Intracardiac Versus Transesophageal Echocardiography for diagnosis of Left Atrial Appendage Thrombosis in Atrial Fibrillation: a Meta-analysis

Guijun He
Chengdu Third People's Hospital
Hanxion Liu
Chengdu Third People's Hospital
Xiaoyu Huang
Chengdu Fourth People's Hospital
Xiaoqi Deng
Chengdu Third People's Hospital
Guosu Yang
Chengdu Third People's Hospital
Luo Duan
Chengdu Third People's Hospital
Lin Cai (cailinwm@163.com)
Chengdu Fourth People's Hospital

Research

Keywords: atrial fibrillation, transesophageal echocardiography (TEE), Intracardiac echocardiography (ICE), and thrombosis

Posted Date: February 4th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-166970/v1

Abstract

Introduction: Left atrial appendage (LAA) thrombus in patients with atrial fibrillation is usually detected by transesophageal echocardiography (TEE). Intracardiac echocardiography (ICE) can be a suitable alternative to detect thrombosis. We performed a meta-analysis of all studies that compared ICE vs. TEE for LAA thrombosis.

Methods: We searched PubMed, Cochrane Library, and Embase for published abstracts and manuscripts until June 1, 2020. Studies reporting clinical outcomes comparing TEE vs. ICE for LAA thrombus in human subjects aged ≥ 18 years were included. Two investigators independently extracted the data and an individual quality assessment was performed. The 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 thrombus was 1.0 (95% CI: 0.91-1.00) vs 0.68 (95% CI: 0.49-0.83),and specificity of ICE and TEE to diagnosis of left atrial appendage thrombus 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 the operation to exclude LAA thrombus.

Intracardiac echocardiography (ICE) is increasingly used to probe the structure of the left atrium and left atrial appendage. Currently, the two methods are unclear about the real events of detecting left atrial appendage thrombus. Therefore, 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 June 1, 2020. Studies only published in the 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 that meaning uneventful AF ablation. (3) The studies had to provide sufficient information to construct the 2×2 contingency table—ie, false and true positives and negatives were provided. If not directly given, get it from the corresponding author via email. (4) TEE and ICE inspection interval is less than 48 hours and the definition of thrombosis consistent or similar,and the anticoagulation standard is consistent. Exclusion criteria:(1) Data cannot be accurately extracted, and it cannot be obtained from the corresponding author. (2) Animal experiments and review kinds of literature. (3) Articles with undetectable thrombus.

2.3 Data extractions and 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]. Carry out the quality assessment, extract data, and cross-check. If opinions are inconsistent, the third researcher will make a joint decision. The extracted data includes basic information, experimental design, and original data (true positives, false positives, true negatives, and false negatives).

2.4 Statistical analysis

2.4.1 Use Q test to detect whether there is the heterogeneity, 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 LAA thrombus in ICE and TEE, 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), the area under the curve (AUC), and Q * statistics were used to evaluate the accuracy of the diagnostic tests ICE vs TEE in the diagnosis of left atrial appendage thrombus [3, 4]. We use the Z test to analyze whether there are differences between the two diagnostic methods. Calculate the Spearman correlation coefficient ρ of true positive rate and false-positive rate, and analyze whether there is a threshold effect. Once Q statistic does not show heterogeneity is not necessary to look for the Spearman correlation coefficient. Deeks linear regression was used to assess whether the included studies had publication bias. The statistical software for this article is Review Manager 5.3, STATA 15, and Meta-Disc 1.4, $P < 0.05$ is 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 finally met the enrollment criteria, and 1108 patients were recruited (TEE = 558 vs. ICE = 550) [5–12]. QUADAS-2 quality graph (Fig. 2,3). Individual study data obtained are shown in Table 1. true positives, false positives, false negatives, and true negatives (Table 2)

3.2 Heterogeneity test

We use 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 and specificity of the forest map are shown in Fig. 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 the ICE and TEE forest plots used to detect the specificity of the left atrial appendage thrombus. The average specificity of ICE in the diagnosis of left atrial appendage thrombosis is 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 thrombus 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 to diagnose left atrial appendage thrombosis is shown in Fig. 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 ($Z = 0.45$, $P > 0.05$), and there was no significant difference between ICE and TEE.

