Intracardiac Versus Transesophageal Echocardiography for diagnosis of left atrial appendage thrombosis in atrial fibrillation: A Meta-analysis

guijun he[1], hanxion liu[1], xiaoqi deng[1], guosu yang[1], han wang[1], duan luo[1], and cai lin[1]

[1]Chengdu Institute of Cardiovascular Diseases

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Abstract

Introduction: Patients with atrial fibrillation excluded left atrial appendage(LAA) thrombosis is typically performed utilizing transesophageal echocardiography (TEE).Intracardiac echocardiography (ICE) can be a suitable alternative to detect thrombosis. Methods: We searched PubMed ,Cochrane Library and Embase for published abstracts and manuscripts until for published abstracts and manuscripts until June1, 2020. Studies reporting clinical outcomes comparing TEE vs. ICE for LAA thrombosis in human subjects aged [?] 18 years were included. Two investigators independently extracted the data and individual quality assessment was performed. Analysis was performed using RevMan 5.3, STATA 15 and Meta-Disc 1.4. Results: Eight eligible studies consisting of 1108 patients (TEE = 558 vs. ICE = 550) were included. The average sensitivity of ICE and TEE to diagnose left atrial appendage thrombosis was 1.0 (95% CI: 0.91-1.00) vs 0.68 (95% CI: 0.49-0.83). The average specificity of ICE and TEE diagnosis of left atrial appendage thrombosis was 1.0 (95% CI: 0.99-1.00) vs 0.98 (95% CI: 0.96-0.99) . The AUC of ICE and TEE were 0.9846 (SEAUC = 0.0196) and 0.9655 (SEAUC = 0.0401), and the Q * statistics were 0.9462 (SEQ * = 0.0406) and 0.9127 (SEQ * = 0.0616), respectively. Z test was performed on Q * statistics (Z = 0.45, P> 0.05), there was no significant difference between ICE and TEE. Conclusion: ICE and TEE have similar diagnostic efficacy for left atrial appendage thrombosis, but ICE has higher sensitivity and specificity, which has certain advantages over TEE and has clinical application prospects

1 Introduction

Atrial fibrillation (AF) is the most common arrhythmia, and the proportion increases with age. The proportion of atrial fibrillation is as high as 8% over 75 years old[1]. The most effective treatment for atrial fibrillation is radiofrequency ablation and cryoablation, but patients need to exclude the left atrium and left atrial appendage (LAA)thrombosis. The main method is to routinely perform transesophageal echocardiography (TEE) before operation to exclude LAA thrombosis. Intracardiac echocardiography (ICE) is increasingly used to define the structure of the left atrium and left atrial appendage. Currently, the two methods are unclear about the real event of detecting left atrial appendage thrombosis, Hence, we performed a meta-analysis.

2.Methods

2.1 Search strategy

We searched PubMed , Cochrane Library and Embase using keywords: atrial fibrillation, transesophageal echocardiography (TEE), Intracardiac echocardiography (ICE) and thrombosis from their inception to June1, 2020. Studies only published in English language be included.

2.2 Study selection

The eligibility criteria for our meta-analysis included: (1) Studies are prospective or retrospective include TEE vs ICE .(2) The clinical result is the gold standard. (3) The studies had to provide sufficient information to construct the 2×2 contingency table—ie, false and true positives and negatives were provided.(4) TEE and ICE inspection interval is less than 48 hours and definition of thrombosis consistent or similar. Exclusion criteria:(1) Data cannot be accurately extracted. (2) Animal experiment and review literatures. (3) Articles with undetectable thrombus.

2.3 Data extractions quality assessment

Two independent reviewers screened the documents according to the pre-established inclusion and exclusion criteria, and included the documents according to the QUADAS-2(quality assessment of diagnostic accuracy studies-2) evaluation criteria[2]. Perform a quality evaluation, extract the data and cross-check, when the opinions are not uniform, the third researcher decides jointly. The extracted data includes basic informations , experimental design and original data (true positives, false positives, true negatives and false negatives).

2.4 Statistical analysis

2.4.1 Heterogeneity analysis Use Q test to analyze whether existing, using I2 to estimate the size of the heterogeneity, and then select the appropriate statistical analysis model for subsequent meta analysis.

