

ORIGINAL ARTICLE

Transarterial Embolization versus Translumber Embolization for Type II Endoleak after Endovascular Abdominal Aortic Aneurysm Repair: A Meta-Analysis

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Objective Type II endoleak is the most common subtype of endoleak as a complication after endovascular aneurysm repair (EVAR). The efficacy of transarterial (TA) embolization and translumber (TL) embolization in the management of type II endoleak remains equipoise. The aim of this study is to compare the technical and clinical success between TA embolization and TL embolization for type II endoleak after EVAR.

Methods The protocol was registered (CRD 42018114453) and the electronic databases (Pubmed, Embase, Web of Science, and Cochrane) were systematically searched till March 2019. The search terms included EVAR, type II endoleak, and embolization. The articles were read and extracted by two authors independently to include randomized control trails and retrospective studies that compared TA embolization and TL embolization in patients who developed type II endoleak after EVAR. The technical and clinical success rates were meta-analyzed with random effect model.

Results A total of 6 articles with 268 patients and 290 type II endoleaks were included. The pooled odds ratio (OR) of technical success rate for TA vs. TL was 0.56 (95% CI, 0.10-3.18; $P=0.51$) and the pooled OR of clinical success rate for TA vs. TL was 0.31 (95% CI, 0.07-1.29; $P=0.11$). As a limitation, 6 articles were all retrospective studies which may lead to bias.

Conclusion Both TA and TL could be effective procedure of embolizations to resolve the type II endoleak. The meta-analysis result indicated that TA embolization was not inferior to TL embolization in technical success and clinical success.

ABDOMINAL aortic aneurysm (AAA) is defined as local aortic dilation and diameter exceed 3cm. It has a prevalence of 7.2% in men older than 50 years old. The associated risk of aneurysm rupture for death can reach up to 90%.^[1] The endovascular aortic aneurysm repair (EVAR) is an effective treatment of AAA and has almost become the first recommended procedure due to its mini invasive and low 30-day mortality. However, EVAR has lots of delayed complications and an inferior late survival compared with open repair.^[2,3] There are a variety of complications after EVAR, such as femoral pseudoaneurysm, endograft migration, endograft occlusion, and endoleak. Endoleak is defined as aneurysm sac that is not completely excluded from the systemic circulation, and it increases the re-intervention rate and rupture risk after EVARs.^[4] The type II endoleak is the most common subtype. Although half of them will resolve spontaneously, about 10%-15% type II endoleak will persist longer than 6 months.^[5,6] The persisting type II endoleak is associated with aneurysm sac expansion,^[7] which may contribute to the delayed adverse outcomes and re-interventions. So when the type II endoleak meets the criteria, i.e., expansion of aneurysm sac longer than 10mm (or>5 mm), or type II endoleak persisting longer than 6 months, the treatment is suggested.^[8,9]

There are several treatments for type II endoleak, such as transarterial (TA) embolization, translumbar (TL) embolization, and laparoscopic ligation of the feeding artery. TA embolization and TL embolization are widely used in multiple vascular surgery centers. Many reviews analyzed the treatment effectiveness of type II endoleak, where most original articles studied TA embolization or TA embolization alternatively.^[10,11] In the present review, we aimed at investigating the technical success and clinical success of TA embolization versus TL embolization for type II endoleak after EVAR.

MATERIALS AND METHODS

Search strategy

The present review was performed according to the PRISMA statement in order to standardize the method.^[12] The registration number of this review is CRD42018114453. The electronic searches were conducted using databases of Pubmed, Embase, Web of Science, and the Cochrane library. The searching terms

are provided in the supplementary material online (*Appendix*). The participants included patients who were diagnosed with type II endoleak, and the induced aneurysm sac expansion > 5 mm or persisting longer than 6 months after EVAR. The interventions include TA embolization and TL embolization. The outcomes were the technical success and clinical success. Technical success was defined as no flow back into aneurysm sac after embolization procedures; clinical success was defined as aneurysm sac shrank or kept stable with no type II endoleak relapse during follow-up. The last search was conducted on the March 27, 2019.

Literature selection

We selected studies of randomized control trails (RCT) and observational studies which investigate treatment effectiveness on the outcomes of type II endoleak between TA embolization and TL embolization. Exclusion criteria were no full-text, less than 10 cases, non-English language, case report, and duplicated publication. Two reviewers (ZX and JL) screened the titles and abstracts of the articles independently. Disagreements were resolved after discussion with the third reviewer (WW).

Data extraction and management

The descriptive, methodological and outcome data were extracted by three reviewers (ZX, JL and WW) independently from each study with a standardized data extraction table recording: author name, country, study design, publication year, criteria for treatment, intervention methods, technical and clinical success rates, and follow-up time.