3.5 Sensitivity analysis

Sensitivity analysis is performed by reducing one article at a time to assess the impact of a study on the meta-analysis. There is no difference in results after excluding each article.

3.6 Publication Bias

We used Deeks to evaluate publication bias for included studies, as shown in Fig. 7. ICE's Deeks linear regression showed $P < 0.05$ and found publication bias. The Deeks linear regression of TEE showed $P > 0.05$, and no bias was found. ICE publication offset may come from the search scope is limited to the published research, and the search for the unpublished research is not performed.

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 spontaneous echo contrast

(SEC); (4) measurement of ejection velocities of the appendages by pulsed-wave Doppler. When being diagnosed with thrombus, TEE and ICE measured similarly low pulsed-wave Doppler velocities of the LAA($\leq$ 20 cm/s). ICE detected a moderate or greater degree of SEC had an appendage ejection Doppler velocity $\leq$ 20 cm/s as measured by TEE. [9]. ICE and TEE have their 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 pain can be performed with ablation operation, and ICE could guide other intracardiac procedures, such as left atrial appendage Occlusion, ventricular premature beat positioning, and ventricular septal ablation. The use of ICE catheter ablation of AF is associated with significantly fewer major complications and lower fluoroscopy and radiofrequency time[13]. Friedman et al analyzed predictors of cardiac perforation in a nationwide registry of 102,398 patients undergoing atrial fibrillation (AF) ablation. In this registry, ICE was used in 73% of patients, and the absence of ICE use was associated with a significantly higher rate of cardiac perforation (odds ratio: 4.85; 95% confidence interval: 4.11 to 5.71; $p < 0.0001$)[14]. However, ICE is expensive, Also, ICE requires further vascular access, The resolution of ICE is lower than that of TEE, and young operators need a certain amount of learning time to master this technology. This article conducted a meta-analysis of the 8 included studies, compared the diagnostic efficacy of ICE and TEE for left atrial appendage thrombus 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 thrombus, 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 display 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. （4）ICE can reduce the number of contrast agents and radiation. 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 language studies may be missed.

5 Conclusion

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.

6 Declarations

Ethical Approval and Consent to participate：

Not applicable

Consent for publication：

yes

Availability of data and materials:

yes

Competing interests:

Not applicable.

Funding:

Not applicable.

Authors' contributions:

1, Guijun He，Cai Lin, 3, Hanxion Liu, 4, Xiaoyu Huang, 5, Xiaoqi Deng,6,Guosu Yang,7, Luo Duan,

Acknowledgments:

Not applicable.

References

1. Laila Staerk, Jason A. Sherer, Darae Ko, et al. Atrial Fibrillation Epidemiology, Pathophysiology, and Clinical Outcomes. Circ Res.2017 Apr 28 ;120(9):1501-1517
2. Whiting PF, Rutjes AW, Westwood ME, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med.2011 Oct 18;155(8):529-36
3. Moses LE, Shapiro D, Littenberg B. Combining independent studies of a diagnostic test into a summary ROC curve: data-analytic approaches and some additional considerations. Stat Med, 1993, 12(14): 1293-1316

