmonary disease, n	15	−0.0022	.631
Diabetes mellitus, n	21	−0.0101	.044
Hypertension, n	23	−0.0006	.158
Renal insufficiency, n	16	−0.0050	.193
Smoking, n	17	−0.0015	.089
Marfan syndrome, n	27	−0.0040	.475
Prior aortic intervention, n	14	0.0041	.144
Technical success, %	18	−0.0053	.601
In hospital/30-d mortality, %	26	0.0026	.510
Mean follow-up period, mo	27	0.0012	.274

The other common reason for reintervention was persistent perfusion of the false lumen and aortic dilation, which result in partial or incomplete thrombosis of the false lumen. Tsai and colleagues³⁵ concluded that partial thrombosis of the false lumen was an important determinant of aortic enlargement and a significant independent predictor of postdischarge mortality. We considered that partial thrombosis occluded the distal reentry tears and resulted in turbulence and a blind sac, which would significantly increase mean arterial and diastolic pressures.

RTAD was an uncommon but a devastating complication in endovascular treatment for type B dissections, especially for arch dissection using the hybrid method.³⁶ In the present study, the incidence of RTAD was 0.92% (16/1742), which was approximately one half that in the study by Canaud and colleagues,³⁷ who demonstrated that excessive oversizing of the proximal stent graft was a risk factor of RTAD. The device oversizing increased per 1%, and the incidence of RTAD increased per 9%. Moreover, the incidence of RTAD was not associated with the proximal endograft configuration.³⁷ At present, the optimal oversizing for type B aortic dissection remains controversial. Previous studies reported that excessive oversizing was a potential risk factor for reintervention after TEVAR.^{16,29} However, many of the included studies reported the range of oversizing,^{8,19–21,24,26,27} except the studies reporting the mean^{11,17,18,29} or median.^{13,16} Although the potential relationship between oversizing and reintervention could not be explored, the selection of oversizing is important. It is important to highlight that an accurate preoperative measurement of the proximal aorta at the transection of the intended landing zone was essential to determine the oversizing.

Our results showed that advanced age of onset was a potential risk factor for reintervention. To our surprise,

however, diabetes mellitus was a protective factor for reintervention. A recent published meta-analysis also suggested that diabetes mellitus may be negatively associated with the presence of thoracic aortic dissection and aneurysm.³⁸ Theivacumar and colleagues³⁹ suggested that diabetes mellitus has a protective effect against aortic dissection. The possible mechanism that diabetes mellitus protected the patients from reintervention should be explored further.

Study Limitations

First, the analysis was composed of only 2403 patients with aortic dissection, which was a relatively small sample for a meta-analysis. However, it should be noted that the number of 27 included studies was more important than the number of patients. Second, the fact that approximately 15.0% of patients underwent prior aortic intervention might cause selection bias. Third, many confounding factors, such as stent-graft brands, types, and generations, length of stent-graft coverage, anesthesia method, and distal reentry tear management, could not be eliminated, because this information was unavailable from most of the included studies. Fourth, the heterogeneity was high, even after sensitivity analysis and subgroup analyses were performed. Nonetheless, the study helps to clarify the true incidence of reintervention after TEVAR and sheds light on the subject.

CONCLUSIONS

Overall, the existing evidence suggests that the incidence of reintervention after TEVAR is relatively high during midterm follow-up. The 3 most common reasons for reintervention are endoleak, false lumen perfusion and aortic dilation, and new dissection. A risk factor of reintervention after TEVAR is advanced age of onset. Diabetes mellitus is a potential protective factor of reintervention. Although it remains an important caveat that these conclusions are based on retrospective studies, the study confirming some of the major findings of previous analyses increases confidence that the results are robust.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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Key Words: aortic dissection, reintervention, endovascular repair

FIGURE E1. Funnel plot of all included studies for reintervention. Publication bias of pooled overall incidence of reintervention was assessed by funnel plot. Each point represents a study, and publication bias exists.