Quality assessment of included studies

Two authors (ZX and JL) independently used the Newcastle-Ottawa scale (NOS) form to assess the quality of non-randomized control studies. We only included studies with NOS scored 5 and above.

Statistical analysis

Dichotomous variables were analyzed by estimating the odds ratio (OR) with 95% confidence interval (CI), and the I^2 statistic was used to assess the heterogeneity between studies. If $I^2 > 50\%$, it was considered high statistical heterogeneity and the random effect model was applied; otherwise, the fixed effect model was used. Funnel plots were created if more than 10 studies were included and publication bias was suspected.

$P < 0.05$ was regarded as statistical significance. The statistical analysis was performed with the RevMan (Version 5.3, Cochrane).

RESULT

Literature searching results

The initial search identified 88 articles. After screening titles and abstracts, 17 articles were included; by reading full text, 6 articles met the selecting criteria (**Figure 1**). All of 6 articles were retrospective studies, including 268 patients and 290 type II endoleaks. The characteristics of included studies were summarized in **Table 1**.

Study quality assessment

The quality assessment (NOS score) of the included studies was summarized in **Table 2**. Due to the heterogeneity of the included studies, we used the random effect model to compare the treatment effects between TA embolization and TL embolization.

Effects of the interventions

Of the 6 included articles, the technical success rates of TA embolization ranged from 40% to 95.7%, and the technical success rate of TL embolization almost reached 100% except in two studies (seen in Table 1). The pooled odds ratio of 6 studies for technical success of TA versus TL was 0.56 (95% *CI*, 0.10-3.18; $P = 0.51$; $I^2 = 62\%$, low quality). Among 5 studies of clinical success (one study had no record on clinical success), the clinical success rate of TA and TL embo-

lization ranged from 11.8% to 78.3% and from 27.3% to 100%, respectively. The pooled *OR* for clinical success was 0.31 (95% *CI*, 0.07-1.29; $P = 0.11$; $I^2 = 70\%$, low quality). A heterogeneity was observed among these 6 studies.

The comparative meta-analysis demonstrated no statistical difference in both technical and clinical success between the two intervention procedures (**Figure 2**). Considering only 6 retrospective articles were included, the funnel plots and sensitivity analysis were not performed.

DISCUSSION

The number of EVARs has increased dramatically since its introduction.^[13] Despite the lower 30 days mortality and minimal invasion, the delayed complications have become the Achilles tender of EVARs.^[14] Endoleak accounts for a large proportion of the complications that leads to the result that aneurysm sac not being excluded from blood circulation. Type I and type III endoleak were regarded as life-threatening due to their acute and severe outcomes, while type II endoleak was benign, and was the most common one as its prevalence can reach 17%-45.6%.^[15-17]

Whether type II endoleak is associated with an increased risk of AAA rupture and mortality is still in controversy. A multicentric study about EVAR showed that type II endoleak did not increase the mortality and the aneurysm-related mortality, but was associated with sac expansion.^[18] The systematic review by Siddloff DA *et al.* suggested that aortic aneurysm rupture after EVAR secondary to an isolated type II endoleak happened in less than 1%.^[10] However, Jones JE *et al.* did a retrospective analysis in 164 patients with type II endoleak, and found that patients with persistent endoleak (>6 months) were at increased risk for aneurysm sac growth compared with patients without persistent endoleak. Additionally, patients with persistent endoleak also had a significantly increased rate of re-intervention and AAA ruptures, which occurred in 4 patients with type II endoleak, demonstrating that persisting type II endoleak may contribute to the high AAA rupture rates and other adverse outcomes.^[9] Van Marrewijk CJ *et al.* found that although type II endoleak may not increase aneurysm rupture risk according to statistic results, it does not mean that type II endoleak was harmless. Adverse outcomes such as aneurysm growth, transfemoral re-intervention, and

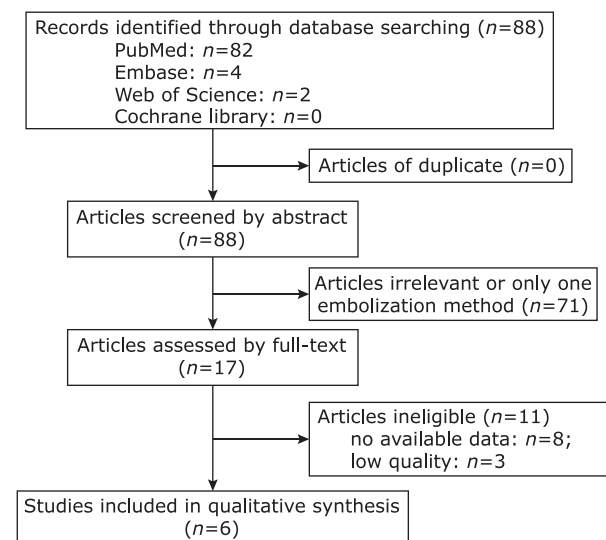


Figure 1. Flow chart of literature selection

Table 1. The basic information of the included studies on TA embolization and TL embolization for type II endoleak