4. Suzuki S, Moro-oka T, Choudhry NK. The conditional relative odds ratio provided less biased results for comparing diagnostic test accuracy in metaanalyses. J Clin Epidemiol, 2004, 57(5): 461-469.
5. Sanjeev Saksena, Jasbir Sra, Luc Jordaens. A Prospective Comparison of Cardiac Imaging Using Intracardiac Echocardiography With Transesophageal Echocardiography in Patients With Atrial Fibrillation The Intracardiac Echocardiography Guided Cardioversion Helps Interventional Procedures Study. Circ Arrhythm Electrophysiol. 2010;3:571-577.
6. Sebastian Stec, Beata Zaborska, Małgorzata Sikora-Fra˛c. First experience with microprobe transoesophageal echocardiography in nonsedated adults undergoing atrial fibrillation ablation: feasibility study and comparison with intracardiac echocardiography. Europace (2011) 13, 51–56.
7. Jian-Fang Ren, Francis E. Marchlinski, Gregory E. Supple. Intracardiac Echocardiographic Diagnosis of Thrombus Formation in the Left Atrial Appendage: A Complementary Role to Transesophageal Echocardiography. Echocardiography 2013;30:72-80.
8. Jakub Baran, Sebastian Stec, Ewa Pilichowska-Paszkiet.Intracardiac Echocardiography for Detection of Thrombus in the Left Atrial Appendage Comparison With Transesophageal Echocardiography in Patients Undergoing Ablation for Atrial Fibrillation: The Action-Ice I Study. Circ Arrhythm Electrophysiol. 2013;6:1074-1081.
9. Elad Anter, Joshua Silverstein, Cory M.Tschabrunn. Comparison of intracardiac echocardiography and transesophageal echocardiography for imaging of the right and left atrial appendages. Heart Rhythm2014;11:1890–1897.
10. Chennai S. Sriram, Javier E. Banchs, Talal Moukabary. Detection of left atrial thrombus by intracardiac echocardiography in patients undergoing ablation of atrial fibrillation. J Interv Card Electrophysiol (2015) 43:227–236.
11. Jakub Baran, Beata Zaborska, Roman Piotrowski. Intracardiac echocardiography for verification for left atrial appendage thrombus presence detected by transesophageal echocardiography: the ActionICE II study. Clinical Cardiology 2017; 1–5
12. Yukinori Ikegami, Kojiro Tanimoto, Kohei Inagawa. Identification of Left Atrial Appendage Thrombi in Patients With Persistent and Long-Standing Persistent Atrial Fibrillation Using Intra-Cardiac Echocardiography and Cardiac Computed Tomography. Circ J.2017 12 25;82(1):46-52
13. La Greca, Cirasa, Di Modica, et al. Advantages of the integration of ICE and 3D electroanatomical mapping and ultrasound-guided femoral venipuncture in catheter ablation of atrial fibrillation. J Interv Card Electrophysiol.2020 Aug 18. DOI: 10.1007/s10840-020-00835-6.
14. Friedman DJ, Pokorney SD, Ghanem A, et al. Predictors of cardiac perforation with catheter ablation of atrial fibrillation. J Am Coll Cardiol EP 2020;6: 635–44.

Tables

Tab 1 General characteristics of included trials

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

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

	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)

LR: likelihood ratio; DOR: diagnostic odds ratio; CI: confidence interval.

Figures

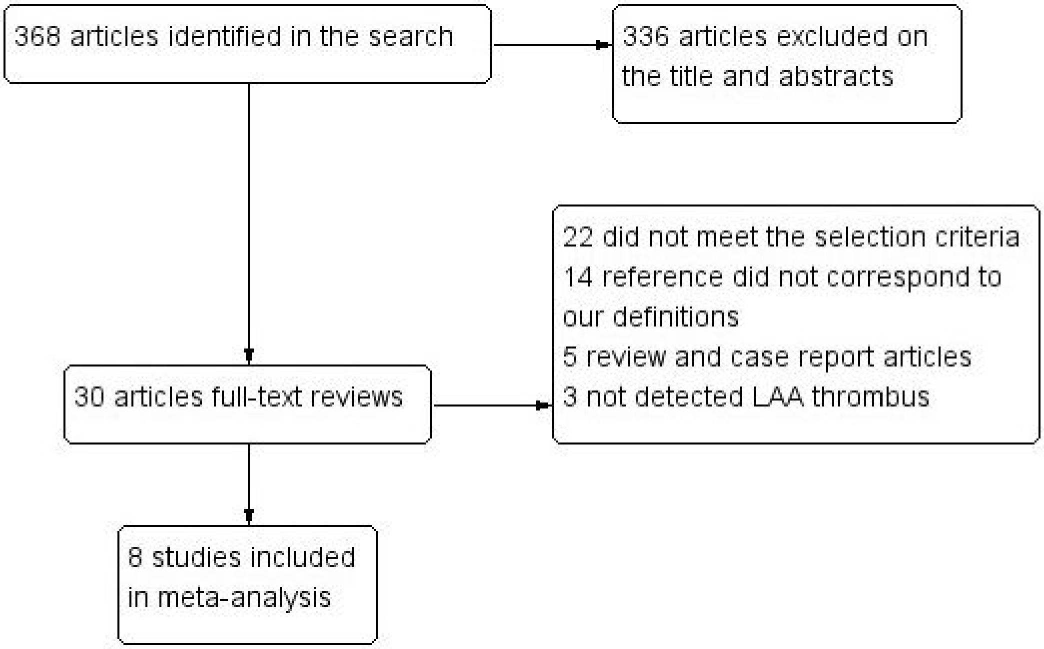

Figure 1

Flow Diagram for the Included Studies.

