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Review Article

Cardiovascular outcomes of emergent vs elective transcatheter aortic valve replacement in severe aortic stenosis: regression matched meta-analysis

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Abstract: Background: Transcatheter aortic valve replacement (TAVR) has been highly increased as the recommended option for patients with a high surgical risk. This study aims to commit a systematic review and meta-analysis to assess the outcomes in severe aortic stenosis patients following emergency transcatheter aortic valve replacement (emergent TAVR) compared to elective TAVR or eBAV followed by elective TAVR. Methods: We conducted a systematic literature search of PubMed, Embase, Cochrane CENTRAL, CINAHL, Science Direct, and Google Scholar. We included nine studies in the latest analysis that reported the desired outcomes. Outcomes were classified into primary outcomes: 30-day all-cause mortality and 30-day readmission rate, and secondary outcomes, which were further divided into (a) peri-procedural outcomes, (b) vascular outcomes, and (c) renal outcomes. Statistical analysis was performed using Stata v.17 (College State, TX) software. Results: A total of 44,731 patients with severe aortic stenosis were included (emergent TAVR n = 4502; control n = 40045). 30-day mortality was significantly higher in the emergent TAVR group (OR: 2.62; 95% CI = 1.76-3.92; P < 0.01). Regarding post-procedural outcomes, the length of stay was significantly higher in the emergent TAVR group (Hedges's g: +4.73 days; 95% CI = +3.35 to +6.11; P < 0.01). With respect to vascular outcomes, they were similar in both groups. Regarding renal outcomes, both acute kidney injury (OR: 2.52; 95% CI = 1.59-4.00; P < 0.01) and use of renal replacement therapy (OR: 2.33; 95% CI = 1.87-2.91; P < 0.01) were significantly higher in emergent TAVR group as compared to the control group. Conclusion: Our study demonstrated that despite increased 30-day mortality and worse renal outcomes, the post-procedural outcomes were similar in emergent and elective TAVR groups. The increased mortality and worse renal outcomes are likely due to hemodynamic instability in the emergent group. The similarity of post-procedural outcomes is evidence of the safety of TAVR even in emergent settings.

Keywords: Emergent TAVR, elective TAVR, aortic stenosis

Introduction

Aortic stenosis (AS) is the most common valvular disease in industrialized countries and carries a poor prognosis if left untreated [1]. The main causes of AS include congenital (bicuspid/unicuspid), calcification of the tri-leaflet valve, and rheumatic disease [2]. Rare causes of AS are metabolic diseases (e.g., Fabry's disease, homozygous type II lipoproteinemia, alkaptonuria, ochronosis), systemic lupus erythematosus, and irradiation [3]. Conditions leading to abnormal calcium and phosphate metabolism such as end-stage kidney disease may also cause AS [4]. The consequences of AS vary according to disease severity. Increased

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bleeding risk, thromboembolic events, infective endocarditis, conduction abnormalities, pulmonary hypertension, heart failure, cardiogenic shock, and sudden death are the main consequences of AS [2]. Diagnosis of severe AS is made by the existence of an aortic transvalvular velocity ≥ 4 m/s, mean transvalvular pressure gradient ≥ 40 mmHg, and aortic valve area (AVA) ≤ 1 cm^2 (with AVA indexed to body surface area ≤ 0.6 cm^2/m^2) [5]. Cardiogenic shock caused by aortic stenosis is becoming increasingly common, heightening operational risks [6]. Over the last ten years, transcatheter aortic valve replacement (TAVR) has been increasingly recommended for candidates of aortic replacement therapy and patients with a high surgical risk [7]. Several trials, notably the PARTNER trials, have recently become the supporting foundation for TAVR. Because of its lower mortality risk, TAVR has been recommended over Surgical Aortic Valve Replacement (SAVR). Compared to other interventions, TAVR is also associated with a lower risk of postprocedural stroke, uncontrolled bleeding, and new-onset atrial fibrillation [8].

TAVR has recently emerged as a viable emergency option for treating aortic stenosis although there are no clear patient selection criteria for emergent TAVR. Large-scale trials examining the efficacy of TAVR, including the PARTNER and CoreValve US Pivotal investigations, have excluded or underrepresented severely decompensated patients [9, 10]. There is little data to support the therapy of aortic stenosis in severely decompensated individuals, and there is a clear literature void here. Some research has been undertaken in the last five years to evaluate the compatibility of TAVR with traditional treatments such as emergency balloon valvuloplasty (eBAV) in critically unwell patients [11].

In patients presenting with cardiogenic shock due to untreated aortic stenosis, TAVR has been linked with improved operative success rates [12-14]. Despite its effectiveness in stabilizing critically ill patients, investigations have revealed a higher risk of in-hospital mortality and kidney injury [11, 15]. Co-morbidities and the nuisance effects of cardiogenic shock are also included when examining the success rate of TAVR in critically sick patients to better understand the elevated mortality rates in such individuals [15]. Compared to elective TAVR patients, emergency TAVR patients had a similar survival rate [16].

The small sample size generated by a single or a few institutions restricts the scope of these investigations. Therefore, it is necessary to conduct the role of urgent or emergent TAVR in patients with severe AS in a wide, nationally representative sample. This study aims to commit a systematic review and meta-analysis to assess the outgrowths in severe aortic stenosis patients following emergency transcatheter aortic valve replacement (emergent TAVR) compared to elective TAVR or eBAV and then elective TAVR.

Methods

Our investigation design and meta-analysis have been presented in line with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) and AMSTAR-2 (Assessing the methodological quality of systematic reviews-2) Guidelines [17, 18]. The checklists of these guidelines are shown in Supplementary Files 1 and 2, respectively. The inclusion criteria of our meta-analysis contain: 1) Adult patients (age > 18) with severe aortic stenosis. 2) Patients undergoing either emergent TAVR in the experimental group and elective TAVR with or without emergent BAV in the control group. 3) Reporting on comparison of emergent TAVR and elective TAVR concerning primary and secondary outcomes. Exclusion criteria were age < 18 years, did not report separate outcomes for emergent or elective TAVR, and no reporting of primary or secondary outcomes of interest. We also eliminated studies that are case reports, clinical spotlight, review articles, and case series.

A literature investigation was committed on PubMed, Embase, Cochrane CENTRAL, CINAHL, Science Direct, and Google Scholar for clinical trials or observational studies with the abovementioned inclusion criteria using a systematic search strategy by PRISMA from the inception till May 2023. The search terms employed using medical subject heading (MeSH) terms and Keywords using Boolean Operators “OR” and “AND” for terms including: “Emergency transcatheter aortic valve replacement” AND “cardiogenic shock” OR “cardiac shock” AND “aortic stenosis” OR “severe aortic stenosis”

OR "cardiac decompensation" with no time, language, and sample size restrictions. The PUBMED keyword occurrence network map is presented in Supplementary File 3.

Study selection

We chose randomized clinical trials (RCTs), pilot trials, and retrospective and prospective studies that met our inclusion criteria. Three authors (MH, HUH, and STR) independently screened the articles; articles that met screening were downloaded into the full text to undergo a second screening phase to evaluate the outcome of interest data. We also did backward snowballing to see the reference of articles with outcomes of interest to find additional studies on our meta-analysis. The data screening was performed under the supervision of a senior author (YS).

Data collection and statistical analysis

The baseline characteristic data were exported to Microsoft Excel and were arranged in Emergent TAVR/Control format. Baseline data elements collected were study design, country of study, follow-up duration, the total number of participants in each study, participants in each arm, their gender proportion, mean age, the proportion of African American patients, body mass index (BMI), the proportion of patients with each New York Heart Association Class, baseline comorbidities including prior history of coronary artery disease (CAD), diabetes mellitus (DM), hypertension (HTN), smoking, prior myocardial infarction (MI), hyperlipidemia (HLD), chronic obstructive pulmonary disease (COPD), peripheral arterial disease (PAD), atrial fibrillation, prior history of stroke, prior interventions such as percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG) and aortic valve intervention, mean Society of Thoracic Surgeons (STS) score %, mean hemoglobin, left ventricular ejection fraction % (LVEF), aortic valve area, aortic valve pressure gradient, peak aortic valve velocity, prior aortic regurgitation. We also collected data on the TAVR approach, i.e., trans-femoral, trans-axillary, or trans-apical approaches.

Outcomes studied were classified into 1) Primary outcome: 30-day all-cause mortality and 30-day readmission rate. 2) Secondary outcomes, which were further divided into (a) peri-procedural outcomes, i.e., length of stay (days), procedural success, paravalvular leak, and pacemaker use, (b) vascular outcomes, i.e., 30-day stroke, vascular complications (includes vessel dissection, rupture, access site hematoma, and the formation of pseudoaneurysms), and major bleeding (any bleeding requiring transfusion), and (c) renal outcomes, i.e., acute kidney injury (AKI) and use of renal replacement therapy (RRT).

Statistical analysis was performed using Stata v.17 (College State, TX) software. Pooled odds-ratio was calculated using the Mantel-Haenszel random-effects model with a probability value of $P < 0.05$, considered statistically significant. For continuous outcomes, Hedges's g was calculated using the Inverse-variance method with a probability value of $P < 0.05$, considered statistically significant. The "test for overall effect" was reported as a z-value corroborating the 95% confidence interval's inference. Higgins I-squared (I^2) was determined to measure statistical heterogeneity where values of ≤ 50% corresponded to low to moderate heterogeneity, while values ≥ 75% indicated high heterogeneity [19]. The publication bias was planned to be depicted graphically and numerically as a funnel plot with Egger's test to be used to estimate funnel-plot asymmetry [20]. Meta-regression was performed to see potential effect modifiers using random effect models for study variance and Knapp-Hartung modification [21, 22]. The quality assessment of the included articles was performed using the Cochrane Risk of Bias (ROB) for randomized studies and the New Castle Ottawa Scale (NOS) for non-randomized studies [23, 24].

Results

Our systematic investigation resulted in 197 articles. After removing duplicates (n = 39), 158 records were screened in the first phase. After duplication removal, 136 articles were excluded, given they didn't meet the inclusion criteria. In the second phase, 22 articles were screened with a full-text review. Of these, 9 studies were included in the final analysis, which reported on our desired outcome (Supplementary File 3) [11, 15, 25-31].

A total of 45,888 patients with severe aortic stenosis and cardiogenic shock were included (emergent TAVR n = 4684; control n = 40934)

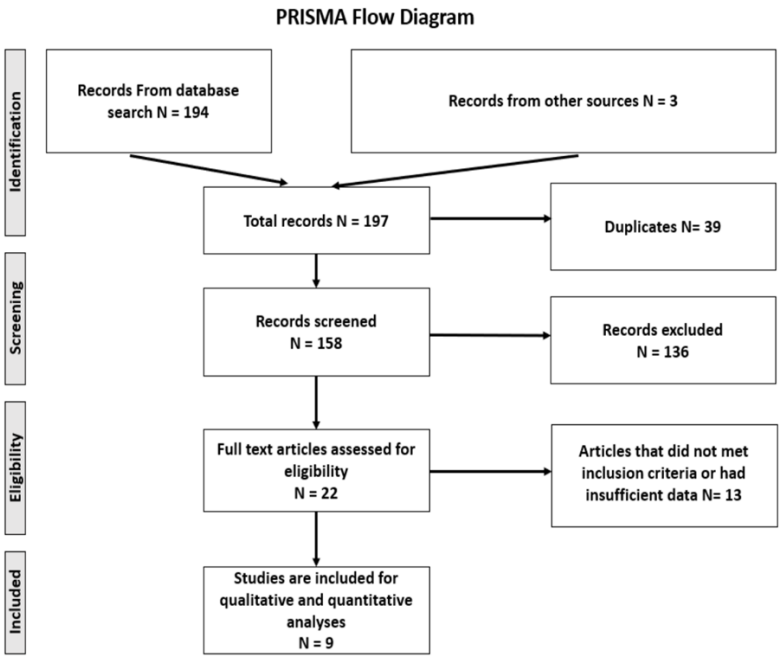

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) Flow of the search strategy for systematic review and meta-analysis.

(**Figure 1**; Supplementary File 3). The mean age of patients with emergent TAVR was 83.14 ± 4.38 years, while the mean age of patients undergoing elective TAVR or emergent BAV with elective TAVR was 83.36 ± 3.45 years, respectively. The Mean STS score % in the emergent TAVR group was 12.14 ± 3.17 while in the control group was 6.4 ± 1.51. The mean LVEF % of the emergent TAVR group was 50.55 ± 7.05 while the control group was 57.61 ± 5.20. The most common comorbidity in the study population was hypertension and the presence of coronary artery disease. Baseline characteristics for both groups are shown in **Table 1**. The study population undergoing emergent TAVR was more likely to be decompensated or in cardiogenic shock and thus hemodynamically unstable, while the study population in control groups was more likely to be hemodynamically stable. Only Bongiovanni et al. had patients with acute cardiac decompensation in both the experimental and control arms [11].

Primary outcomes

30-day all-cause mortality which was reported by all nine studies [11, 15, 25-31]. When the emergent TAVR was compared against the control group, 30-day mortality was significantly higher in the emergent TAVR group (OR: 2.28; 95% CI = 1.63-3.19; P < 0.01). 30-day readmission rates were reported in 4 studies [25-27, 31] (**Figure 3**). It was significantly higher in the emergent TAVR group (OR: 1.28; 95% CI = 1.05-1.57; P = 0.01). Forest Plots for primary outcomes are shown in **Figure 2**.

Secondary outcomes

In terms of post-procedural outcomes, length of stay was studied in five studies, procedural success in five studies, paravalvular leak in seven studies, and pacemaker use was studied in all nine studies [11, 15, 25-31]. The length of stay was significantly higher in the emergent TAVR group (Hedges's g: +5.18 days; 95% CI = +1.67 to +8.69; P < 0.01). Procedural success (OR: 0.99; 95% CI = 0.94-1.03; P = 0.58), paravalvular leak (OR: 1.04; 95% CI = 0.97-1.11; P = 0.30), and pacemaker use (OR: 1.04; 95% CI = 0.97-1.11; P = 0.71) did not show any significant difference. Forest plots of procedural outcomes are shown in **Figure 4**.

With respect to vascular outcomes, 30-day stroke was studied in six studies, vascular complications were mentioned in seven studies, while major bleeding was discussed in seven studies [11, 15, 25-31]. No vascular outcome was significantly different in either group. 30-day stroke (OR: 1.12; 95% CI = 0.74-1.70; P = 0.59), vascular complications (OR: 1.35; 95% CI = 0.80-2.27; P = 0.26) and major bleeding (OR: 1.24; 95% CI = 0.91-1.70; P = 0.18) were similar in both groups. Forest plots of vascular outcomes are shown in **Figure 5**.

Regarding renal outcomes, acute kidney injury was discussed in eight studies [7, 11, 21, 23-27] while the use of renal replacement therapy was studied in five studies [11, 21-24]. Both acute kidney injury (OR: 2.71; 95% CI = 1.66-4.42; P < 0.01) and use of renal replacement therapy (OR: 2.36; 95% CI = 1.93-2.89; P < 0.01) were significantly higher in the emergent TAVR group as compared to the control group.