Studies	Country	Research type	Criteria for intervention	No. of patients	No. of endoleaks	TA		TL		Materials	Follow-up
						Technical success	Clinical success	Technical success	Clinical success		
Marcelin <i>et al.</i> , 2017 ^[30]	France	Retrospective study	Persistent after 6 months and increasing sac size > 5 mm	28	29	16/22 (72.7%)	NS	1/7 (14.3%)	NS	onyx	20 ± 12 months (range 6 - 49 months)
Haq <i>et al.</i> , 2017 ^[31]	UK	Retrospective study	Increasing sac size > 5 mm	28	28	7/17 (41.2%)	2/17 (11.8%)	3/11 (27.3%)	3/11 (27.3%)	coils or embolizing agent	3.11 years (median)
Massis <i>et al.</i> , 2012 ^[32]	USA	Retrospective study	Increase of sac size > 5 mm within 6 month, or sac > 6 cm or change in sac morphology, or change in position or orientation of stent graft in sac	95	101	58/65 (89.2%)	21/29 (72.4%)	36/36 (100%)	18/24 (75%)	onyx	15 weeks
Nevala <i>et al.</i> , 2010 ^[33]	Finland	Retrospective study	Increasing sac size or persistent after 3 months	14	14	4/10 (40%)	2/9 (22.2%)	3/3 (100%)	3/3 (100%)	coils, thrombin, gelatin, onyx, glue	NS
Stavropoulos <i>et al.</i> , 2009 ^[29]	USA	Retrospective study	Persistent > 1 month and aneurysm expansion	84	85	22/23 (95.7%)	18/23 (78.3%)	62/62 (100%)	45/62 (72.6%)	coils, n-butyl cyanoacrylate	18.7 months (range 1-84 months)
Baum <i>et al.</i> , 2002 ^[34]	USA	Retrospective study	Persistent > 1 month	19	33	17/20 (85%)	4/20 (20%)	13/13 (100%)	12/13 (92.3%)	coils, thrombin	13.1/8.4 months

TA, transarterial; TL, translumbar; NS, not stated.

Table 2. Quality assessment results of included studies employing the Newcastle-Ottawa Scale

Studies	Adequate case definition	Representativeness	Selection of controls	Definition of controls	Comparability	Ascertainment of exposure	Same method of ascertainment	Non-Response rate	Total score
Marcelin <i>et al.</i> , 2017 ^[30]	★	★	n/a	★	n/a	★	★	n/a	5
Haq <i>et al.</i> , 2017 ^[31]	★	★	n/a	★	★	★	★	n/a	6
Massis <i>et al.</i> , 2012 ^[32]	★	★	n/a	★	n/a	★	★	n/a	5
Nevala <i>et al.</i> , 2010 ^[33]	★	★	n/a	★	n/a	★	★	n/a	5
Stavropoulos <i>et al.</i> , 2009 ^[29]	★	★	n/a	★	★	★	★	n/a	6
Baum <i>et al.</i> , 2002 ^[34]	★	★	n/a	★	★	★	★	n/a	6