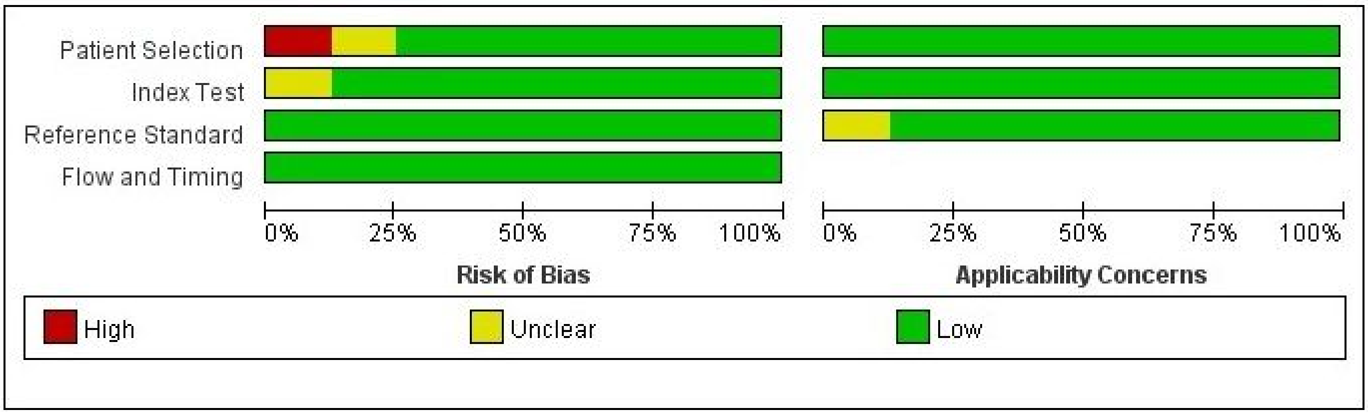

Figure 2

Methodological quality graph.