Table 1. Baseline demographics of patients undergoing emergent TAVR or elective TAVR with or without BAV

Study			Chen et al. 2020	Bianco et al. 2020	Landes et al. 2015	Frerker et al. 2016	Kolte et al. 2018	Enta et al. 2020	Bongiovanni et al. 2017	Kabahizi et al. 2021	Elbaz-Greener et al. 2019
Study Design			Retrospective Cohort	Retrospective analysis	Retrospective single-center analysis	Retrospective analysis	Retrospective data from Registry	Retrospective data from Registry	Multicenter retrospective cohort study	Retrospective data from Registry	Retrospective data from registry
Country			USA	USA	Israel	Germany	USA	Japan	Germany	UK	Canada
Follow-up duration				Yearly till 5 years		365 days	338-394 days	250 days	2 years	1 year	
Total participants - n			602	1193	369	771	40,042	1613	141	1157	2170
Patients	Emergent TAVR/Control	n	139/463	247/946	27/158	27/744	3,952/36090	87/1526	23/118	182/975	429/1741
Males	Emergent TAVR/Control	%	57.55/57.55	53/53	44.5/44.5	44.4/44.4	51.9/51.9	29.9/29.9	82.61/82.61	57.7/53.34	55.2/53.8
Females	Emergent TAVR/Control	%	42.45/41.47	47/51.2	55.5/55.1	55.6/53.1	48.1/48.4	70.1/70.4	17.39/15.84	42.3/46.66	44.8/46.2
Age	Emergent TAVR/Control	Mean ± SD	85.25 ± 2.59/85.5 ± 2.29	81.5 ± 3.45/82.75 ± 2.59	80.1 ± 9.7/81.5 ± 6.2	78 ± 9/80 ± 7	83.5 ± 2.9/83.5 ± 2.9	84.9 ± 7/84.3 ± 5	76 ± 11.4/81.2 ± 6.2	80.1 ± 7/82 ± 2.1	81.3 ± 8.9/81.9 ± 7.2
African American	Emergent TAVR/Control	%	0.72/1.73	2.8/1.8			3.4/2.7				
BMI	Emergent TAVR/Control	Mean ± SD	26.52 ± 2.01/26.47 ± 1.99	27.68 ± 2.47/27.18 ± 2.18		27.1 ± 6.1/26 ± 4.7		21.3 ± 2.3/22.2 ± 3.6			
NYHA class 1	Emergent TAVR/Control	%	0.72/0	0/0.5			1.7/2.9				
NYHA class 2	Emergent TAVR/Control	%	7.91/15.33	1.6/12.2	0/8.2		5.2/16.8				
NYHA class 3	Emergent TAVR/Control	%	74.82/75.81	33.6/63.3	37/75.7		39.7/64.8				
NYHA class 4	Emergent TAVR/Control	%	11.51/5.4	59.9/8.5	63/20.9		52.8/14.6		100/100		
CAD	Emergent TAVR/Control	%		96.7/94.2		70.4/61.7	99.8/99.8		65.2/59.4		59.9/73.5
Diabetes Mellitus	Emergent TAVR/Control	%	38.85/34.13	44.1/40.9	48.1/27.8	40.7/30.6	39.4/35.2	33.3/26.3		21.9/18	49.2/44.8
Hypertension	Emergent TAVR/Control	%	92.09/89.42	89.1/89.2	92.6/90.5	81.5/86.7	91.3/90	74.7/78.8			92.1/94.4
Smoker	Emergent TAVR/Control	%	3.6/3.02	11.3/5.7			5.8/4.6	8.1/2.4			
Prior MI	Emergent TAVR/Control	%	30.94/29.37	47.8/36.8	14.8/5.7		33.5/22.9	14.9/6.8	17.4/37.5		
Dyslipidemia	Emergent TAVR/Control	%		82.6/80.3	85.2/83.5			46/42.5			59.4/67.1

COPD	Emergent TAVR/Control	%	35.97/37.58	14.2/8.1	18.5/17.1	22.2/16.8	33.63/25.17	17.4/18.5		18.6/20.3	37.1/35.5
Peripheral artery disease	Emergent TAVR/Control	%	20.14/25.92	33.6/36.5	22.2/13.9	33.3/23.2	32.9/30.3	31/14.4	17.4/9.4	23/20.3	5.8/5.4
Atrial fib	Emergent TAVR/Control	%	47.48/47.08	48.6/41	44.4/24.7	51.9/44.8	50.7/40.6	35.6/20.2	30.4/46.9	23/19.1	31.9/25.4
Prior PCI	Emergent TAVR/Control	%		36.8/34.6			35.3/34.7	31/26.5	30.43/28.12		28.2/35.4
Prior CABG	Emergent TAVR/Control	%	26.62/23.54	29.2/25.9	22.2/20.3		25.3/28.3	10.3/7.2	8.7/6.3	12/14.3	22.6/24.4
Prior stroke	Emergent TAVR/Control	%	12.23/9.94	14.6/12.8	29.6/16.5	14.8/14.1	13.4/11.7	23/13.8	8.7/6.3	4.9/7	
Prior aortic valve intervention	Emergent TAVR/Control	%	10.79/14.25	16.2/7.2			17.8/5.7			15.9/16.4	17.2/10.6
STS score	Emergent TAVR/Control	Mean ± SD	6.925 ± 1.26/5.332 ± 1.12		9.7 ± 6.1/6.3 ± 4		12.3 ± 3/6.4 ± 1.5	14.2 ± 3.7/6.7 ± 1.3		5.79 ± 4.13/4.56 ± 2.69	
Hb	Emergent TAVR/Control	Mean ± SD			10.6 ± 1.5/12.2 ± 2		10.8 ± 0.8/11.9 ± 1	10.8 ± 1.9/11.2 ± 2			
LVEF	Emergent TAVR/Control	Mean ± SD	50 ± 5.78/56 ± 5.77			39.5 ± 15.4/52.4 ± 13.2	50.7 ± 6.6/57.7 ± 4.3	47.9 ± 16.1/58.5 ± 11.9			
Aortic valve area (cm^2)	Emergent TAVR/Control	Mean ± SD	0.625 ± 0.22/0.625 ± 0.22		0.59 ± 0.19/0.65 ± 0.17	0.7 ± 0.2/0.8 ± 0.3		0.56 ± 0.15/0.64 ± 0.17			
Mean AV pressure gradient (ΔP)	Emergent TAVR/Control	Mean ± SD	46.25 ± 4.91/44.25 ± 4.34	49.3 ± 18.3/48.5 ± 13.4	51 ± 18/51 ± 13	35.1 ± 16.8/38.4 ± 15.6		50.2 ± 20/50.5 ± 18			
Peak velocity	Emergent TAVR/Control	Mean ± SD	4.125 ± 0.29/4.15 ± 0.31				4 ± 0.3/4 ± 0.3	4.5 ± 0.84/4.6 ± 0.78			
Aoritc regurg	Emergent TAVR/Control	%		36.65/36.59		11.5/31.3	26.23/25.13	10.3/9.6	4.3/12.9		
Transfemoral approach	Emergent TAVR/Control	%	82.73/80.78	82.2/79.5	96.3/88	92.6/78.4	75.4/78.7	82.8/81.3			82.1/81.6
Transaxillary approach	Emergent TAVR/Control	%	7.2/6.91	12.6/11.2	3.7/12	7.4/8.3	0.1/0.3				
Transapical approach	Emergent TAVR/Control	%	9.35/10.15	0.4/4.9	3.7/12	–-/12.7	14.7/13.5				

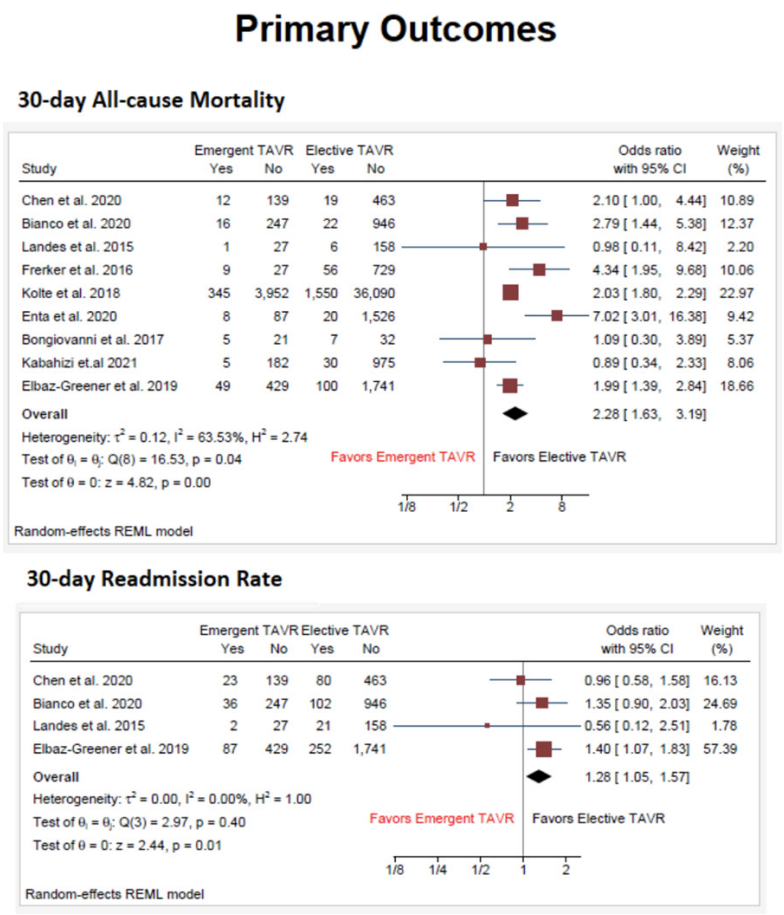

Figure 2. Forest plot for Primary Outcome (30-day mortality and 30-day readmissions).

Forest plots for renal outcomes are shown in **Figure 6**.

Univariate meta-regression

We performed univariate meta-regression against demographics (age, male and female sex), comorbidities (HTN, DM, HLD, CAD, smoking, BMI, atrial fibrillation, and baseline LVEF), prior procedures (prior PCI, prior CABG, and prior AV replacement), the surgical risk based on STS score %, and TAVR approach method (trans-apical, trans-femoral and trans-axillary). Univariate meta-regression results are presented in **Table 2** and their respective bubble plots are shown in Supplementary Figures 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11. For 30-day all-cause mortality, effect modification was seen with sex and hypertension. Length of stay was modified by several factors such as age, HTN, DM, smoking, CAD, and prior PCI. Vascular complications were modified by HTN and prior PCI status. Major bleeding was affected by the presence of atrial fibrillation (likely because of increased anti-coagulation) and transfemoral approach. AKI was modified by baseline LVEF and the trans-axillary approach of TAVR. Procedural success, paravalvular leak, pacemaker use, 30-day stroke, use of RRT, and 30-day readmissions were not modified by any of the variables studied.

Publication bias

Although we initially planned for a publication bias estimation using the methods explained above, however, since our final analysis included less than 10 studies, we did not perform a publication bias testing as per Cochrane Handbook recommendations [32].

Quality assessment

Since all the studies included in the final analysis were retrospective observational studies, their quality was assessed by the Newcastle-Ottawa Scale (**Table 3**).

Heterogeneity

Most of the outcomes studied showed low to moderate heterogeneity. The only outcomes showing high heterogeneity were the presence of AKI (I^2 = 76.36%) and the length of stay (I^2 = 99.97%). It was self-explicable. Firstly, as per the Cochrane Handbook of the Systematic Review and Meta-analysis, if the number of included studies is less than ten, it is not possible to differentiate between true heterogeneity and findings merely by chance [32]. Secondly, the high percentage of variability could be explained by the sampling error due to the retrospective nature of the studies involved.

Discussion

Herein we committed a systematic review and meta-analysis of 45,888 patients which demonstrated a significant relationship between emergency transcatheter aortic valve replacement (emergent TAVR) and an increase in

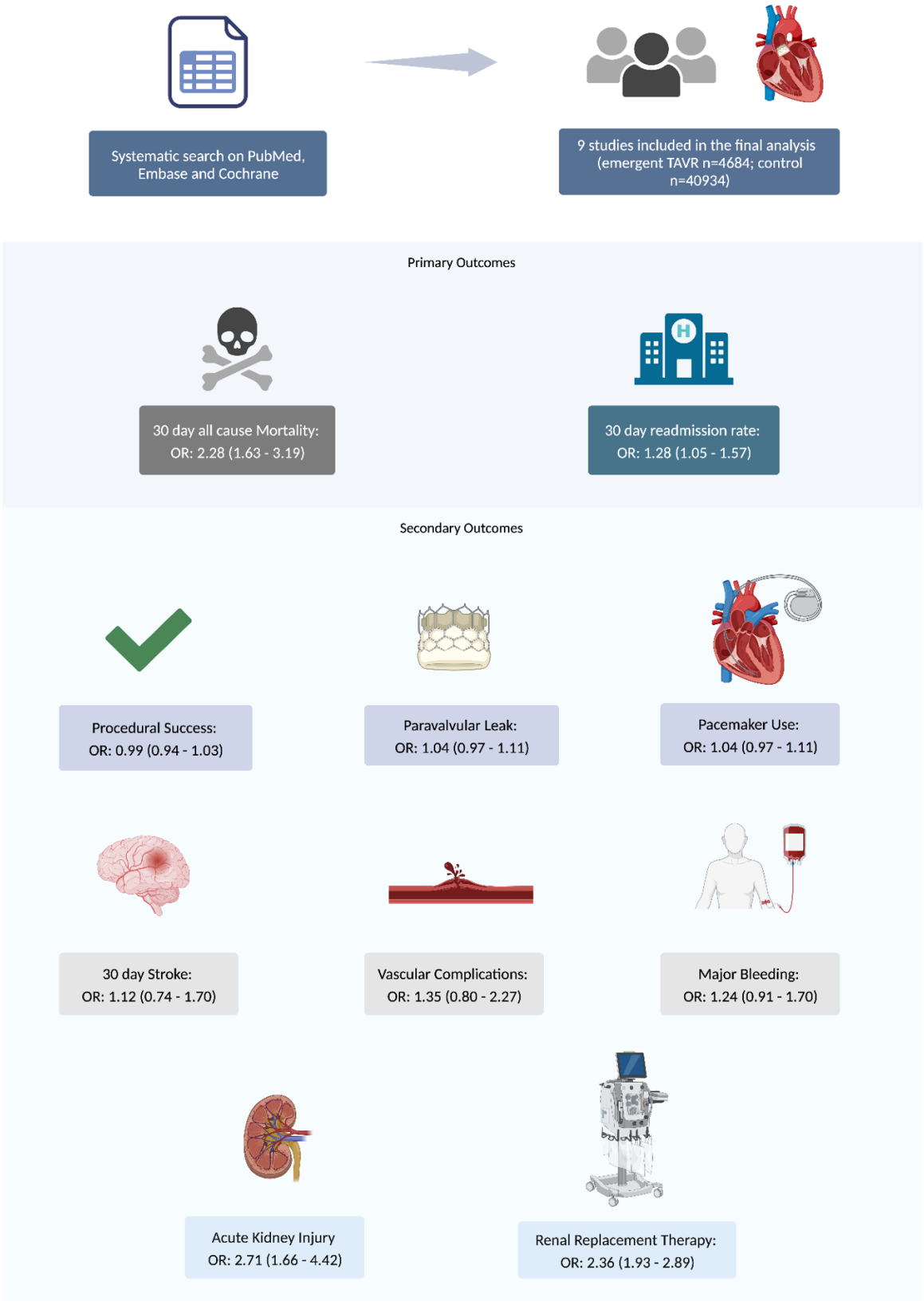

Figure 3. Graphical Abstract: Summarized primary and secondary outcomes of patients undergoing emergent TAVR or elective TAVR with or without BAV.