2.4.2 We tabulated true positives, false negatives, false positives, and true negatives in patients with sepsis and systemic inflammatory response syndrome, stratified by study. We used the numbers to calculate sensitivity and specificity and a corresponding CI. The Mose's constant linear model was used to fit the SROC curve, and the diagnostic odds ratio (DOR), aera under curve (AUC) and Q * statistics were used to evaluate the accuracy of the diagnostic tests ICE vs TEE in diagnosis of left atrial appendage thrombosis [3,4]. We used the Z test to analyze whether there is difference in the two diagnosis. Calculate the Spearman correlation coefficient ρ of true positive rate and false positive rate, and analyze whether there is a threshold effect. Using Deeks linear regression to evaluate whether the included studies have publication bias. The statistical software for this article is Review Manager 5.3,STATA 15 and Meta-Disc 1.4, $P < 0.05$ was considered statistically significant.

3 Results

3.1 Search results

A total of 30 relevant citations were identified (Fig. 1). After a detailed evaluation of these studies, 8 studies ultimately met the inclusion criteria enrolling 1108 patients (TEE = 558 vs. ICE = 550)[5-12]. QUADAS-2 quality graph (Fig. 2,3). Individual study data obtained is shown in Table 1. True positives, false positives, false negatives, and true negatives (Table 2)

3.2 Heterogeneity test

We used DOR as the effect size to analyze the heterogeneity of ICE and TEE respectively. The Q test shows that Cochran-Q is 1.75 and 6.15 respectively. That means heterogeneity between studies is small.

3.3 The sensitivity, specificity in the forest map shown in Figure 4. The average sensitivity of ICE to diagnose left atrial appendage thrombosis was 1.0 (95% CI: 0.91-1.00), and the average sensitivity of TEE was 0.68 (95% CI: 0.49-0.83). Figure 5 shows a forest map of ICE and TEE for detecting the specificity of left atrial appendage thrombosis. The average specificity of ICE diagnosis of left atrial appendage thrombosis was 1.0 (95% CI: 0.99-1.00), and the average specificity of TEE was 0.98 (95% CI: 0.96-0.99). In addition, the positive likelihood ratio (PLR) of left atrial appendage thrombosis diagnosed by ICE and TEE was 84.00 (95% CI: 31.56-223.55) vs 25.75 (95% CI: 6.70-98.95); Negative likelihood ratio (NLR) was 0.10 (95% CI: 0.04-0.26) vs 0.47 (95% CI: 0.26-0.86), DOR was 872.70 (95% CI: 208.12-3659.42) vs 89.46 (95% CI: 24.64-324.76), the data is shown in Table 3.

3.4 The SROC curve of ICE and TEE diagnose left atrial appendage

thrombosis shown in Figure 6. The AUC of ICE and TEE were 0.9846 (SEAUC = 0.0196) and 0.9655 (SEAUC = 0.0401), and the Q * statistics were 0.9462 (SEQ * = 0.0406) and 0.9127 (SEQ * = 0.0616), respectively. Z test was performed on Q * statistics (Z = 0.45, P> 0.05), there was no significant difference between ICE and TEE.

3.5 Calculate the Spearman correlation coefficient ρ of the logarithm of sensitivity and (1-specificity) log, ρ values of ICE and TEE are -0.185 and -0.054, respectively, and P are both> 0.05, suggesting that there is no threshold effect.

3.6 Sensitivity analysis

Sensitivity analysis was carried out by reducing one article at a time to evaluate the impact of a single study on this meta-analysis. The combined DOR and 95% CI calculated after deleting one document. There is no difference in results after excluding each article.

3.7 Publication Bias

We uses Deeks to evaluate publication bias for included studies, as shown in Figure 7. ICE's Deeks linear regression showed P <0.05, and publication bias was found; TEE's Deeks linear regression showed P> 0.05, and no publication bias was found. ICE publication offsets may come from research that is limited to published studies, and to unpublished studies.