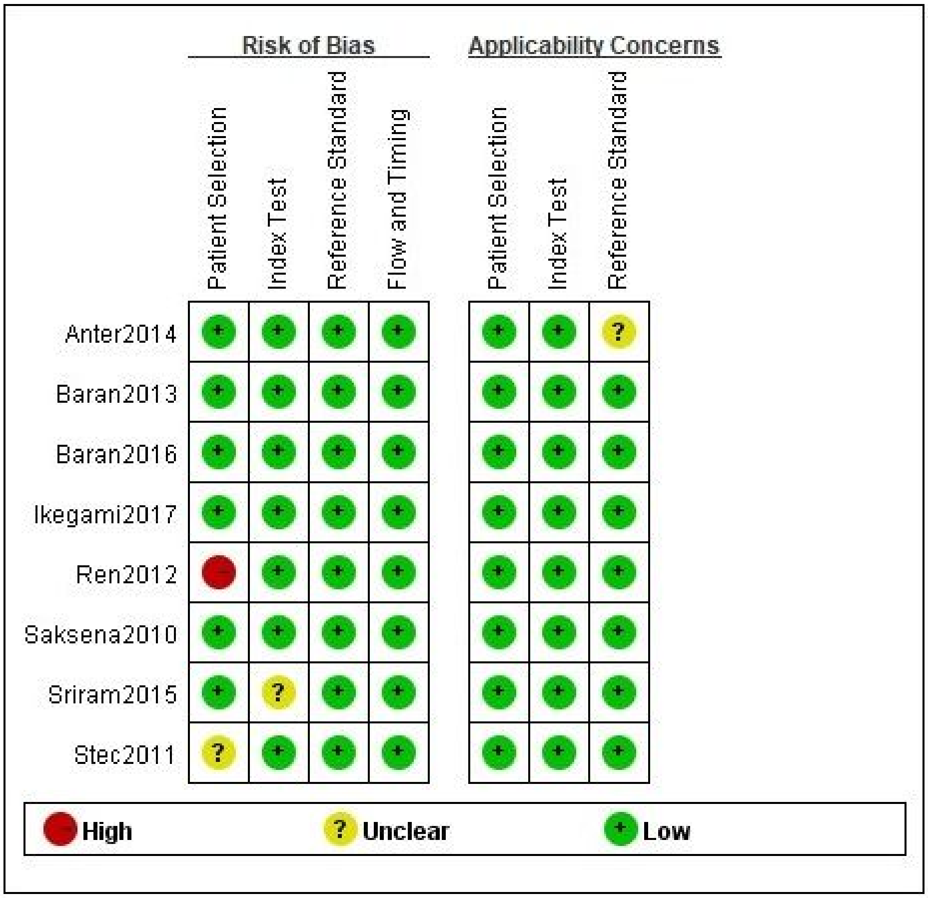

Figure 3

Methodological quality graph

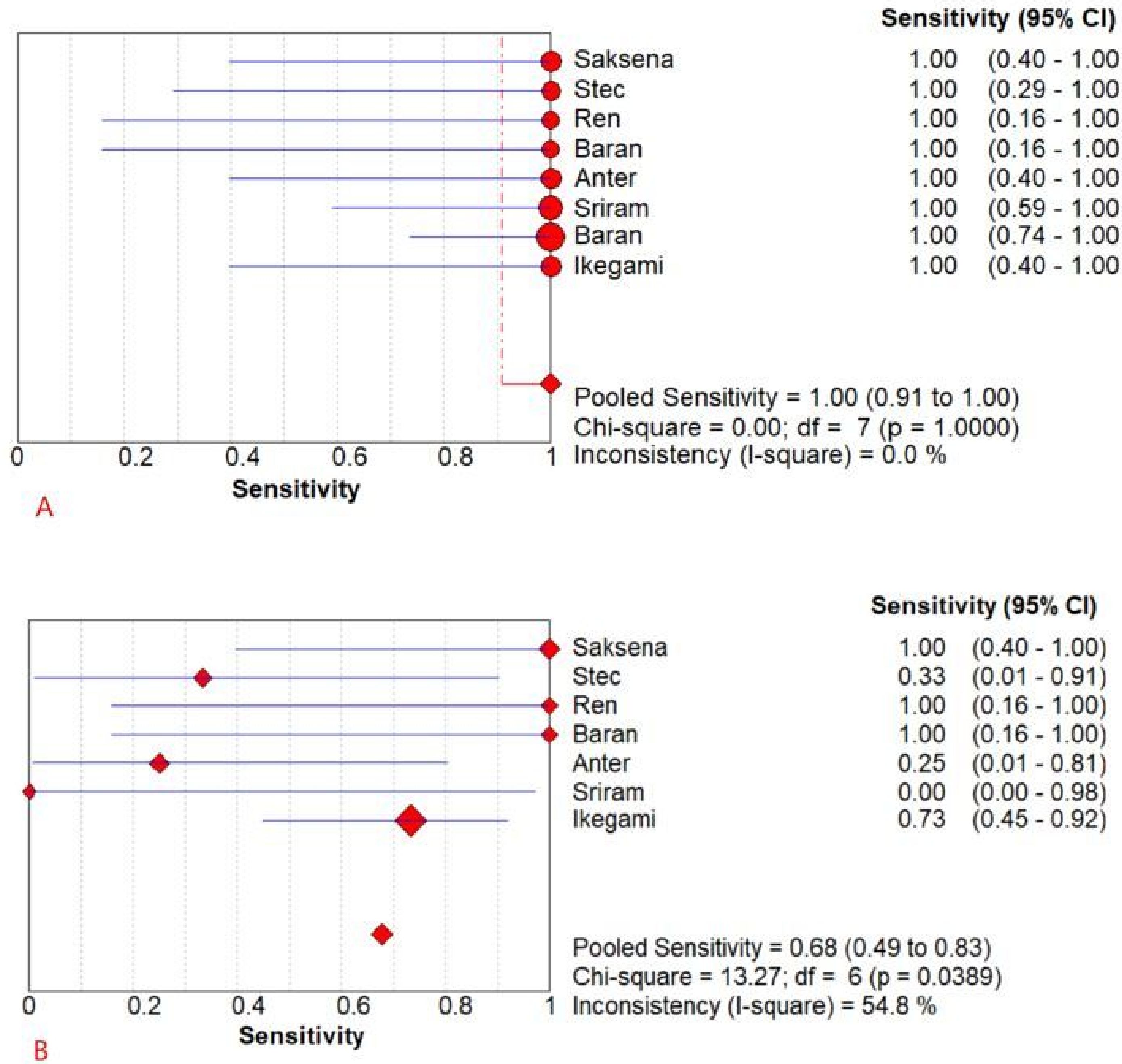

Figure 4

Forest plots of the sensitivity of ICE(A) and TEE (B)