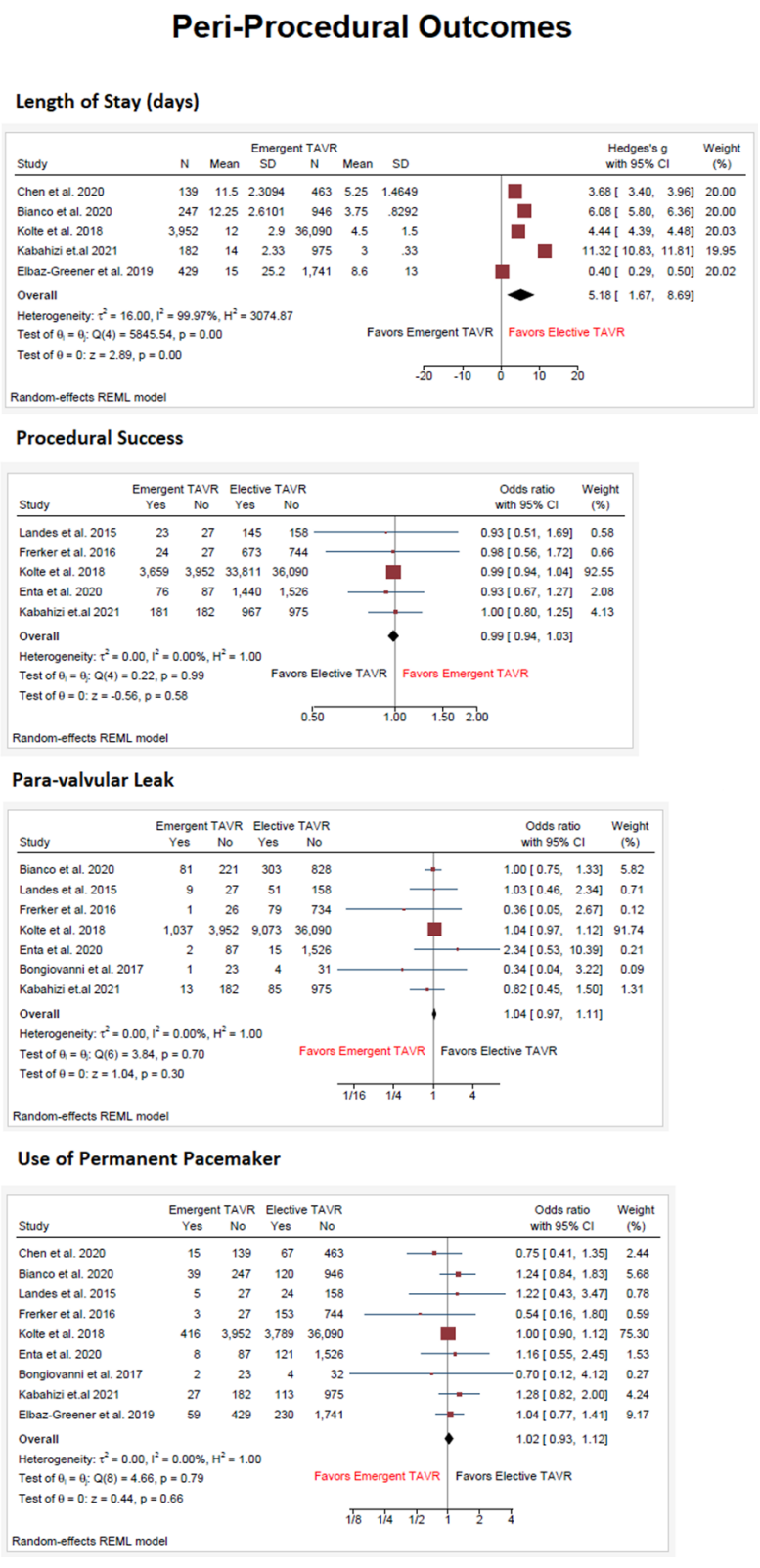

Figure 4. Peri-procedural outcomes of patients undergoing emergent TAVR or elective TAVR with or without BAV.

30-day mortality rate with increased length of hospital stay, elevated incidence of acute kidney injury, and use of renal replacement therapy. In addition, it demonstrated an enhanced trend of readmissions associated with emergent TAVR. However, most of these outcomes could be explained by the presence of baseline hemodynamic instability and cardiogenic shock present at baseline. Moreover, it is to be noted that mean LVEF and STS scores were worse in patients undergoing emergent TAVR compared to patients undergoing elective TAVR with or without BAV. In other words, there is a bias that exists with our study because the nature of the population requiring emergent TAVR has a higher burden of comorbidities. However, despite being high-risk, other outcomes such as major bleeding, stroke, procedural success, pacemaker implantation, and vascular complications, no discernible differences were found between the two groups. This shows that the TAVR procedure is safe even in emergent settings. Aparisi et al. conducted a systematic review that is congruent with our findings of major bleeding, stroke, and need for permanent pacemaker placement which is not significantly different between emergent TAVR and elective group. It also demonstrates a similar finding of reduced incidence of AKI in the elective group, which transcribes into decreased hospital stay and reduced need for the ini-

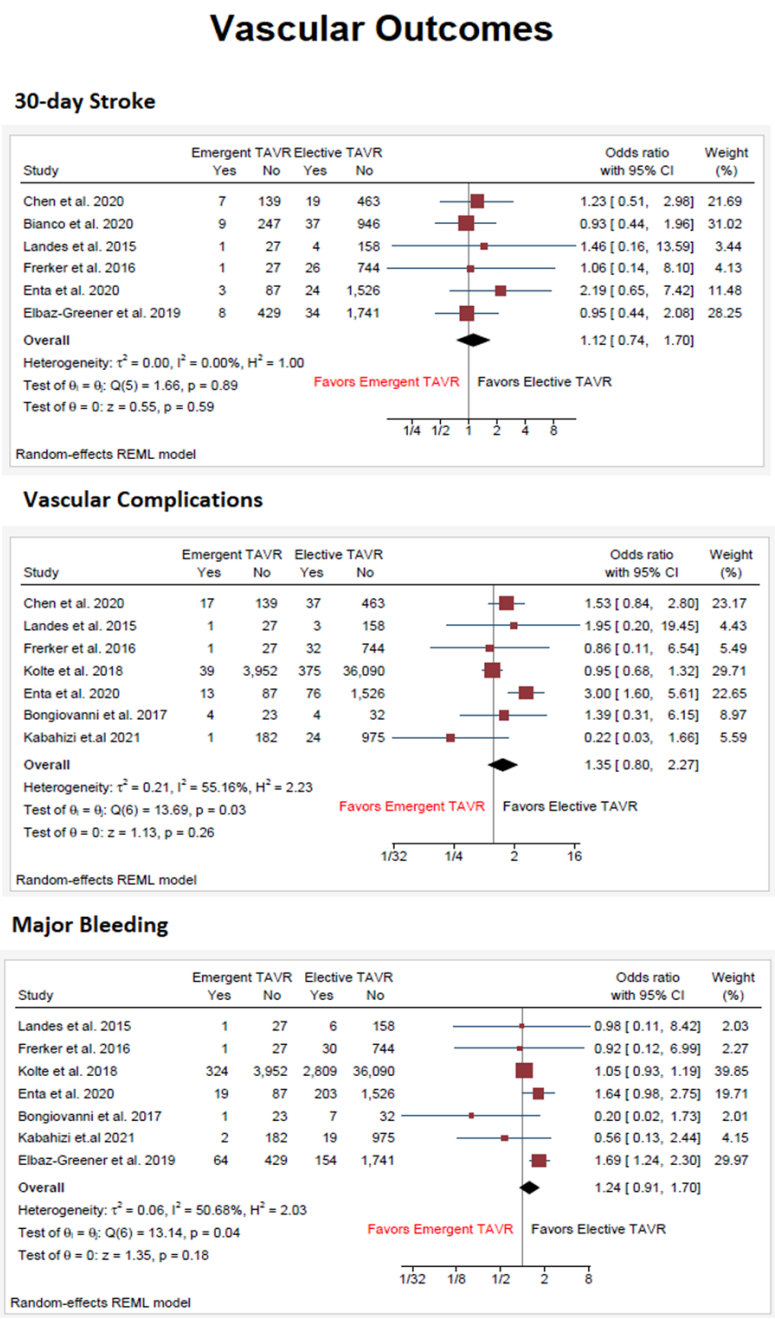

Figure 5. Vascular outcomes of patients undergoing emergent TAVR or elective TAVR with or without BAV.

tiation of dialysis as compared to our analysis which revealed an increased length of stay in the emergent arm [33]. There are considerable differences between the two studies; herein meta-analysis and systematic review include studies comparing eBAV with both elective TAVR and emergent TAVR, whereas Aparisi et al. meta-analysis only included studies with control groups made up of patients undergoing elective TAVR. This broadens the scope of our investigation because eBAV is also regarded as a treatment option for patients with severe aortic stenosis [34].

Patients with severe AS and cardiogenic shock have a higher 5-year all-cause mortality of 60% regardless of the nature of treatment and valvular therapy approach [6]. The emergent TAVR arm demonstrated an elevated 30-day mortality risk, prioritizing the determination of factors conditioning this increased mortality. The patients who required emergent TAVR had an elevated baseline interventional risk as compared to the elective procedures due to an exaggerated load of comorbidities and deterioration of LV function. 30-day all-cause mortality in patients undergoing elective TAVR was shown to be significantly lower than those undergoing emergent TAVR, according to Aparisi et al. [33]. These results conform with our study's findings. The high frequency of mortality in patients requiring emergent TAVR could partially be explained by significant baseline medical comorbidities in this patient population. Kabahizi et al. which is included in our final analysis performed a descriptive analysis on 1157 patients, of which 84% and 16% underwent elective and emergency TAVR, respectively. Their analysis revealed a similar 30-day mortality rate between the two groups [30]. Though this contrasts with our findings of increased 30-day mortality in emergency TAVR. These findings translate and transcribe into the utility, benefit, and importance of emergent TAVR in high-risk patients. Interestingly, as mentioned above, baseline characteristics

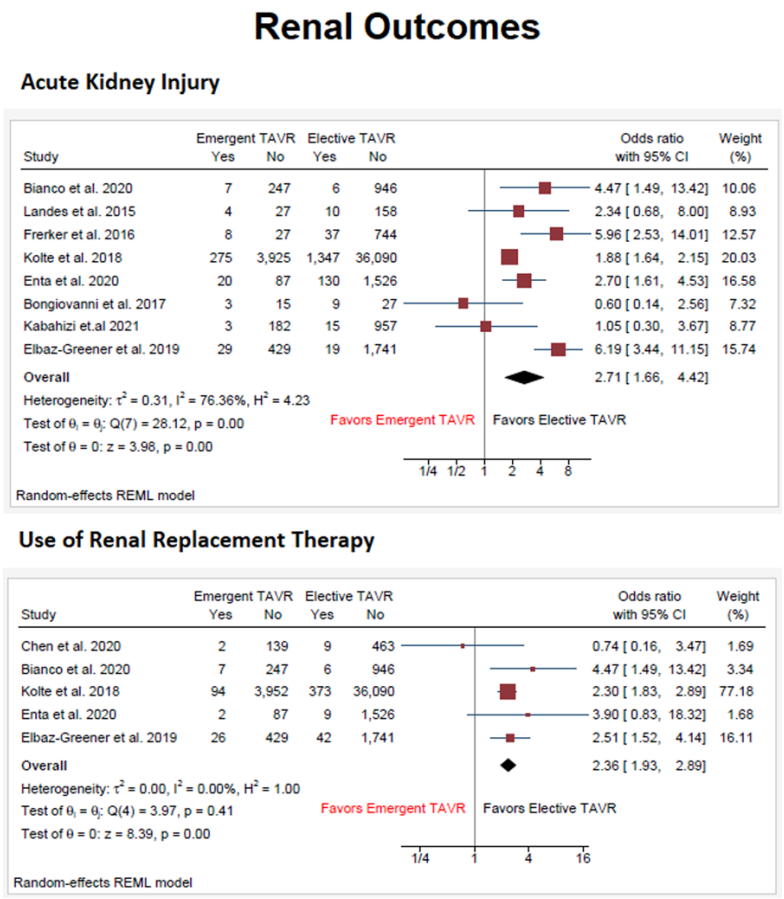

Figure 6. Renal outcomes of patients undergoing emergent TAVR or elective TAVR with or without BAV.

such as left ventricular systolic dysfunction, poor mobility, and severe liver disease are attributed to the worsening of mortality in other studies. However, once they are accounted for, the difference in mortality slims down to almost negligible between the two groups. Therefore, despite the presence of the aforementioned high-risk baseline characters in urgent TAVR, Kabahizi et al. analysis revealed no difference between the two arms [30]. In our analysis, we found a significant correlation between emergent TAVR and the development of AKI. This is congruent with prior studies of elective TAVR as well. This highlights the importance of multiple pre-operative and perioperative factors in the development of AKI. Ram et al. predicted that preoperative factors are baseline comorbidities that are present more in the emergent arm, which includes the presence of CKD, hypertension, higher STS score or EURO SCORE risk score, diabetes mellitus, peripheral arterial disease, or COPD [35]. Current literature reveals an inverse relationship between baseline GFR and the subsequent development of AKI [36]. Ram et al. also demonstrated that intraoperative risk factors contributed highly to the development of AKI, with the number of units of blood being transfused as the most common and important indicator. Some patients had granular casts in their urinalysis signifying possible ATN. Aeroembolisms and cholesterol embolization during transcatheter intervention are potential sources causing renal damage [35]. In addition, the use of nephrotoxic agents and intraoperative hypotension with rapid pacing during the deployment of balloon-expandable Edwards SAPIEN valves is also associated with AKI [37]. Additionally, our meta-analysis showed that emergent TAVR considerably increases the 30-day mortality rate, which is associated with a decline in renal function in emergency patients. In addition to that, sepsis which is predicted by AKI, is considered an independent prognostic factor for mortality. CKD, peripheral artery disease, diabetes mellitus, and deterioration of LV function are mainly risk factors for developing AKI [33]. To prevent the incidence of AKI a strategy can be employed which includes but is not limited to the idea of simple hydration with crystalloids and depending on the patient's hemodynamics and volume status; an aggressive diuresis with early supportive measures. Prophylactic dialysis which was investigated in TAVI patients who carry a high risk of developing AKI, may be beneficial in emergency settings [35, 38].

Our study indicates that the subjects in emergent TAVR had a higher 30-day mortality rate than the elective arm. Huang et al. did a study that corroborates with our findings of increased 30-day mortality in the emergent TAVR group in high-risk nonsurgical candidates [12]. Patients

Table 2. Univariate Meta-regression of potential effect modifiers for all study outcomes