4 Discussion

ICE and TEE mainly evaluate LAA through the following methods: (1) measurement of LAA length, width, and cross-sectional area; (2) evaluation for thrombus; (3) evaluation for sponta- neous echo contrast (SEC); (4) measurement of ejection velocities of the appendages by pulsed-wave Doppler. When be diagnosed with thrombus, TEE and ICE measured similarly low pulsed-wave Doppler velocities of the LAA([?]20 cm/s). ICE detected a moderate or greater degree of SEC had an appendage ejection Doppler velocity [?]20 cm/s as measured by

TEE. [9]. ICE and TEE have their own advantages and limitations. TEE will cause more discomfort for patients, requiring fasting and drinking, and damage to the esophagus. The merit of TEE is low cost.

Less painful can be performed with ablation operation, and ICE could guide other intracardiac procedures, such as ventricular premature beat positioning, ventricular septal ablation. However, ICE is expensive, and The operation will be canceled if the LAA thrombosis is found , which will cause considerable losses for the patients. This article conducted a meta-analysis of the 8 included studies, compared the diagnostic efficacy of ICE and TEE for left atrial appendage thrombosis by combining diagnostic effect amounts and SROC curves, Finally, the credibility of this meta-analysis was evaluated by sensitivity analysis and test publication bias. The results combined DOR of ICE and TEE were 872.70 and 89.46, respectively, suggesting that both have a significant correlation with left atrial appendage thrombosis, and the correlation of ICE is higher. The SROC curve shows that the AUC of ICE and TEE are 0.9846 (SEAUC = 0.0196) and 0.9655 (SEAUC = 0.0401), and the Q * statistics are 0.9462 (SEQ * = 0.0406) and 0.9127 (SEQ * = 0.0616), respectively. Z test was performed on Q * statistics (Z = 0.45, P> 0.05), there was no significant difference between ICE and TEE. It shows that ICE is not significantly better than TEE for LAA thrombus identification ability. The main reasons we consider ICE better than TEE:(1)TEE probe obviously can be positioned only in the esophagus, whereas the ICE probe can be placed in various sites inside the cardiac chambers, and more conducive to understanding the real situation of left atrial appendage thrombus and structure. (2) TEE requires good cooperation from the patients to better observe LAA, and poor synergism may lead to negative results. (3) ICE can visualize the LAA more clearly, because the short distance to the LAA allows for the visualization of the entire LAA and each pectinate muscle, along with a thrombus that could be hidden between them. The heterogeneity among the studies included in this article is relatively small. Limitations of this meta-analysis: the number of cases reported in the relevant literature retrieved is not large enough, and more randomized controlled trials are needed to verify the reliability of the results .Four studies were performed in a retrospective fashion, which might become a limitation of this meta-analysis .

The retrieved literature is not comprehensive. The search scope is limited to the published research,some gray documents other languages studies may be missed. In summary, ICE and TEE have similar diagnostic efficacy for left atrial appendage thrombosis, but ICE has higher sensitivity and specificity, ICE may be more appropriate for patients who require transseptal puncture. which has certain advantages over TEE and has clinical application prospects.

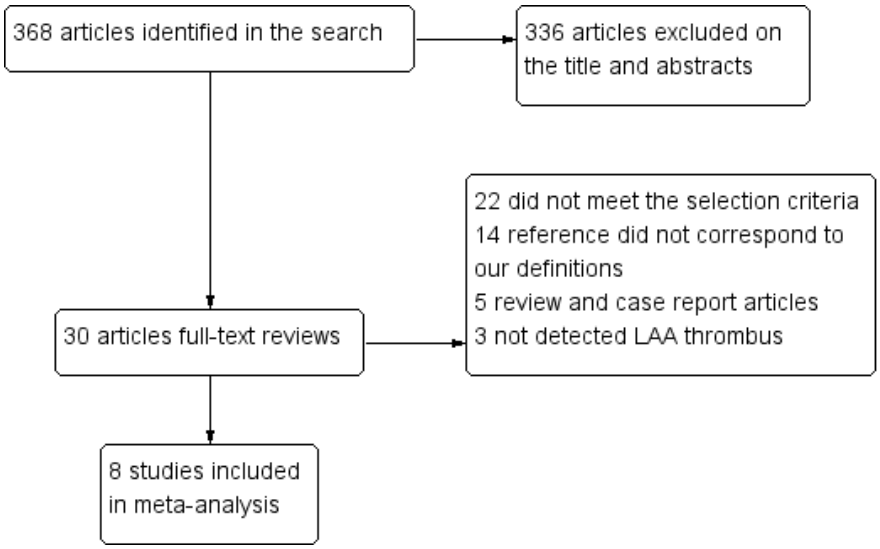

Figure 1: Flow Diagram for the Included Studies.