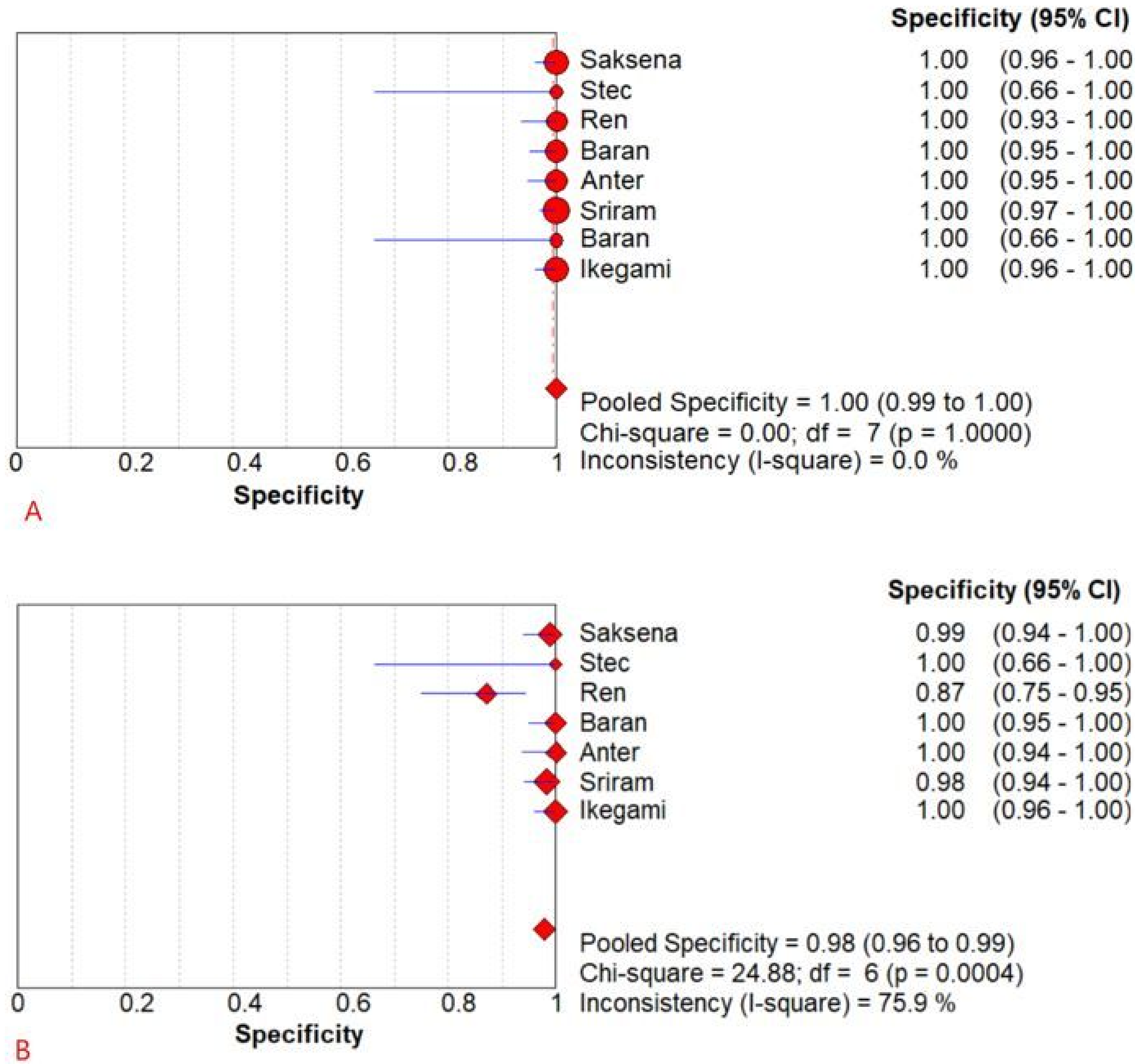

Figure 5

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