	Meta-regression of potential effect modifiers																			
	30-day Mortality		30-day Readmissions		Length of Stay		Procedural Success		Para-valvular Leak		Pacemaker Use		Stroke		Vascular Complications		Major Bleeding		AKI		Use of RRT	
	Co-efficient	*p*-value	Co-efficient	*p*-value	Co-efficient	*p*-value	Co-efficient	*p*-value	Co-efficient	*p*-value	Co-efficient	*p*-value	Co-efficient	*p*-value	Co-efficient	*p*-value	Co-efficient	*p*-value	Co-efficient	*p*-value	Co-efficient	*p*-value
Demographics																						
Age	0.717	0.452	-0.086	0.251	-0.827	0.506	-0.004	0.898	0.085	0.206	-0.04	0.417	0.088	0.462	0.112	0.343	0.138	0.289	0.017	0.905	-0.119	0.353
Male	-0.041	0.002	-0.003	0.943	0.116	0.911	0.003	0.656	-0.028	0.192	-0.0038	0.773	-0.026	0.298	-0.02	0.209	-0.022	0.197	-0.025	0.218	-0.025	0.44
Female	0.0407	0.002	0.009	0.821	0.007	0.992	-0.003	0.655	0.028	0.194	0.006	0.641	0.024	0.331	0.02	0.22	0.023	0.192	0.025	0.214	0.029	0.356
Cormorbidity																						
HTN	-0.083	0.001	0.023	0.787	-1.4	< 0.001	0.004	0.702	-0.021	0.644	-0.003	0.871	-0.046	0.356	-0.066	0.03	-0.009	0.76	0.008	0.85	-0.028	0.56
DM	0.007	0.778	0.037	0.153	-0.349	0.001	-0.00011	0.986	0.0056	0.704	-0.0038	0.689	-0.042	0.259	0.045	0.52	0.02	0.379	0.053	0.063	0.011	0.682
HLD	-0.028	0.212	-0.009	0.649	*	*	*	*	-0.021	0.283	0.0048	0.625	-0.016	0.366	*	*	-0.001	0.927	0.004	0.793	0.01	0.68
CAD	-0.009	0.914	*	*	0.149	0.02	*	*	0.0249	0.175	0.007	0.89	-0.001	0.942	-0.006	0.722	0.005	0.841	-0.004	0.883	-0.0005	0.964
Smoking	0.036	0.833	*	*	0.472	< 0.001	*	*	-0.026	0.778	0.0778	0.172	-0.073	0.51	0.046	0.93	*	*	0.242	0.184	0.26	0.1
BMI	-0.168	0.068	*	*	*	*	*	*	-0.154	0.357	-0.018	0.856	-0.14	0.247	-0.152	0.098	*	*	0.128	0.128	-0.08	0.8
Atrial Fibrillation	0.012	0.533	-0.01	0.373	-0.129	0.474	0.0038	0.928	0.005	0.637	-0.0069	0.303	-0.008	0.733	-0.01	0.742	-0.022	0.006	0.013	0.647	-0.008	0.582
LVEF	-0.063	0.526	*	*	*	*	0.0033	0.922	0.13	0.363	0.0805	0.257	0.053	0.73	0.0382	0.808	-0.002	0.982	-0.146	0.006	0.41	0.689
Prior Procedures																						
Prior PCI	-0.054	0.542	*	*	1.39	< 0.001	*	*	-0.044	0.631	-0.002	0.945	-0.09	0.352	-0.17	0.002	-0.065	0.247	0.07	0.616	-0.029	0.687
Prior CABG	-0.004	0.881	0.031	0.715	-0.473	0.098	0.0012	0.841	0.008	0.659	-0.0097	0.444	-0.044	0.246	-0.035	0.18	0.009	0.772	0.043	0.231	-0.02	0.607
Prior AV Replacement	-0.0994	0.22	0.05	0.739	1.1	0.296	*	*	-0.054	0.444	0.035	0.429	-0.002	0.993	-0.325	0.247	-0.064	0.78	-0.13	0.631	-0.013	0.946
Surgical Risk																						
STS Score	0.247	0.084	*	*	-1.168	0.444	-0.005	0.853	0.063	0.381	-0.018	0.703	0.133	0.452	0.212	0.276	0.233	0.1	0.167	0.177	0.366	0.115
TAVR Approach																						
Transfemoral	0.034	0.514	-0.07	0.282	-0.405	0.556	-0.005	0.728	-0.0046	0.835	0.0047	0.823	0.035	0.725	0.068	0.334	0.076	0.006	0.035	0.522	0.0203	0.697
Transaxillary	0.0331	0.161	0.08	0.228	0.123	0.462	-0.004	0.878	-0.004	0.72	0.0094	0.704	-0.058	0.614	0.063	0.183	-0.0142	0.886	0.092	0.007	0.036	0.781
Transapical	-0.0161	0.672	-0.053	0.241	-0.161	0.236	0.009	0.839	0.003	0.778	-0.0189	0.428	0.0322	0.656	-0.11	0.148	0.0168	0.922	-0.04	0.603	-0.063	0.605

P < 0.05 shows that our study had no effect modifiers in our studied outcomes.

Table 3. Newcastle Ottawa Scale (NOS) Assessment for included studies

Study	NOS Score
Chen et al. 2020 [22]	7/9
Bianco et al. 2020 [21]	7/9
Landes et al. 2015 [27]	7/9
Frerker et al. 2016 [25]	7/9
Kolte et al. 2018 [11]	7/9
Enta et al. 2020 [24]	7/9
Bongiovanni et al. 2017 [7]	9/9
Kabahizi et al. 2021 [26]	7/9
Elbaz-Greener et al. 2019 [23]	7/9

in emergency settings are much more likely to experience cardiac arrest due to ventricular tachycardia and ventricular fibrillation as well as increased bleeding complications; mechanical circulatory support devices (MCS) used during emergent TAVR have been strongly associated with worse short- and long-term outcomes [39]. Huang et al. demonstrated that the use of MCS in high-risk patients as a bailout strategy (e.g., in cardiac arrest and CPR during the procedure) has the worst outcomes. However, the use of MCS before the procedure was associated with decreased mortality; highlighting that early hemodynamic monitoring and stabilization can provide better outcomes [12].

Furthermore, we demonstrated that post-procedural outcomes such as stroke, perioperative myocardial infarction, and paravalvular leak were not significantly different between the two groups. Kolte et al. reviewed the STS registry for patients who underwent emergent TAVR and revealed similar findings between the two groups in accordance with our results [15].

Mack et al. randomized trial revealed favorable outcomes when urgent TAVR was compared to medical therapy alone [40]. Therefore urgent TAVR provides an excellent and novel approach for patients with severe aortic stenosis and higher comorbidity burden, which otherwise would lead to increased morbidity and mortality.

Limitations

Our study has the following limitations. Included studies are retrospective since only one multicenter randomized study could be found on the present topic. Second, because of the emergent nature of the procedure and its implications in the population which has a higher burden of baseline comorbidities makes it is difficult to extrapolate it to other populations. Third, because the inclusion criteria for patients who were eligible for urgent TAVR varied between studies, there may be heterogeneity in the results. Despite the visualization of worse outcomes in this study, there is a need to do further research to explore the utility of emergent TAVR in non-surgical high-risk patients. As described above, there exists a visible bias due to the nature of the procedure; emergent patients include debilitated patients who have high baseline comorbidities that increase the apparent mortality rate and depict worse outcomes. Therefore, more studies are required to delineate the implication of baseline comorbidities on the emergent nature of the procedure to accurately assess the utility and benefits of this procedure, especially in high-risk populations. This study also implies that pre-procedural stabilization of subjects can potentially improve outcomes, decrease mortality, and improve vascular complications, the length of stay, and the incidence of AKI. Future studies can be conducted by increasing our inclusion criteria, improving baseline comorbidities, incorporating timely MCS if required, and then studying the effects on mortality and other outcomes on a prospective randomized trial to better risk stratify emergent TAVR. Regarding effect modifiers, we could not perform multivariate meta-regression due to the limitations of the data. Further studies are warranted to further elucidate the effects of potential effect modifiers of our study.

Conclusions

Emergent TAVR is a promising procedure for severely debilitated, surgically high-risk patients with post-operative outcomes similar to the patients electively treated. Recognition of comorbidities and their earlier optimization can lead to decreased mortality and promising outcomes. Further prospective cohort studies are required to validate our findings.

Disclosure of conflict of interest

None.

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PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	3
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	4
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	5
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	5
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	5
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	5
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	5
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	5-6
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	5-6
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	5-6
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	6
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	6
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	6
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	6
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	6
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	6
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	6
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	6
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	6
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	7
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	-
Study characteristics	17	Cite each included study and present its characteristics.	7
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	7
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	-
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	7
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	7
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	9
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	9
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	9
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	9
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	10
	23b	Discuss any limitations of the evidence included in the review.	10
	23c	Discuss any limitations of the review processes used.	-
	23d	Discuss implications of the results for practice, policy, and future research.	-
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	-
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	-
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	-
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	-
Competing interests	26	Declare any competing interests of review authors.	-
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	-

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71
For more information, visit: http://www.prisma-statement.org/

Supplementary File 1. Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) checklist.

AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both

1. Did the research questions and inclusion criteria for the review include the components of PICO?

For Yes:
- ☑ Population
- ☑ Intervention
- ☑ Comparator group
- ☑ Outcome

Optional (recommended)
- ☐ Timeframe for follow-up

☑ Yes
☐ No

2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?

For Partial Yes:
The authors state that they had a written protocol or guide that included ALL the following:
- ☑ review question(s)
- ☑ a search strategy
- ☑ inclusion/exclusion criteria
- ☑ a risk of bias assessment

For Yes:
As for partial yes, plus the protocol should be registered and should also have specified:
- ☐ a meta-analysis/synthesis plan, if appropriate, *and*
- ☐ a plan for investigating causes of heterogeneity
- ☐ justification for any deviations from the protocol

☐ Yes
☑ Partial Yes
☐ No

3. Did the review authors explain their selection of the study designs for inclusion in the review?

For Yes, the review should satisfy ONE of the following:
- ☑ *Explanation for* including only RCTs
- ☐ OR *Explanation for* including only NRSI
- ☐ OR *Explanation for* including both RCTs and NRSI

☑ Yes
☐ No

4. Did the review authors use a comprehensive literature search strategy?

For Partial Yes (all the following):
- ☑ searched at least 2 databases (relevant to research question)
- ☑ provided key word and/or search strategy
- ☑ justified publication restrictions (e.g. language)

For Yes, should also have (all the following):
- ☐ searched the reference lists / bibliographies of included studies
- ☐ searched trial/study registries
- ☐ included/consulted content experts in the field
- ☐ where relevant, searched for grey literature
- ☐ conducted search within 24 months of completion of the review

☐ Yes
☑ Partial Yes
☐ No

5. Did the review authors perform study selection in duplicate?

For Yes, either ONE of the following:
- ☑ at least two reviewers independently agreed on selection of eligible studies and achieved consensus on which studies to include
- ☐ OR two reviewers selected a sample of eligible studies and achieved good agreement (at least 80 percent), with the remainder selected by one reviewer.

☑ Yes
☐ No

6. Did the review authors perform data extraction in duplicate?

For Yes, either ONE of the following:
- ☑ at least two reviewers achieved consensus on which data to extract from included studies
- ☐ OR two reviewers extracted data from a sample of eligible studies and achieved good agreement (at least 80 percent), with the remainder extracted by one reviewer.

☑ Yes
☐ No

7. Did the review authors provide a list of excluded studies and justify the exclusions?

For Partial Yes:	For Yes, must also have:	
☑ provided a list of all potentially relevant studies that were read in full-text form but excluded from the review	☐ Justified the exclusion from the review of each potentially relevant study	☐ Yes ☑ Partial Yes ☐ No

8. Did the review authors describe the included studies in adequate detail?

For Partial Yes (ALL the following):	For Yes, should also have ALL the following:	
☑ described populations ☑ described interventions ☑ described comparators ☑ described outcomes ☑ described research designs	☐ described population in detail ☐ described intervention in detail (including doses where relevant) ☐ described comparator in detail (including doses where relevant) ☐ described study's setting ☐ timeframe for follow-up	☐ Yes ☑ Partial Yes ☐ No

9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?

RCTs		
For Partial Yes, must have assessed RoB from	For Yes, must also have assessed RoB from:	
☐ unconcealed allocation, *and* ☐ lack of blinding of patients and assessors when assessing outcomes (unnecessary for objective outcomes such as all-cause mortality)	☑ allocation sequence that was not truly random, *and* ☑ selection of the reported result from among multiple measurements or analyses of a specified outcome	☑ Yes ☐ Partial Yes ☐ No ☐ Includes only NRSI
NRSI		
For Partial Yes, must have assessed RoB:	For Yes, must also have assessed RoB:	
☐ from confounding, *and* ☐ from selection bias	☑ methods used to ascertain exposures and outcomes, *and* ☑ selection of the reported result from among multiple measurements or analyses of a specified outcome	☑ Yes ☐ Partial Yes ☐ No ☐ Includes only RCTs

10. Did the review authors report on the sources of funding for the studies included in the review?

For Yes	
☑ Must have reported on the sources of funding for individual studies included in the review. Note: Reporting that the reviewers looked for this information but it was not reported by study authors also qualifies	☑ Yes ☐ No

11. If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?

RCTs

For Yes:

- ☑ The authors justified combining the data in a meta-analysis
  - ☑ AND they used an appropriate weighted technique to combine study results and adjusted for heterogeneity if present.
  - ☑ AND investigated the causes of any heterogeneity

☑ Yes ☐ No ☐ No meta-analysis conducted

For NRSI

For Yes:

- ☑ The authors justified combining the data in a meta-analysis
  - ☑ AND they used an appropriate weighted technique to combine study results, adjusting for heterogeneity if present
  - ☑ AND they statistically combined effect estimates from NRSI that were adjusted for confounding, rather than combining raw data, or justified combining raw data when adjusted effect estimates were not available
  - ☐ AND they reported separate summary estimates for RCTs and NRSI separately when both were included in the review

☐ Yes ☐ No ☐ No meta-analysis conducted

12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?

For Yes:

- ☐ included only low risk of bias RCTs
- ☑ OR, if the pooled estimate was based on RCTs and/or NRSI at variable RoB, the authors performed analyses to investigate possible impact of RoB on summary estimates of effect.

☑ Yes ☐ No ☐ No meta-analysis conducted

13. Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?

For Yes:

- ☑ included only low risk of bias RCTs
- ☐ OR, if RCTs with moderate or high RoB, or NRSI were included the review provided a discussion of the likely impact of RoB on the results

☑ Yes ☐ No

14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?

For Yes:

- ☐ There was no significant heterogeneity in the results
- ☑ OR if heterogeneity was present the authors performed an investigation of sources of any heterogeneity in the results and discussed the impact of this on the results of the review

☑ Yes ☐ No

15. If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?

For Yes:

- ☑ performed graphical or statistical tests for publication bias and discussed the likelihood and magnitude of impact of publication bias

☑ Yes ☐ No ☐ No meta-analysis conducted

16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?

For Yes:

- ☑ The authors reported no competing interests OR
- ☐ The authors described their funding sources and how they managed potential conflicts of interest

☑ Yes ☐ No

To cite this tool: Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, Moher D, Tugwell P, Welch V, Kristjansson E, Henry DA. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ. 2017 Sep 21;358:j4008.

Supplementary File 2. AMSTAR-2 (Assessing the methodological quality of systematic reviews-2) Guidelines checklist.

Supplementary File 3. Research Question, PICO, MeSH, Keywords, and Search Strategy

Research Question:

Comparison of emergent Transcatheter Aortic Valve Replacement against Elective Transcatheter Aortic Valve Replacement with or without emergent Baloon Aortic Valvuloplasty

PICO:

Population: Severe Aortic Stenosis

Intervention: Emergent Transcatheter Aortic Valve Replacement

Comparison: Elective Transcatheter Aortic Valve Replacement with or without emergent Baloon Aortic Valvuloplasty

Outcome:

1) **Primary outcomes** studied include *30-day mortality* and 3*0-day readmission rate*.

2) **Secondary outcomes** which were further divided into (a) peri-procedural outcomes, i.e., length of stay (days), procedural success, paravalvular leak, and pacemaker use, (b) vascular outcomes, i.e., 30-day stroke, vascular complications (includes vessel dissection, rupture, access site hematoma, and the formation of pseudoaneurysms), and major bleeding (any bleeding requiring transfusion), and (c) renal outcomes, i.e., acute kidney injury (AKI) and use of renal replacement therapy (RRT).

Study type: Odds ratio to compare binary outcomes and Hedges' g to compare continuous outcomes meta-analyses.