TABLE E1. Search strategies in PubMed and Embase databases (June 2, 2015)

Search	Query	Items found	Time
PubMed			
#3	Search#1 AND#3 Filters: Humans; English	120	23:28:00
#2	Search ((reintervention*[Title/Abstract]) OR secondary intervention*[Title/Abstract]) OR re-intervention*[Title/Abstract] Filters: Humans; English	4604	23:27:19
#1	Search (TEVAR[Title/Abstract]) OR thoracic endovascular aortic repair[Title/Abstract] Filters: Humans; English	728	23:26:29
Embase			
#3	#1 AND#2	170	-
#2	reintervention:ab,ti OR 'secondary intervention':ab,ti OR 're intervention':ab,ti AND [english]/lim AND [humans]/lim AND [embase]/lim	5563	-
#1	tevar:ab,ti OR 'thoracic endovascular aortic repair':ab,ti AND [english]/lim AND [humans]/lim AND [embase]/lim	1125	-

TEVAR, Thoracic endovascular aortic repair.

TABLE E2. Sensitivity analysis of included studies using random effect model

Omitting study	Proportion	95% CI	Tau ²	I ² %
Wilkinson and colleagues ⁶ 2013	0.1553	0.1207-0.1899	0.0059	85.4
Nozdrzykowski and colleagues ⁷ 2013	0.1493	0.1157-0.1829	0.0055	84.9
Jia and colleagues ⁸ 2013	0.1599	0.1239-0.1960	0.0065	84.4
Garbade and colleagues ⁹ 2010	0.1522	0.1180-0.1863	0.0057	85.2
Chemelli-Steingrubler and colleagues ¹⁰ 2010	0.1538	0.1195-0.1881	0.0058	85.4
Jánosi and colleagues ¹¹ 2015	0.1500	0.1163-0.1837	0.0055	84.2
Huang and colleagues ¹² 2015	0.1599	0.1249-0.1949	0.006	84.1
Faure and colleagues ¹³ 2015	0.1489	0.1154-0.1823	0.0055	84.8
Song and colleagues ¹⁴ 2014	0.1546	0.1204-0.1889	0.0058	85.4
Kitamura and colleagues ¹⁵ 2014	0.1538	0.1194-0.1882	0.0058	85.3
Hanna and colleagues ³ 2014	0.1490	0.1154-0.1826	0.0055	84.7
Faure and colleagues ¹⁶ 2014	0.1477	0.1144-0.1810	0.0054	84.5
Weng and colleagues ¹⁷ 2014	0.1570	0.1219-0.1922	0.0061	85.4
Lee and colleagues ¹⁸ 2013	0.1444	0.1121-0.1767	0.0049	83.2
Shu and colleagues ¹⁹ 2013	0.1599	0.1246-0.1953	0.0061	84.1
Mani and colleagues ²⁰ 2012	0.1508	0.1168-0.1847	0.0056	84.9
Lombardi and colleagues ²¹ 2012	0.1552	0.1207-0.1897	0.0059	85.4
Andacheh and colleagues ²² 2012	0.1531	0.1187-0.1875	0.0058	85.2
Steuer and colleagues ²³ 2011	0.1465	0.1135-0.1795	0.0052	84.0
Shu and colleagues ²⁴ 2011	0.1597	0.1249-0.1945	0.0059	84.6
Kim and colleagues ²⁵ 2011	0.1507	0.1168-0.1846	0.0056	85.0
Kang and colleagues ²⁶ 2011	0.1497	0.1160-0.1835	0.0055	84.7
Xu and colleagues ²⁷ 2010	0.1588	0.1236-0.1940	0.0061	85.2
Parsa and colleagues ²⁸ 2010	0.1497	0.1160-0.1834	0.0055	84.8
Zhang and colleagues ²⁹ 2015	0.1572	0.1212-0.1933	0.0065	85.4
VIRTUE 2014 ³⁰	0.1495	0.1159-0.1832	0.0055	84.4
Nienaber and colleagues ³¹ 2009	0.1517	0.1176-0.1859	0.0057	85.0
Pooled estimate	0.1529	0.1193-0.1864	0.0057	84.8

CI, Confidence interval.