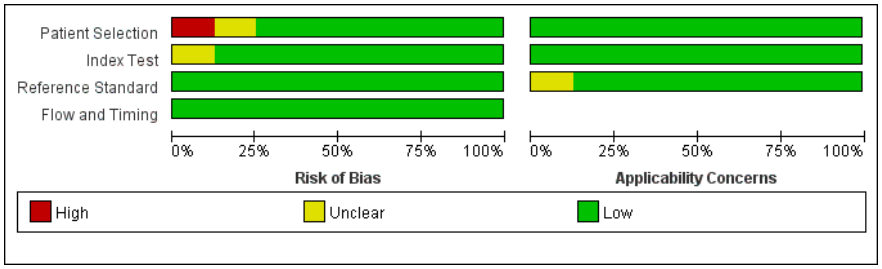

Figure 2:Methodological quality graph.

Figure 3:Methodological quality graph

Auther	Year	Type of study	Mean age	Male(%)	Permanent AF(%)	Patients enrolled (ICE vs.TEE)
Saksena	2010	Prospective	58	84.2	91	95 vs 95
Stec	2011	Retrospective	49	66.7	25	12 vs 12
Ren	2012	Retrospective	57.8	NA	NA	56 vs 56
Baran	2013	Prospective	54	74	13	76 vs 76
Anter	2014	Prospective	60.5	73	NA	71 vs 69
Sriram	2015	Retrospective	62.6	73.8	29.5	122 vs 122
Baran	2016	Prospective	65	57	57	21 vs 21
Ikegami	2017	Retrospective	69	83	69	97 vs 107

Tab 1 General characteristics of included trials

			ICE					TEE		
Author	Year	TP	FP	FN	TN		TP	FP	FN	TN
Saksena	2010	4	0	0	91	Saksena	2010	4	1	0	90
Stec	2011	3	0	0	9	Stec	2011	1	0	2	9
Ren	2012	2	0	0	54	Ren	2012	2	7	0	47
Baran	2013	2	0	0	74	Baran	2013	2	0	0	72
Anter	2014	4	0	0	67	Anter	2014	1	0	3	58
Sriram	2015	7	0	0	115	Sriram	2015	0	2	1	119
Baran	2016	12	0	0	9	Baran	2016	12	9	0	0
Ikegami	2017	4	0	0	93	Ikegami	2017	11	0	4	92

Tab 2 Summary of results of ICE and TEE in included studies, TP=true positive. FP=false positive. TN=true negative. FN=false negative

	Pooled sensitivity (95%CI)	Pooled specificity (95%CI)	Pooled Positive LR (95%CI)	Pooled Negativee LR (95%CI)	Pooled DOR (95%CI)
ICE	1.0 (0.91-1.00)	1.0 (0.99-1.00)	84.00 (31.56-223.55)	0.10 (0.04-0.26)	872.70 (208.12-3659.42)
TEE	0.68 (0.49-0.83)	0.98 (0.96-0.99)	25.75 (6.70-98.95)	0.47 (0.26-0.86)	89.46 (24.64-324.76)

Tab 3 Pooled sensitivity, pooled specificity, and pooled likelihood ration of ICE and TEE

LR: likelihood ration; DOR: diagnostic odd ratio; CI: confidence interval.