MeSH Terms & Keywords:

Aortic Stenosis

Cardiogenic Shock

Transcatheter Aortic Valve Replacement

Balloon Aortic Valvuloplasty

Mortality

Stroke

Pacemaker placement

Renal replacement therapy

Acute kidney injury

Vascular complications

Treatment Outcome

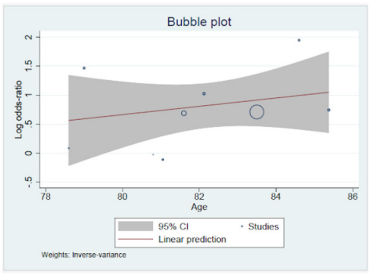
Humans

Mesh Terms Table

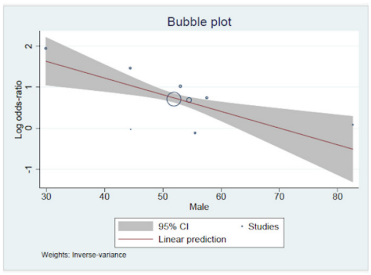
Population	Intervention	Comparison	Outcome	Study Type
"Shock, Cardiogenic"[Mesh] AND "Aortic Valve Stenosis"[Mesh]	"Emergency Treatment"[Mesh] AND "Transcatheter Aortic Valve Replacement"[Mesh]			
Aortic Valve Stenoses	Emergency Therapies			
Aortic Stenosis	Emergency Therapy			
Stenoses, Aortic	Emergency Treatments			
Aortic Valve Stenoses	Transcatheter Aortic Valve Implantation			

Bubble Plots for Meta Regression for 30-day Mortality

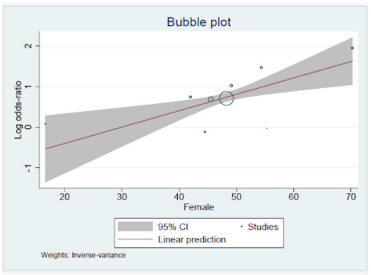
Age



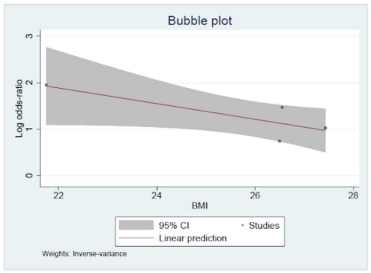
Male



Female



BMI



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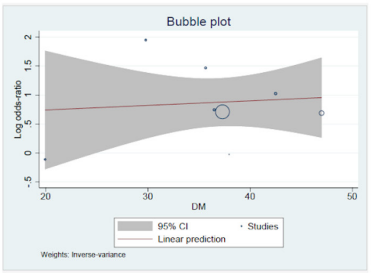
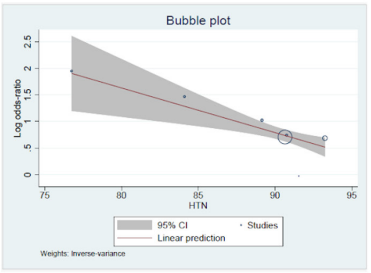
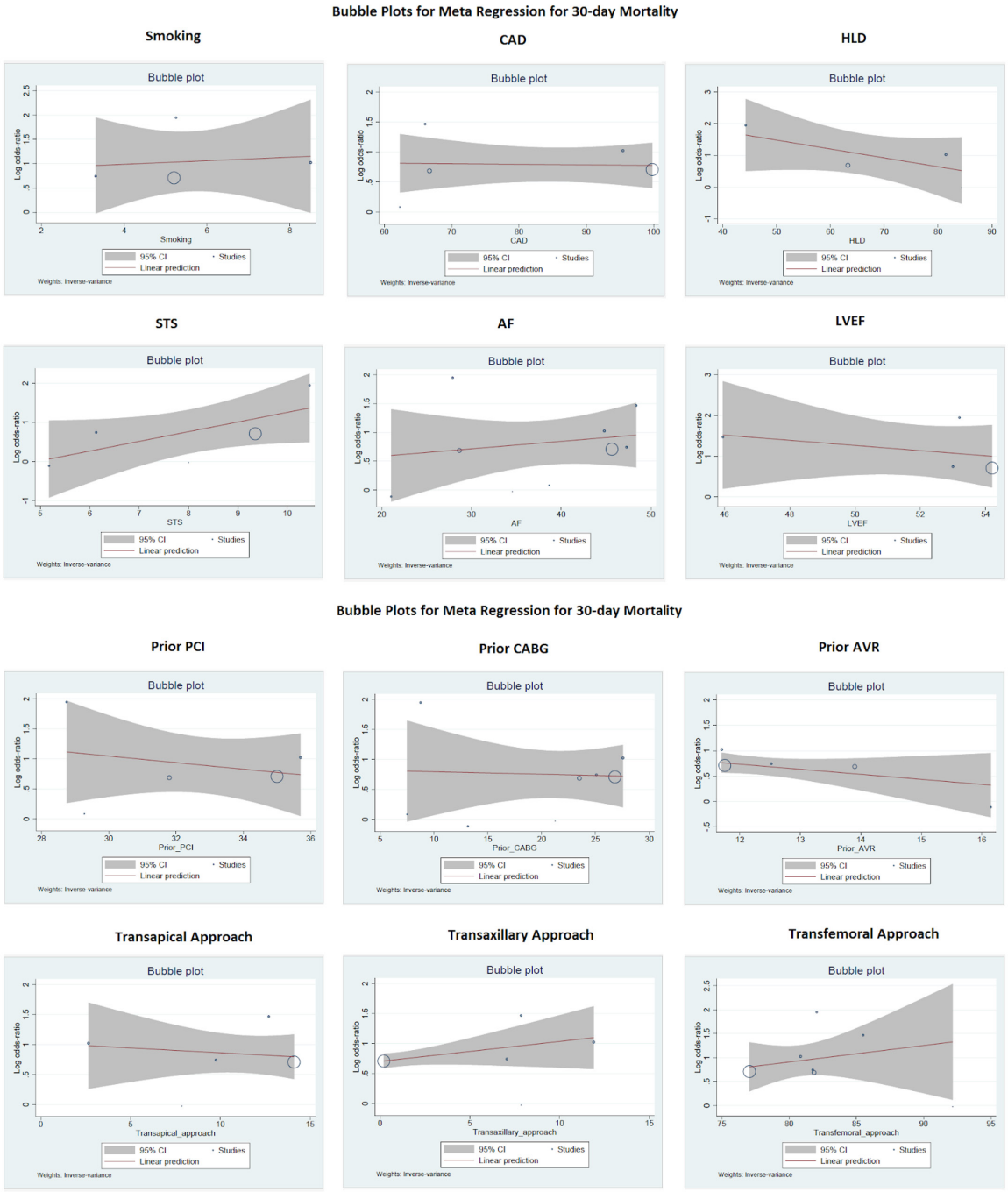
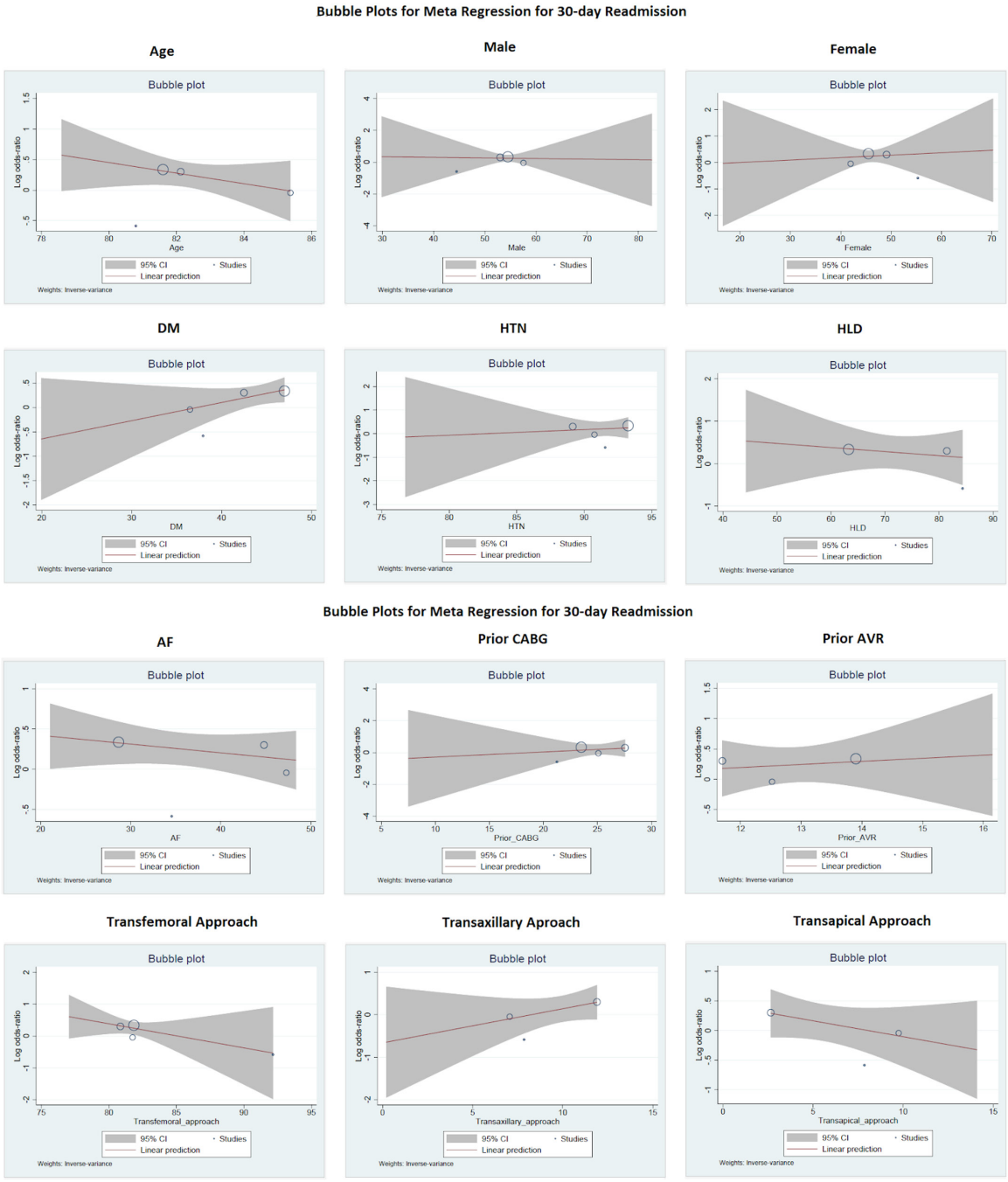


Hypertension

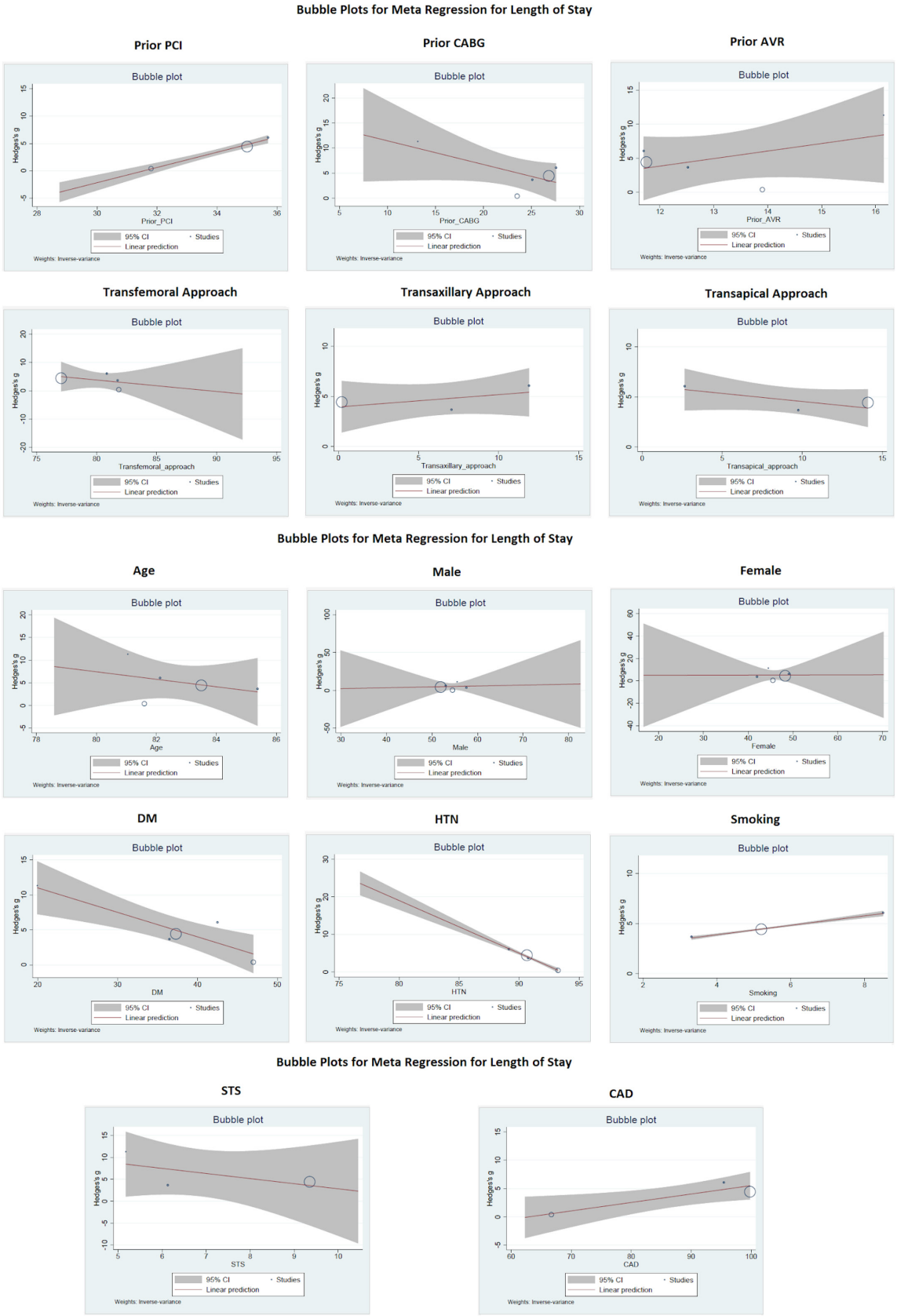




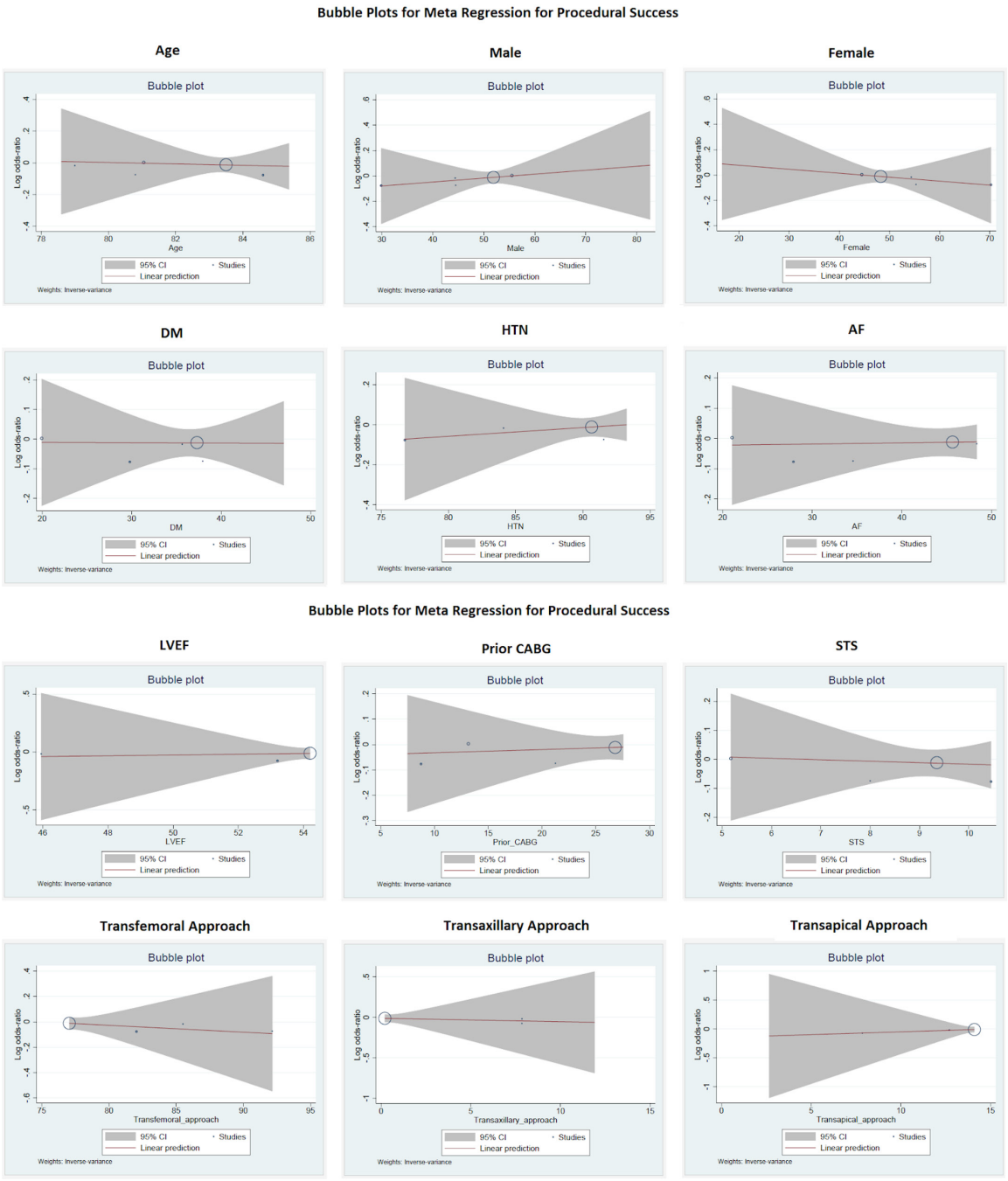
Supplementary Figure 1. Bubble plots of 30-day Mortality.