TABLE E3. Reasons for reintervention after endovascular repair for aortic dissections

Study	Patients, n	Total number: Reintervention causes
Wilkinson and colleagues ⁶ 2013	49	5: 2 AAA; 3 Type I endoleak
Nozdrzykowski and colleagues ⁷ 2013	32	9: 2 Distal-organ malperfusion; 7 Stent-graft migration
Jia and colleagues ⁸ 2013	208	9: 3 Endoleak; 6 Distal aorta rupture
Garbade and colleagues ⁹ 2010	46	NR
Chemelli-Steingruber and colleagues ¹⁰ 2010	38	5: 2 Type III endoleak; 3 RTAD
Jánosi and colleagues ¹¹ 2015	142	NR
Huang and colleagues ¹² 2015	81	2: 2 Type I endoleak
Faure and colleagues ¹³ 2015	24	8: 4 Type I endoleak; 1 Type II endoleak; 1 Stent-graft migration; 1 New dissection; 1 New aneurysm
Song and colleagues ¹⁴ 2014	20	2: 2 New dissection
Kitamura and colleagues ¹⁵ 2014	45	NR
Hanna and colleagues ³ 2014	50	13: 4 Type I endoleak; 3 Metachronous aortic pathology separate from the initially treated dissection; 3 False lumen dilation; 2 Type II endoleak; 1 RTAD
Faure and colleagues ¹⁶ 2014	41	13: 2 Stent-graft migration; 7 Type I endoleak 1 Type II endoleak; 3 Aneurysm evolution
Weng and colleagues ¹⁷ 2013	99	8: 8 Stent-graft-induced new dissection
Lee and colleagues ¹⁸ 2013	71	27 (25 patients): 1 Iatrogenic dissection; 2 Spontaneous dissection; 1 Extension of dissection; 9 Type I endoleak; 11 Enlargement of dissection; 2 Rupture of dissection; 1 True lumen collapse
Shu and colleagues ¹⁹ 2013	127	4: 3 Perfusion of false lumen; 1 Right renal artery compressed
Mani and colleagues ²⁰ 2012	58	NR
Lombardi and colleagues ²¹ 2012	40	4: 1 Liver and gall bladder ischemia; 1 Renal failure; 1 Retrograde dissection; 1 Stent-graft migration
Andacheh and colleagues ²² 2012	73	11: 7 Endoleak; 4 Persistent distal perfusion of false lumen
Steuer and colleagues ²³ 2011	60	19: 10 Aortic dilation; 2 Left arm claudication; 1 Left arm rest pain; 1 Subclavian steal syndrome; 2 Type II endoleak; 1 Aneurysm; 2 Stenting of the left renal artery
Shu and colleagues ²⁴ 2011	45	1: 1 Type I endoleak
Kim and colleagues ²⁵ 2011	41	12 (9 patients): 7 Type I endoleak; 3 Distal reperfusion; 2 RTAD
Kang and colleagues ²⁶ 2011	76	19: 3 RTAD; 10 Aortic enlargement; 2 Type I endoleak; 1 Type II endoleak; 3 Stent-graft and true lumen collapse
Xu and colleagues ²⁷ 2010	84	4: 3 Endoleak; 1 RTAD
Parsa and colleagues ²⁸ 2010	55	13: 1 LCCA coverage; 1 Iliac arterial rupture; 1 Stent-graft migration; 1 LCCA dissection; 1 Aortic dilation; 1 Aortoesophageal fistula; 2 Stent-graft collapse; 3 False lumen dilation; 2 Metachronous aortic pathology
Zhang and colleagues ²⁹ 2015	252	24: 3 Type I endoleak; 2 Type II endoleak; 5 New dissection; 4 New aneurysm; 5 False lumen dilation; 2 RTAD; 2 Redissection; 1 Right iliac artery occlusion
VIRTUE 2014 ³⁰	100	22: 15 Type I endoleak; 1 Type III endoleak; 2 Aortic rupture; 2 RTAD; 2 Others
Nienaber and colleagues ³¹ 2009	72	13: 7 False-lumen flow and diameter expansion; 1 RTAD; 1 Malperfusion; 4 Others
Total, n	2029	247: 82 Endoleak; 49 False lumen perfusion and aortic dilation; 17 New dissection; 16 RTAD; 14 Organ malperfusion; 12 Stent-graft migration; 11 Enlargement of dissection; 10 Aortic rupture; 8 Stent-graft induced new dissection; 6 New aneurysm; 6 True lumen collapse; 5 AAA; 3 Redissection; 1 Aortoesophageal fistula; 1 Iliac arterial rupture; 6 Others

AAA, Abdominal aortic aneurysm; NR, not reported; RTAD, retrograde type A aortic dissection; LCCA, left common carotid artery