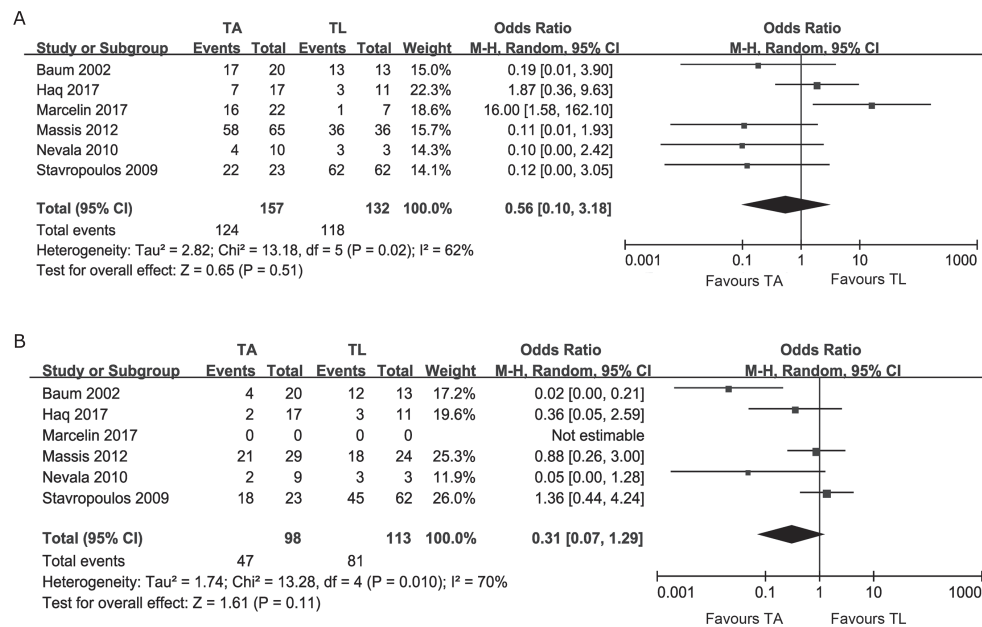


Figure 2. Forest plot showing the pooled odds ratios of the studies comparing technical success and clinical success between two interventions of TA and TL in treatment of type II endoleak.

A. Comparison of the technical success rates; B. comparison of the clinical success rates. TA, transarterial (embolization); TL, translumbar (embolization).

transabdominal secondary procedures (e.g. laparoscopic branch vessel clipping) occurred in 55% patients with type II endoleak in 3 years, comparing to in 15% patients without any endoleaks ($P < 0.0001$).^[19] Some situations where type II endoleak could not be detected^[20,21] may also contribute to the unclear correction between type II endoleak and AAA rupture risk. Additionally, some occult type I endoleaks and type III endoleaks existing behind the phenomenon type II endoleaks contributed to growth of aneurysm sac.^[22] Type II endoleaks may have potential associations with AAA ruptures after EVAR.

Half of the type II endoleaks resolved spontaneously, so conservative treatment was recommended as the first choice.^[23] The *Society for Vascular Surgery Practice Guidelines* recommend treatment to type II endoleak be implemented when the sac expands to diameter > 5 mm.^[8] Meanwhile, the *Clinical Practice Guideline of European Society of Vascular Surgery* recommends intervention for patients with type II endoleak when the sac diameter exceeding 10 mm during follow-up.^[24] Many clinical practitioner tend to regard 5 mm growth of a sac or persisting 6 month as the criteria for performing treatment.^[25-28]

Up to now, there is a variety of methods that can be used to eliminate type II endoleak, such as TA embolization, TL embolization, and laparoscopic liga-

tion of feeding vessels. In general, embolization is the most prevailing measure to occlude type II endoleak in vascular surgery departments. In TA embolization, percutaneous transfemoral or transbrachial is used for access, and either superior mesenteric artery-middle colic artery - inferior mesenteric artery or external iliac artery-lumbar artery is selected according to the origin of type II endoleak. The materials that can be delivered include coils, Onyx® (ethylene vinyl alcohol copolymer) and glue. TL embolization is an alternative way to eliminate type II endoleak, especially when internal iliac or inferior mesenteric arteries were occluded. The endoleak is identified by the fluoroscopic marks in advance, the aneurysm sac is then punctured and the sheathed needles are positioned into the endoleak. After embolization of the endoleak sac, endoleak angiography should be performed to verify that the procedure is successful.^[29]

Some meta-analysis or systematic reviews compared the technical or clinical success rates between TA embolization and TL embolization for type II endoleak. Ultee KHJ *et al.* pointed out that technical successes of TA embolization was 84.0% (95% CI: 77.2%–89.8%; $I^2 = 56.2\%$), while for TL embolization, this was 98.7% (95% CI: 95.6%–100%; $I^2 = 0.0\%$).^[11] In another systematic review published recently, TL embolization had a higher clinical success rate than TA embolization

(81% vs. 62.5%; $P=0.024$), but the articles included in these reviews investigated only one intervention retrospectively and the review analyzed the two interventions separately.^[10] In present review, all included 6 studies investigated the technical and clinical success of both TA and TL embolization, and all stated explicitly the criteria of clinical success which was not heterogeneous. TL embolization may have an advantage over TA in technical and clinical success according to the results of original articles, but our analysis indicate that there are no statistical differences between these two procedures. In future, more studies comparing the outcomes of TA embolization with TL embolization after EVARs are needed to reduce the underlying bias.

The present review has several limitations. All studies included are retrospective studies and there has no RCTs. The low quality of evidences may bring bias to this study. In addition, beside the embolization methods, the materials used in embolization procedures also affect the clinical success rates, but the subgroup division could not be conducted for the small quantity of studies included. In conclusion, both TA and TL embolization could be effective to resolve type II endoleak when the induced aneurysm sac expansion >5mm in 6 months or persists longer than 6 months. Although in most studies, TL showed minor advantage over TA, result of this meta-analysis indicated that TA was not inferior to TL in technical success and clinical success.

Conflict of interests

None.

Supplementary material

Appendix is available online at <http://cmsj.cams.cn/EN/10.24920/003618>.

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