Supplementary Figure 2. Bubble plots for 30-day readmission rate.



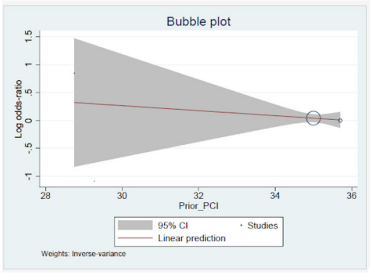
Supplementary Figure 3. Bubble plots of Length of Stay.



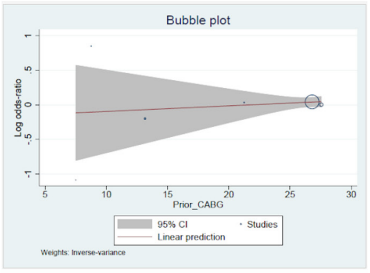
Supplementary Figure 4. Bubble plots of Procedural Success.

Bubble Plots for Meta Regression for Para-valvular Leak

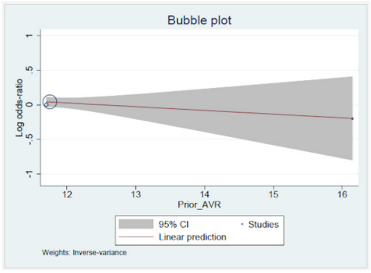
Prior PCI



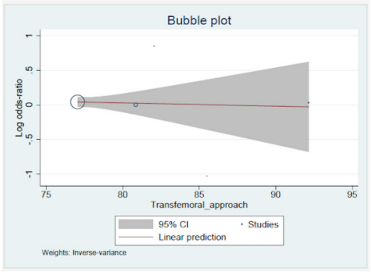
Prior CABG



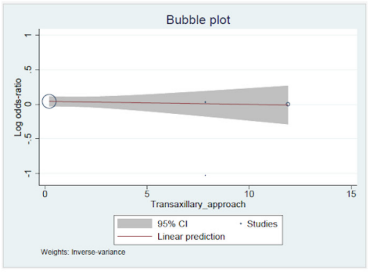
Prior AVR



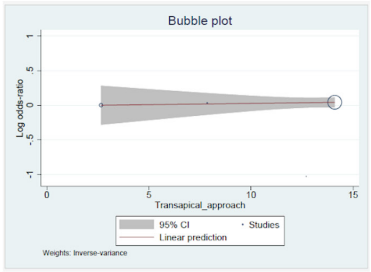
Transfemoral Approach



Transaxillary Approach

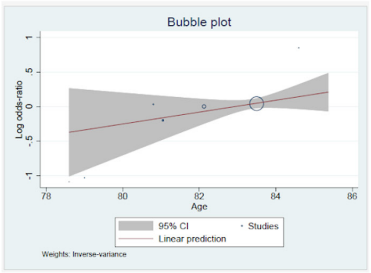


Transapical Approach

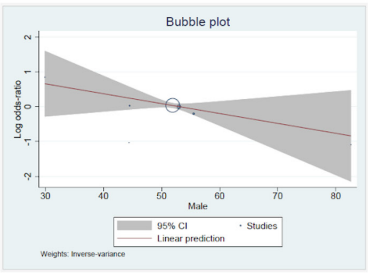


Bubble Plots for Meta Regression for Para-valvular Leak

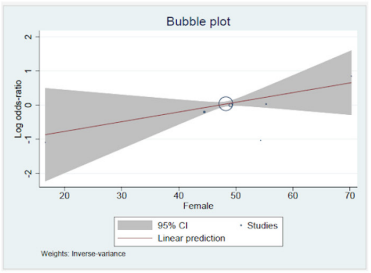
Age



Male



Female



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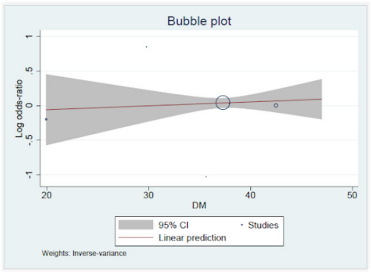

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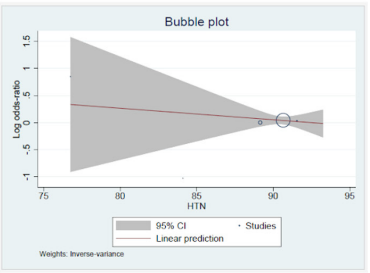

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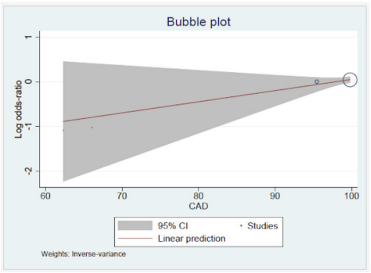
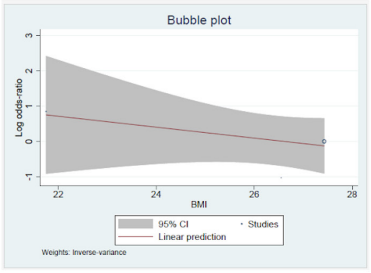
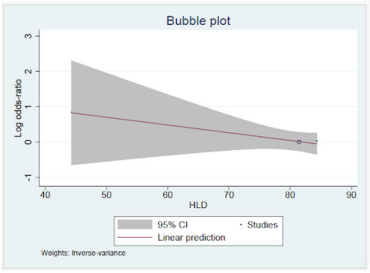


Bubble Plot for Meta Regression for Para-valvular Leak

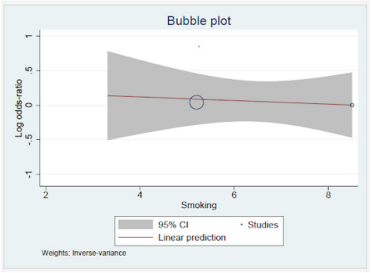
BMI

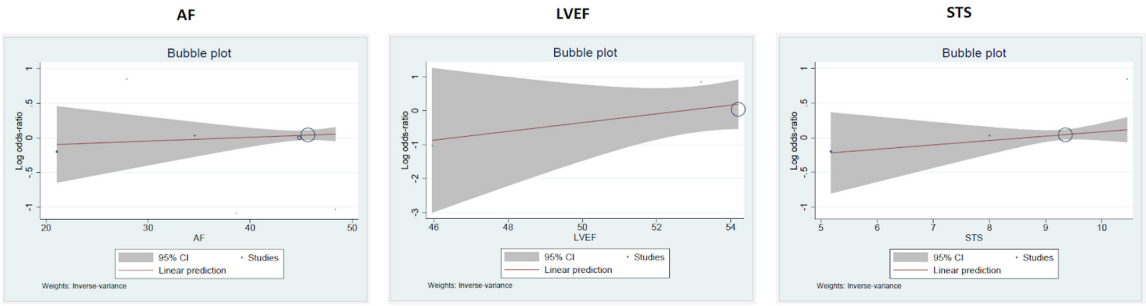


HLD

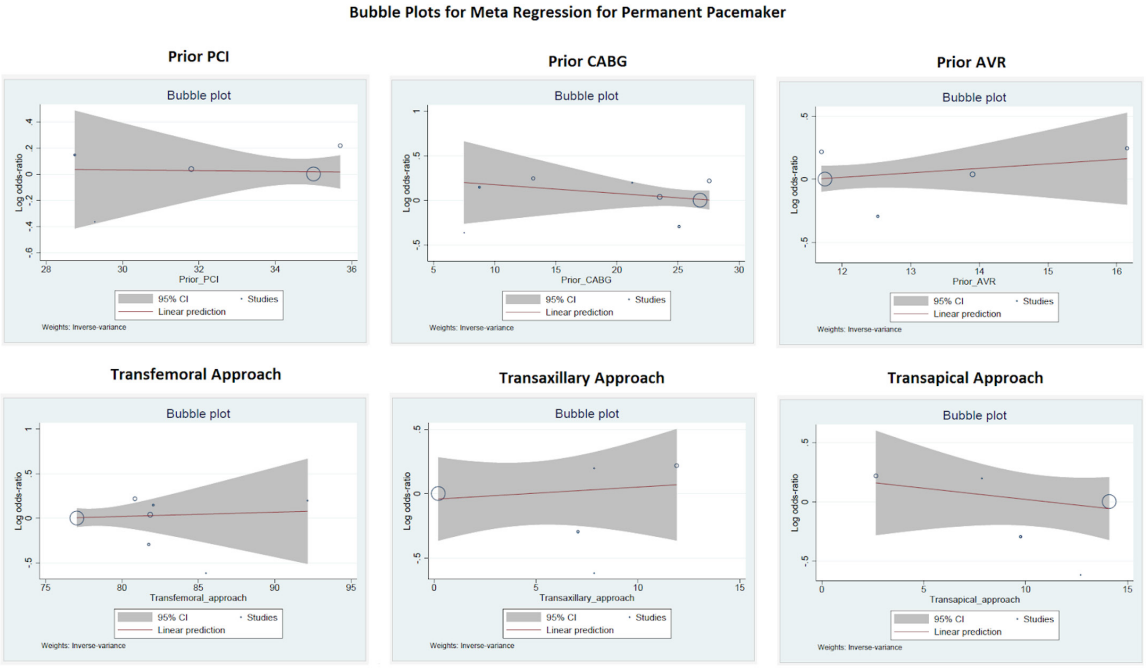


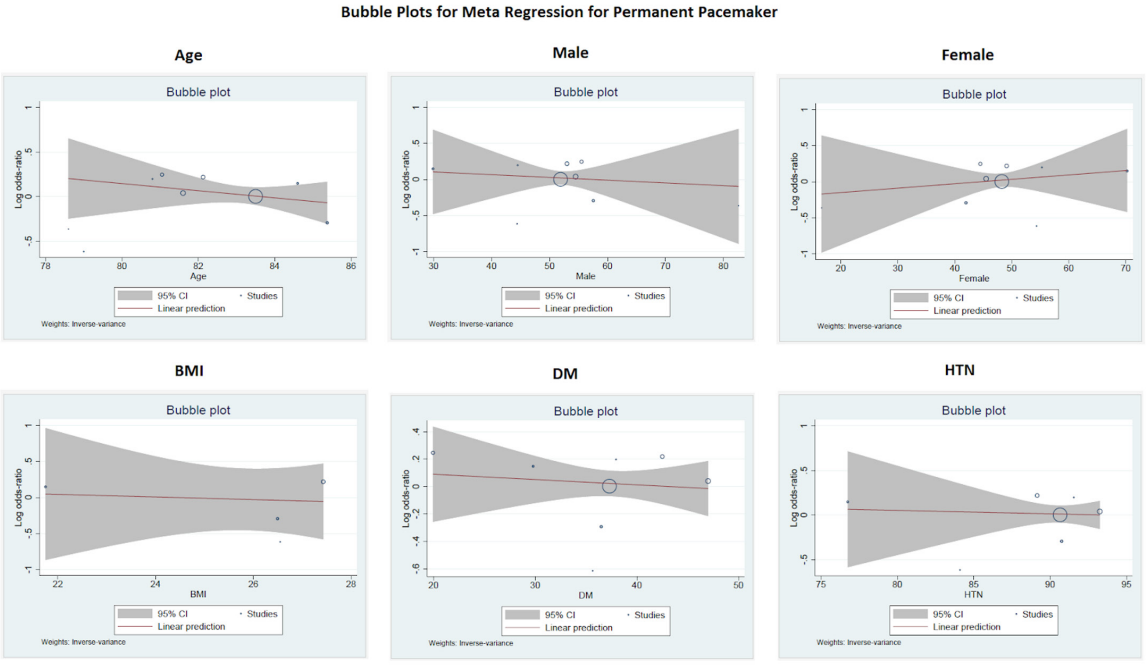
Smoking

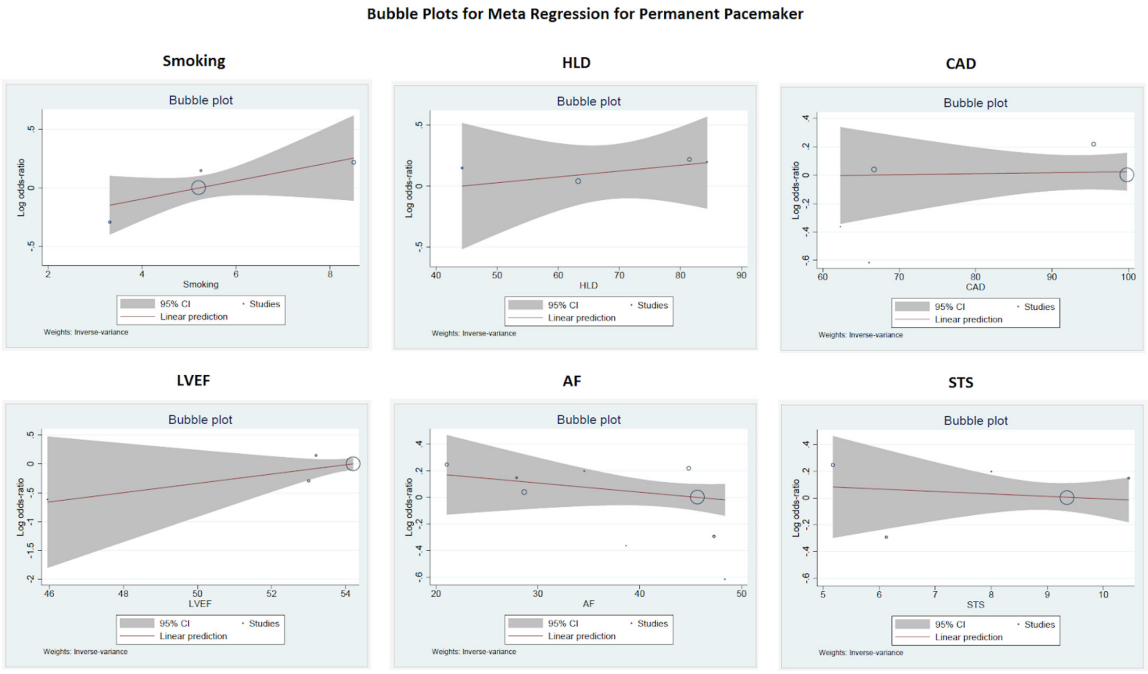




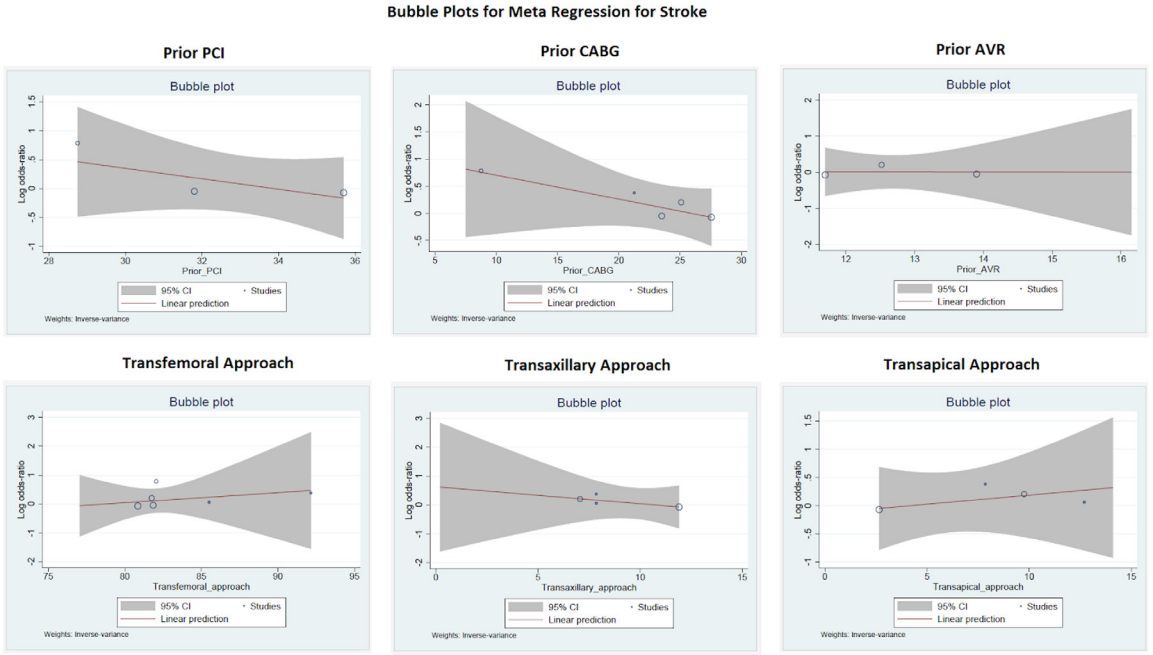
Supplementary Figure 5. Bubble plots of Paravalvular Leak.