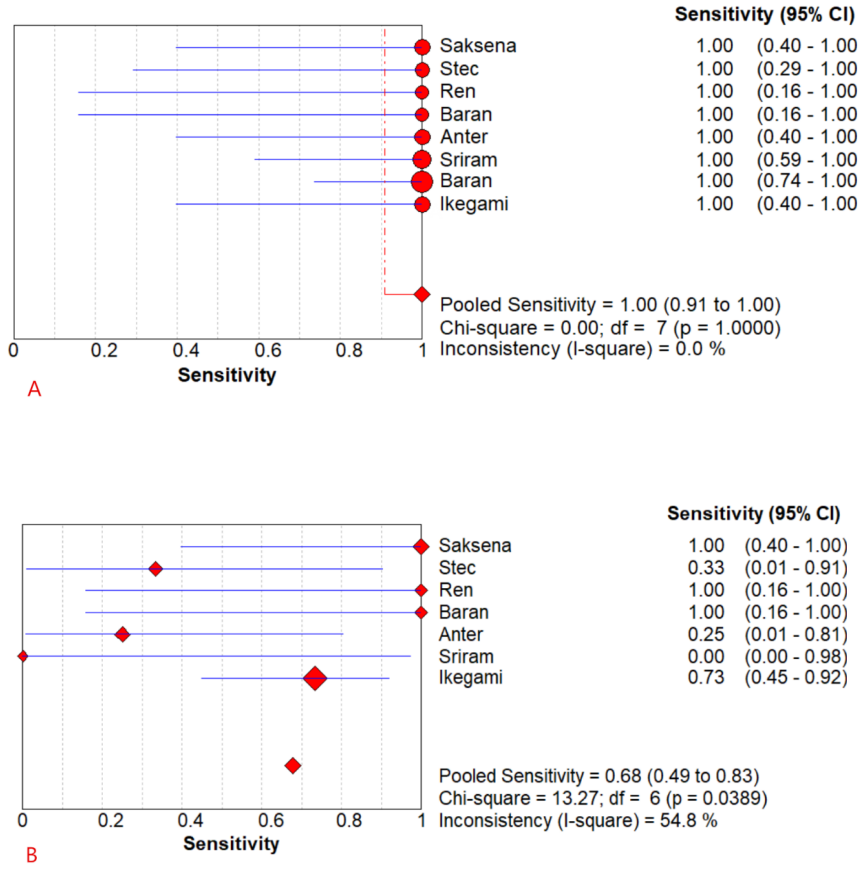

Fig 4 Forest plots of sensitivity of ICE(A) and TEE (B)

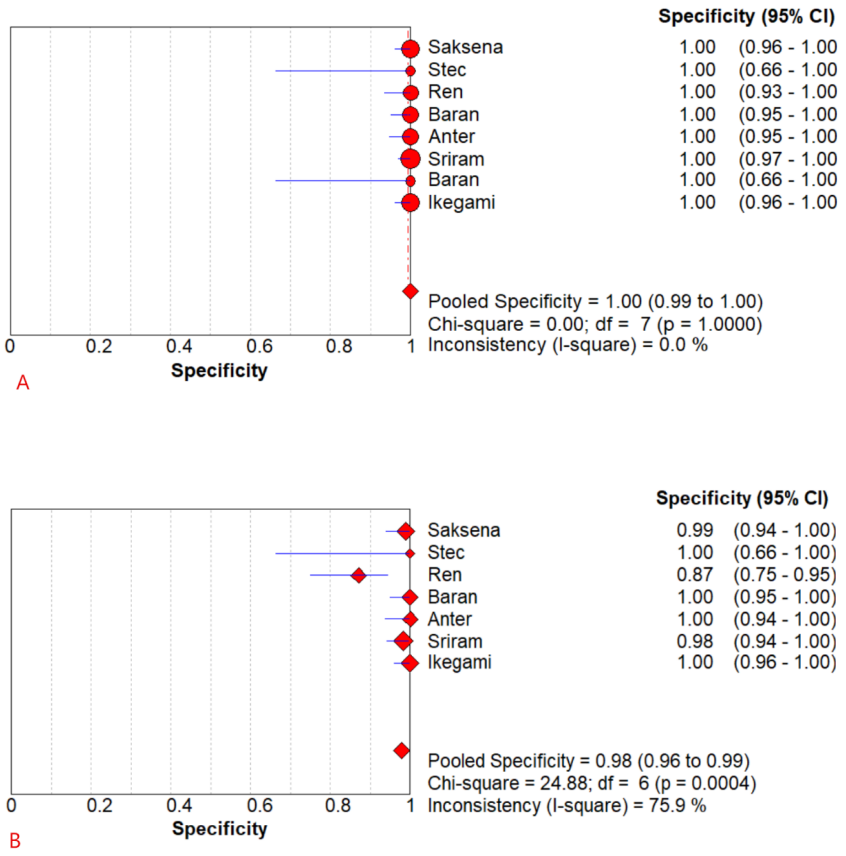

Fig 5 Forest plots of specificity of ICE(A) and TEE (B)