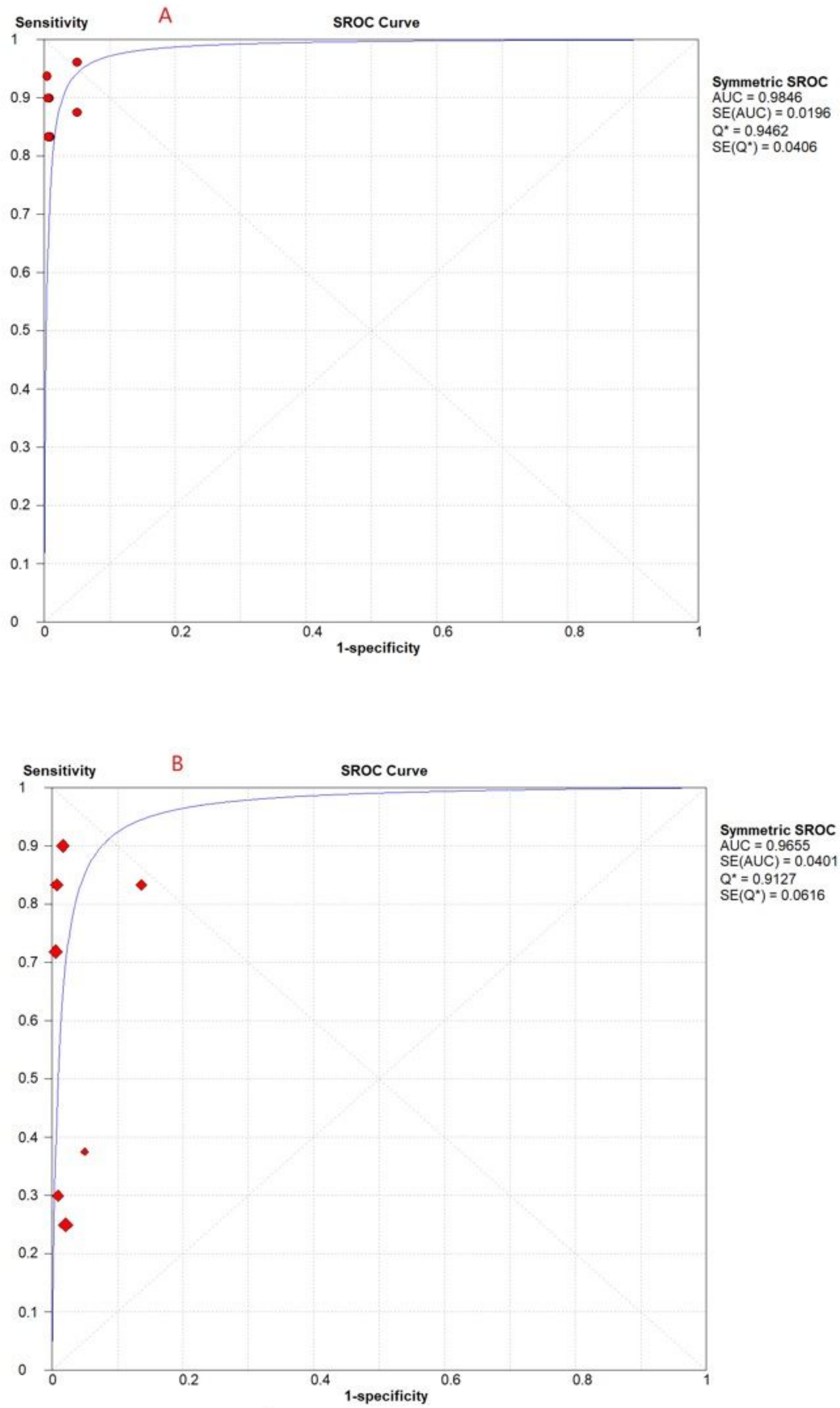

Figure 6

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