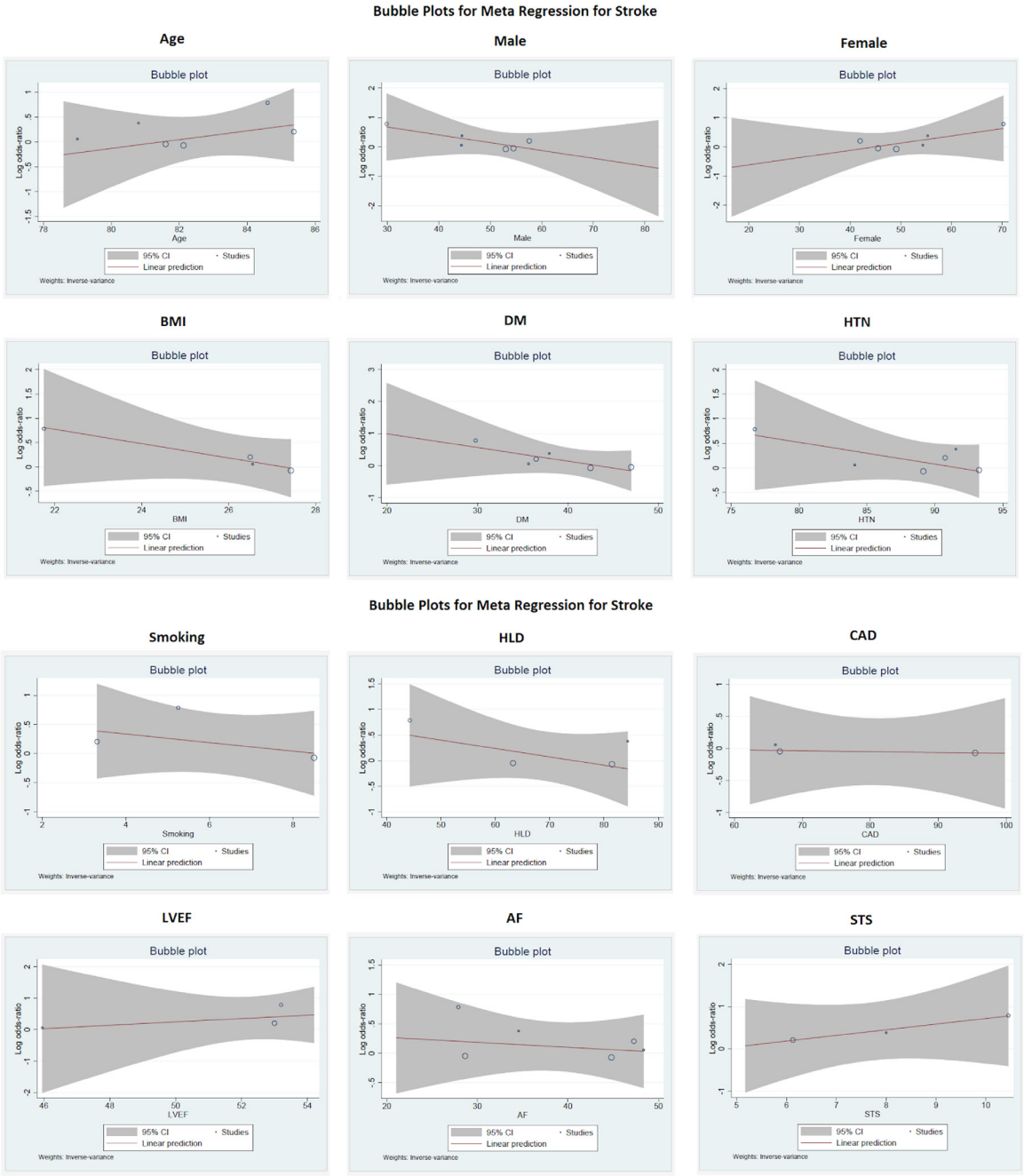






Supplementary Figure 6. Bubble plots of Pacemaker Use.

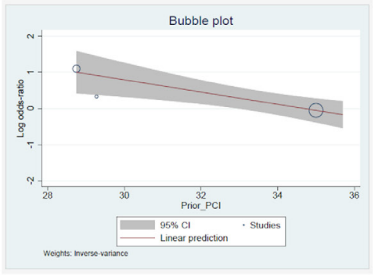




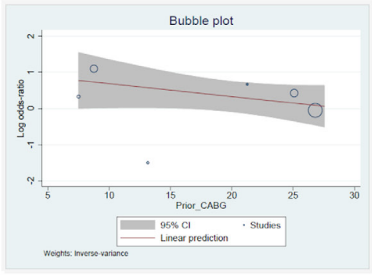
Supplementary Figure 7. Bubble plots of 30-day Stroke.