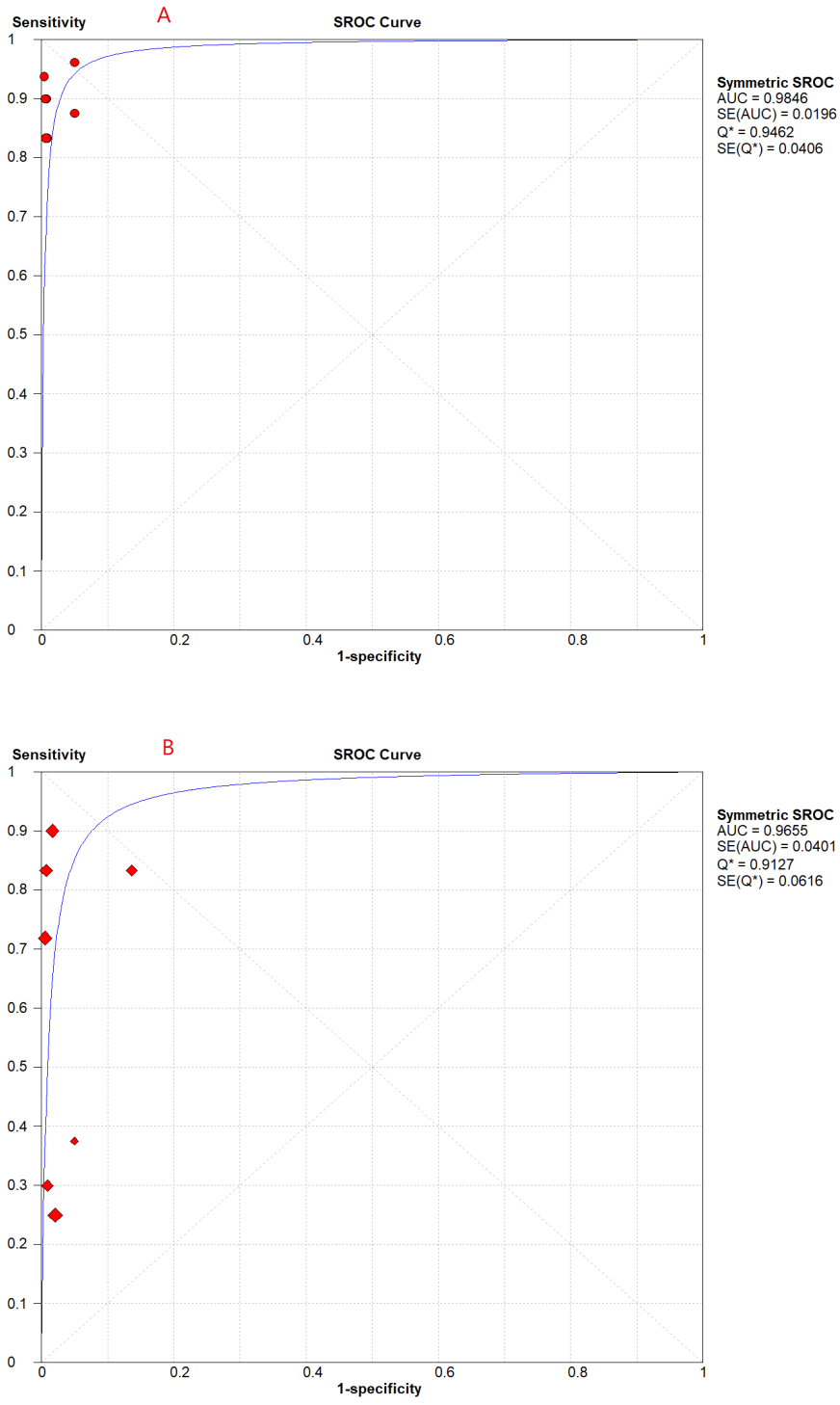

Fig 6 SROC curve of ICE(A) and TEE (B)