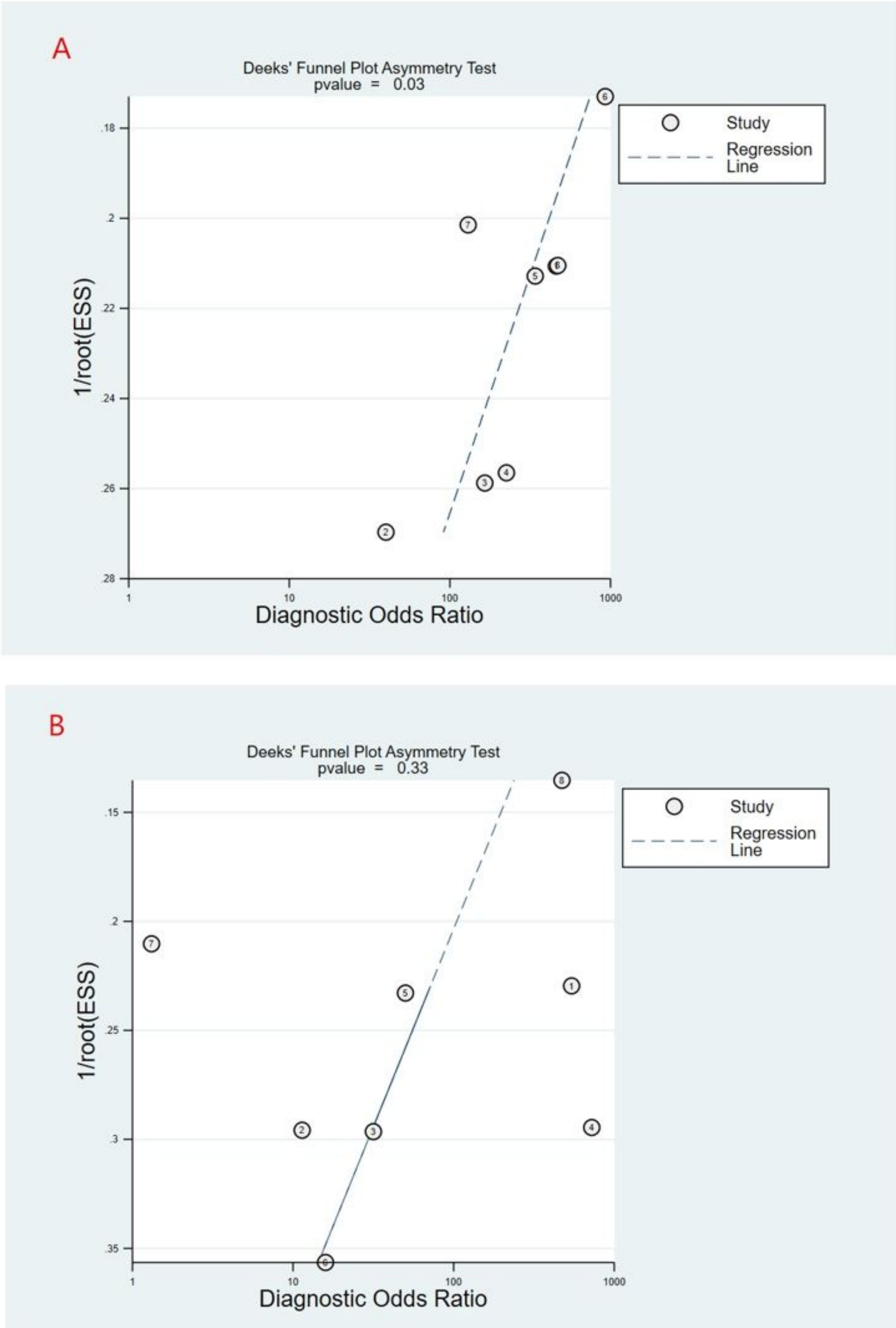

Figure 7

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