Bubble Plots for Meta Regression for Vascular Complication

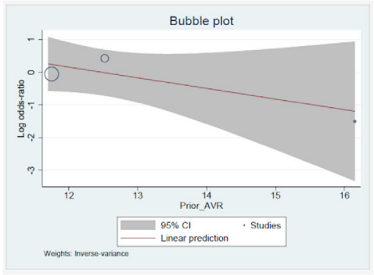
Prior PCI



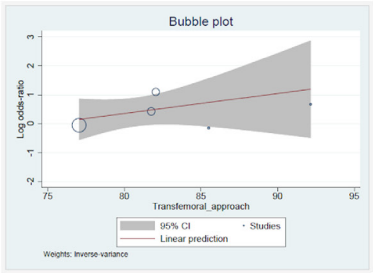
Prior CABG



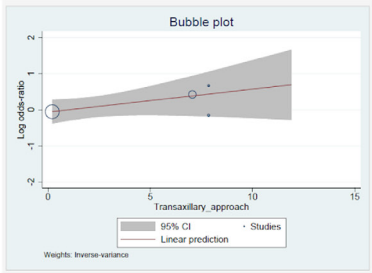
Prior AVR



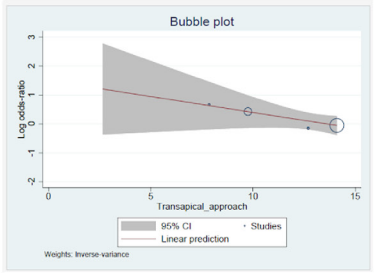
Transfemoral Approach



Transaxillary Approach

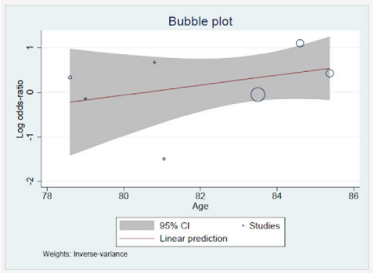


Transapical Approach

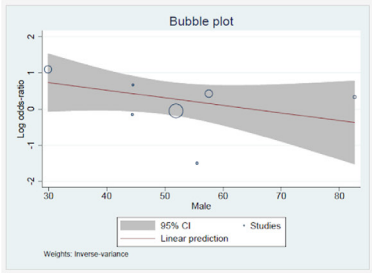


Bubble Plots for Meta Regression for Vascular Complication

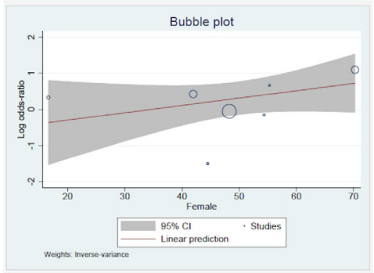
Age



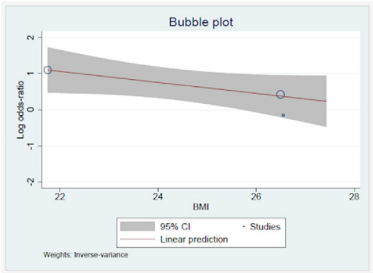
Male



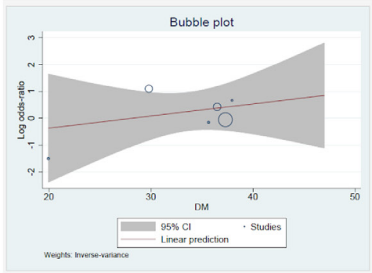
Female



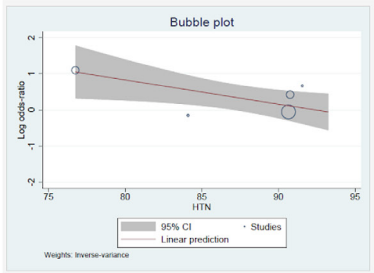
BMI

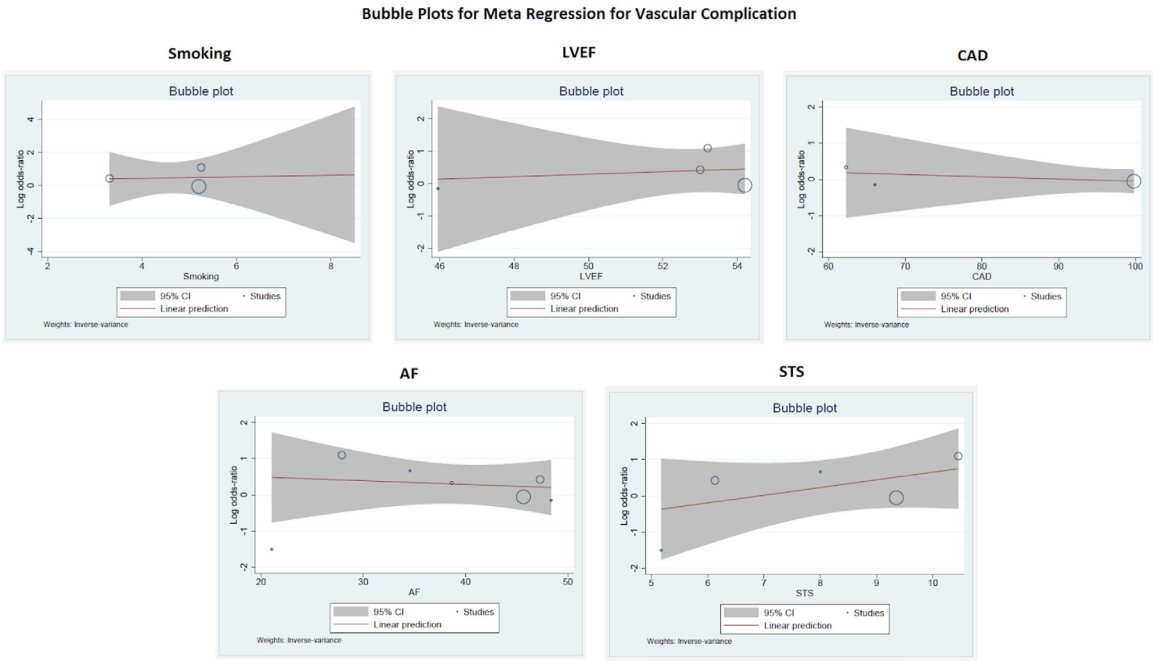


DM

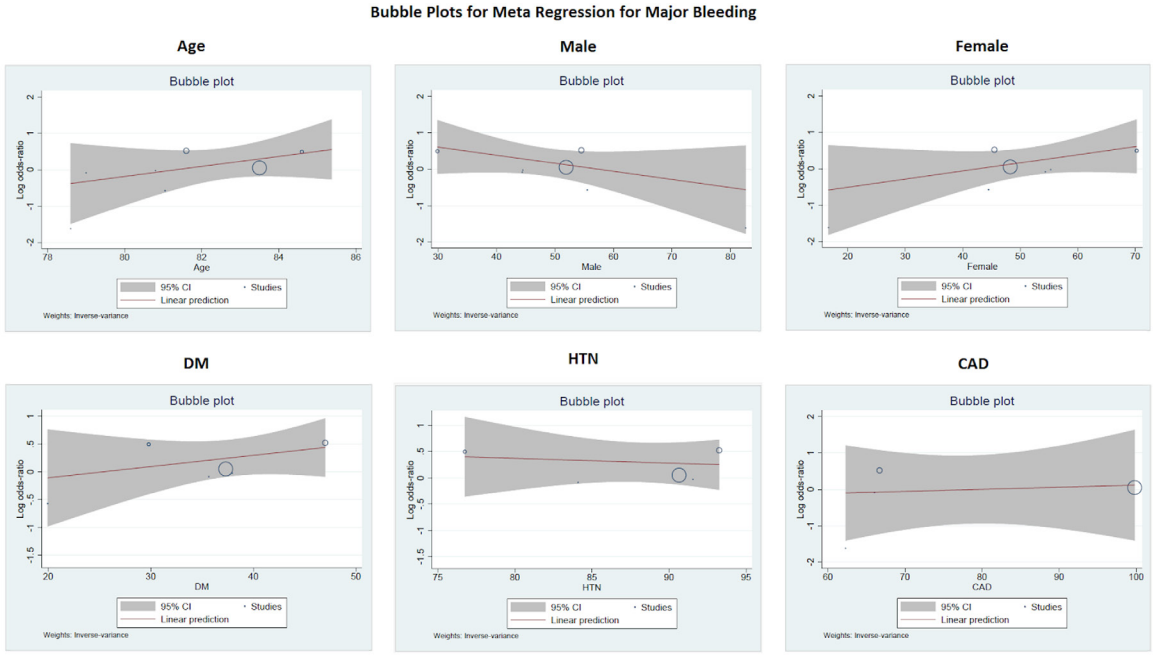


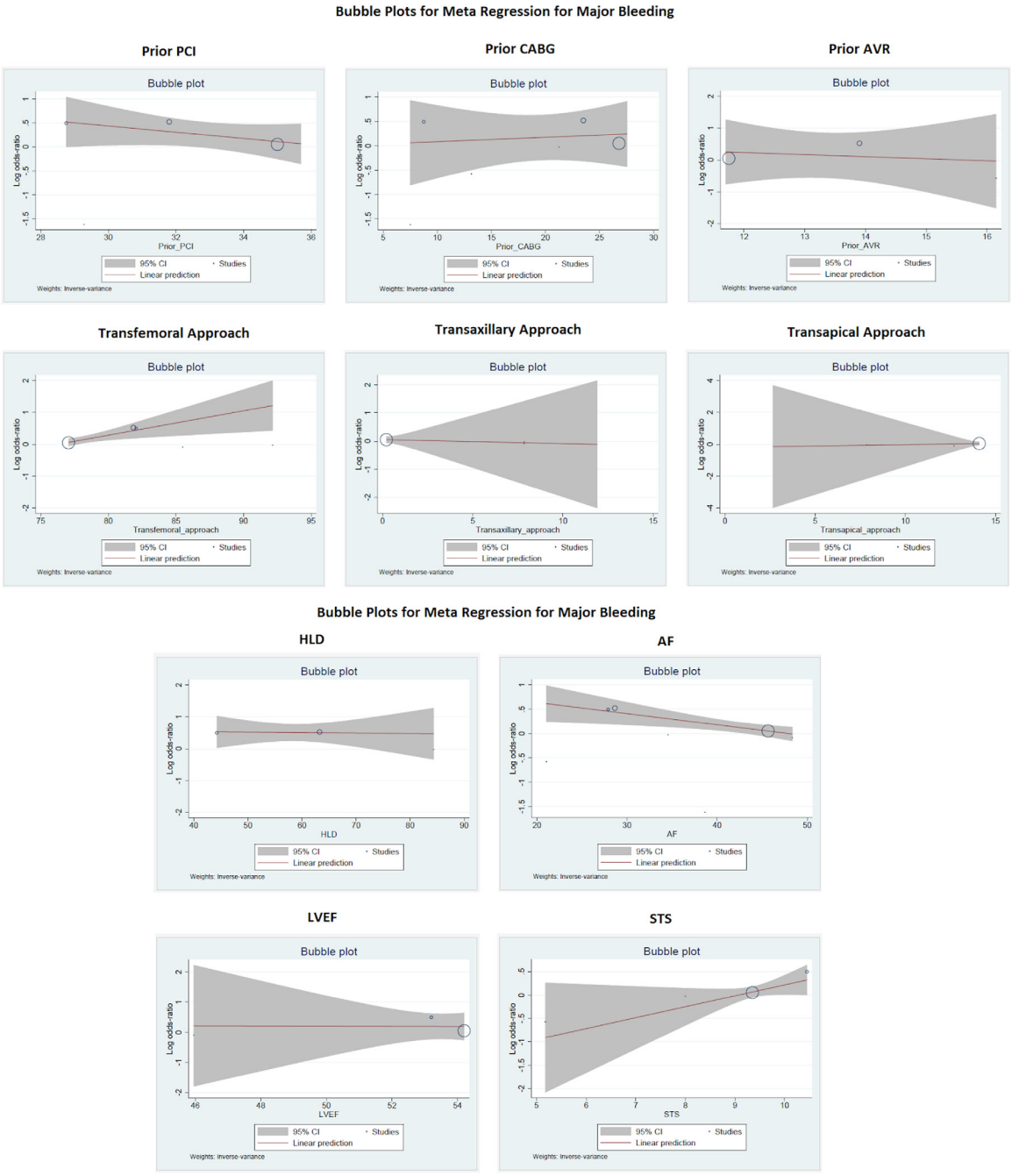
HTN





Supplementary Figure 8. Bubble plots of Vascular Complications.

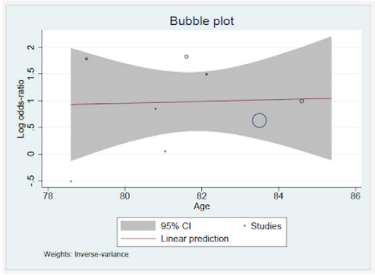




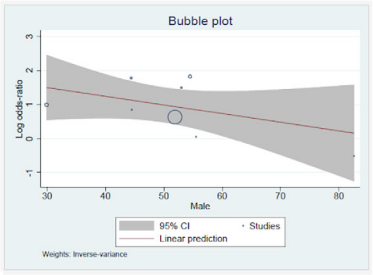
Supplementary Figure 9. Bubble plots of Major Bleeding.

Bubble Plots for Meta Regression for Acute Kidney Injury

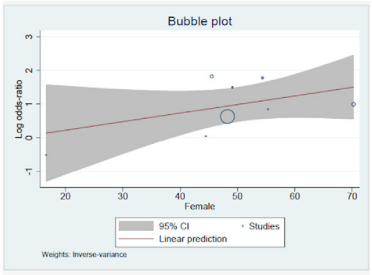
Age



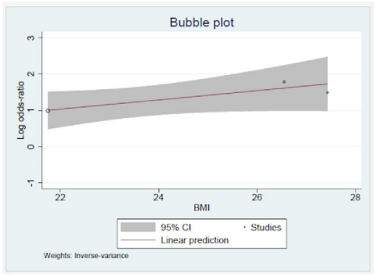
Male



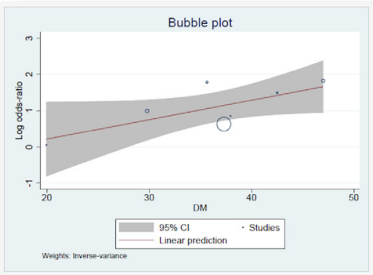
Female



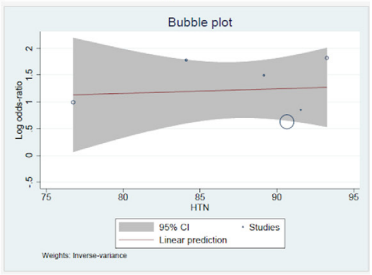
BMI



Diabetes Mellitus

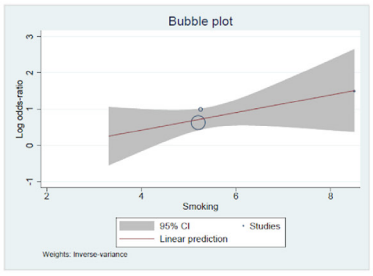


Hypertension

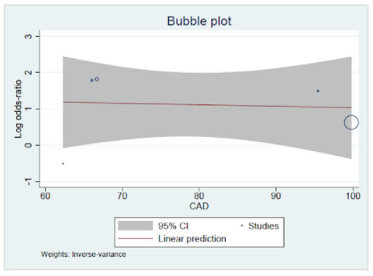


Bubble Plot for Meta Regression for Acute Kidney Injury

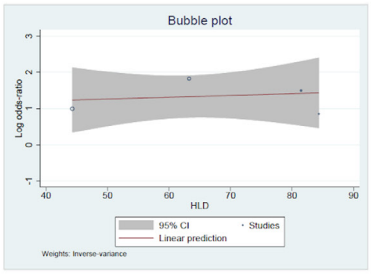
Smoking



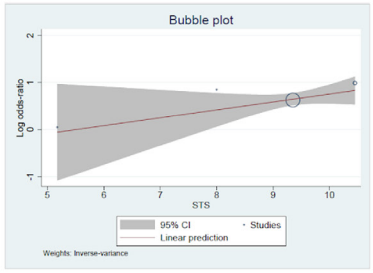
CAD



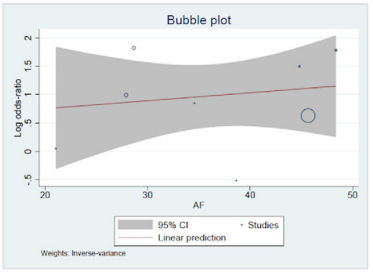
HLD



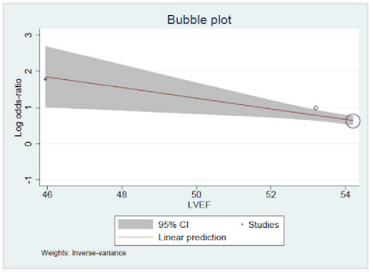
STS

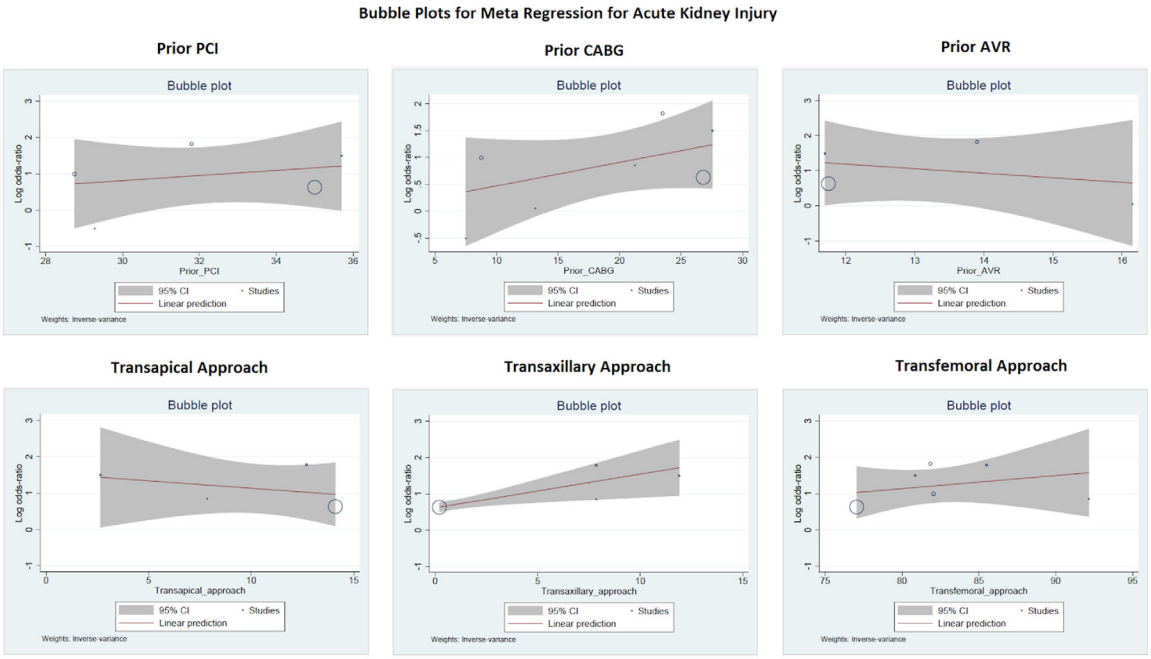


AF

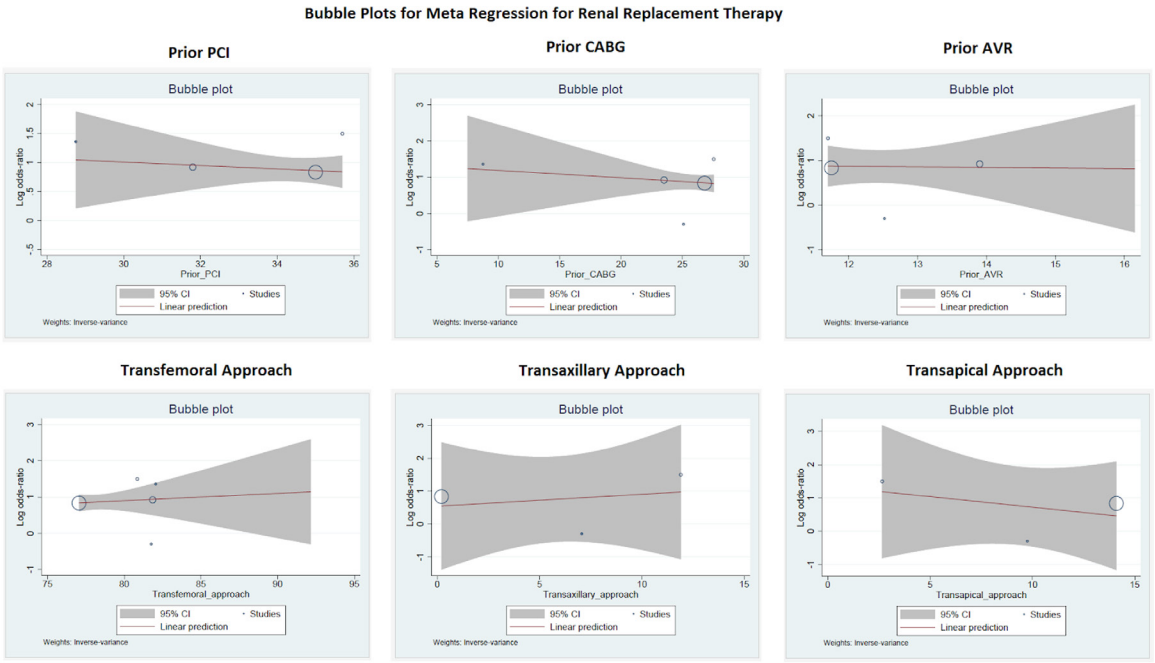


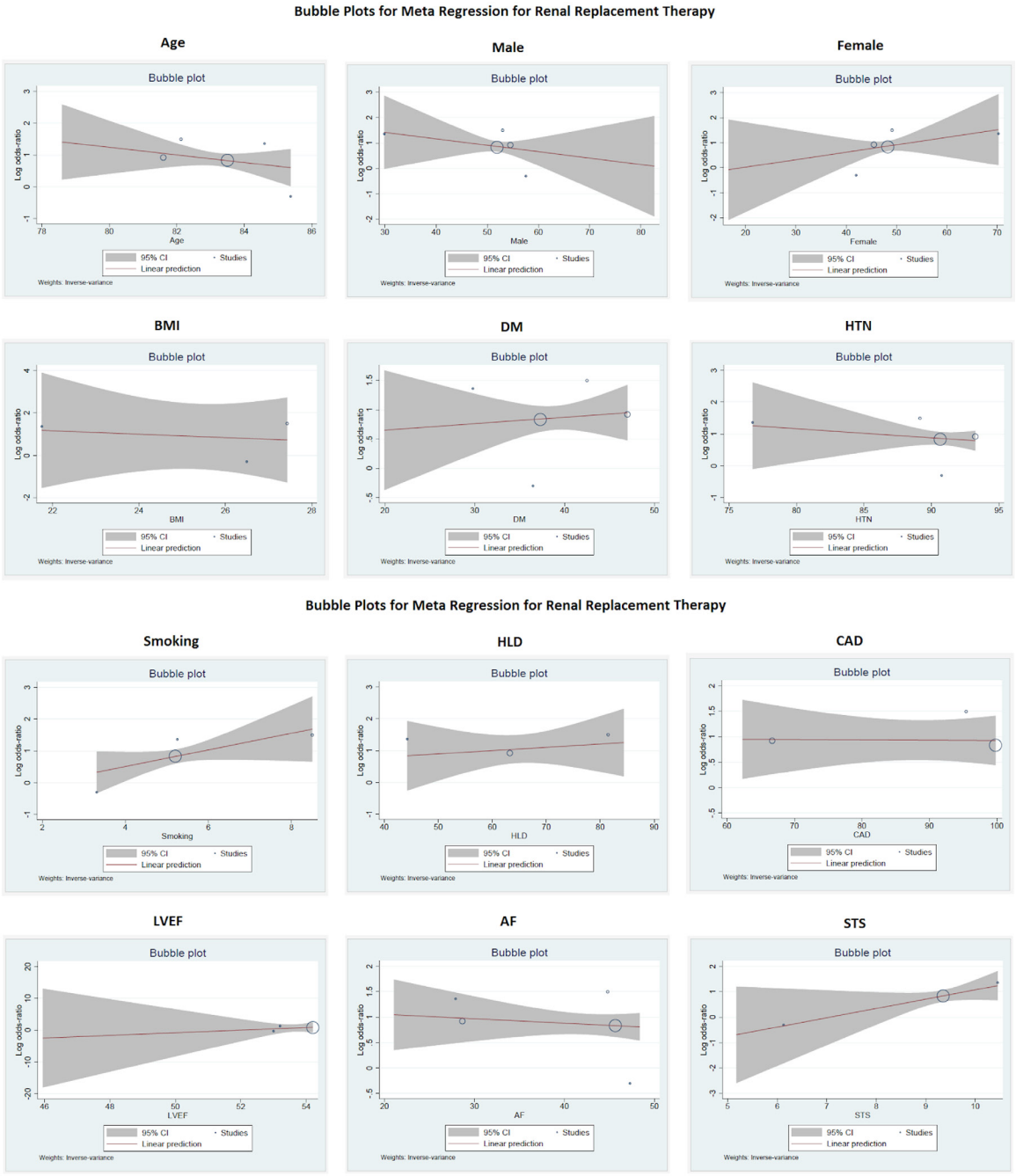
LVEF





Supplementary Figure 10. Bubble plots of Acute Kidney Injury.





Supplementary Figure 11. Bubble plots of Renal Replacement Therapy.