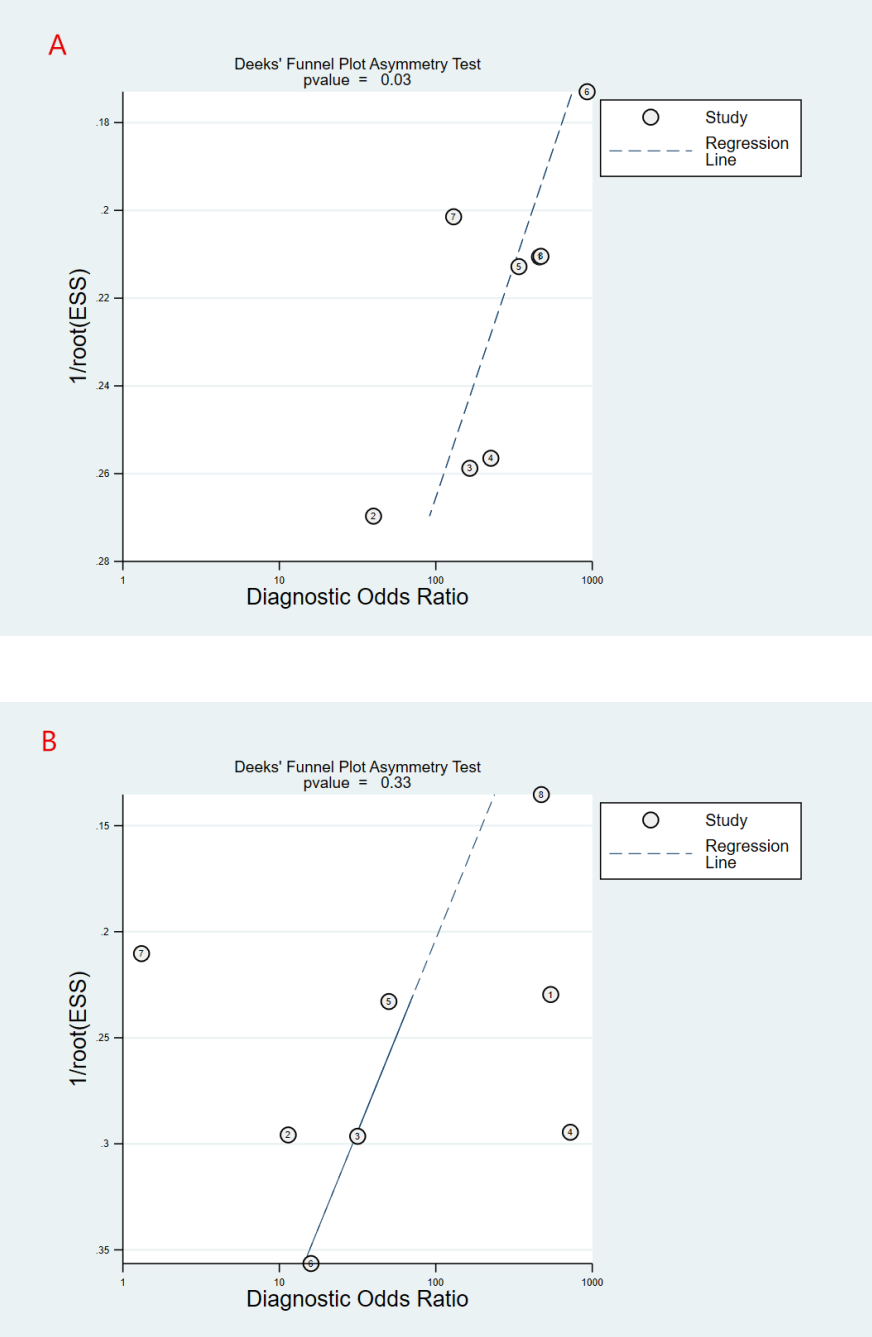

Fig 7 Funnel graph for ICE(A) and TEE (B)

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