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## Cardiovascular Outcomes of Transradial Versus Transfemoral Percutaneous Coronary Intervention in End-Stage Renal Disease: A Regression-Based Comparison

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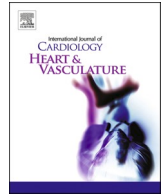
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# Cardiovascular outcomes of transradial versus transfemoral percutaneous coronary intervention in End-Stage renal Disease: A Regression-Based comparison

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## ABSTRACT

**Background:** Limited data is available on the comparison of outcomes of transradial (TR) and transfemoral (TF) access for percutaneous coronary intervention (PCI) in patients with end-stage renal disease (ESRD).

**Methods:** Online databases were queried to compare cardiovascular outcomes among TR and TF in ESRD patients. The outcomes assessed included differences in mortality, cerebrovascular accidents (CVA), periprocedural myocardial infarction (MI), bleeding, transfusion, and periprocedural cardiogenic shock (CS). Unadjusted odds ratios (OR) were calculated using a random-effect model.

**Results:** A total of 6 studies including 7,607 patients (TR-PCI = 1,288; TF-PCI = 6,319) were included. The overall mean age was 67.7 years, while the mean age for TR-PCI and TF-PCI was 69.7 years and 67.9 years, respectively. TR-PCI was associated with lower incidence of mortality (OR 0.46 95 % CI 0.30–0.70,  $p < 0.05$ , I<sup>2</sup> 0.00 %), bleeding (OR 0.45 95 % CI 0.29, 0.68,  $p < 0.05$ , I<sup>2</sup> 3.48 %), and transfusion requirement (OR 0.52 95 % CI 0.40, 0.67,  $p < 0.05$ , I<sup>2</sup> 0.00 %) (Fig. 1). There were no differences among TR-PCI and TF-PCI for periprocedural MI, periprocedural CS, and CVA outcomes.

**Conclusion:** TR access was associated with lower mortality, bleeding, and transfusion requirement as compared to TF access in patients with ESRD undergoing PCI.

## 1. Introduction

The prevalence of coronary artery disease (CAD) in end-stage renal disease (ESRD) patients remains high since ESRD is an independent risk factor for CAD.[1] Despite advancements in percutaneous coronary intervention (PCI) with newer generation stents, lower profile delivery

systems, PCI in ESRD patients remains a challenge due to a greater cardiovascular burden with severely calcified coronaries, lower ejection fraction, and complications associated with the procedure including high mortality risk.[2,3].

The transradial (TR) PCI approach is reported to have a higher procedural success rate of up to 90 %.[4] In addition, TR-PCI has been

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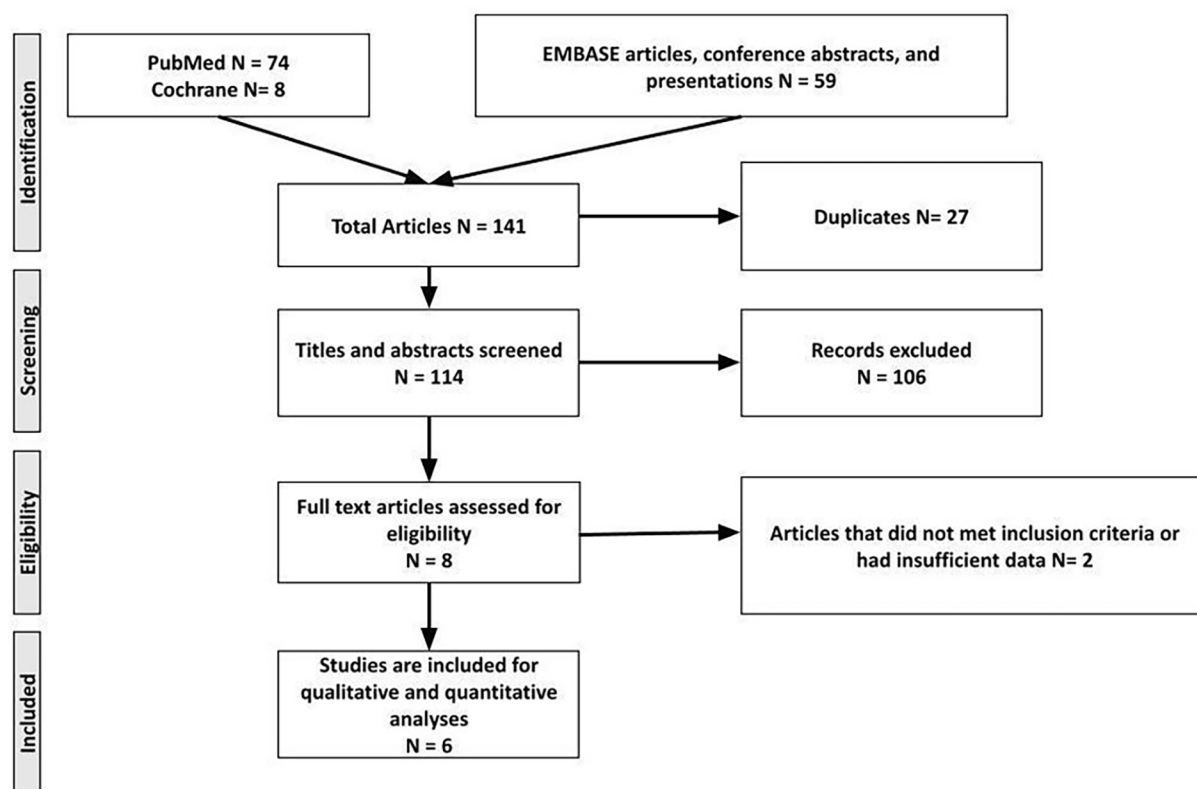


Fig. 1. The Preferred Reporting Items for Systematic Reviews and meta-Analyses (P.R.I.S.M.A.).

associated with a lower risk of bleeding, vascular complications, shorter hospital stay, and overall lower healthcare costs compared with the transfemoral (TF) approach, given better cardiovascular outcomes.[2,5] However, TR-PCI is not frequently pursued among ESRD patients on hemodialysis given the presence of arteriovenous fistula (AVF) or the need to preserve radial artery, a preferred choice of arterial conduit for dialysis access through a fistula.[6].

Although most clinical studies have reported the cardiovascular outcomes of TR-PCI compared to the TF approach for PCI, very few studies reported outcomes in patients with ESRD.[6–13] The literature has shown different results of comparison of TR. versus TF in ESRD, therefore, we sought to do a *meta-analysis* with a regression model to rule out any effect modifier to fully delineate the effect on cardiovascular outcomes in such a patient group

The objective of this *meta-analysis* was to explore the safety and efficacy of the TR compared TF -access for percutaneous coronary artery intervention in patients with end-stage renal disease.

## 2. Methods

Our *meta-analysis* was performed using the “Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (P.R.I.S.M.A. A.)” strategy and “meta-analysis of Observational Studies in Epidemiology (MOOSE)” protocol.[14,15] We searched electronic databases (MEDLINE-PubMed & E.M.B.A.S.E. and Cochrane Central Registry) from inception up to July, 7th 2021, using a Boolean operator (“OR” and “AND”) to combine two sets of keywords and medical subject headings (MeSH), including “Transradial access”, “Transfemoral access”, “Percutaneous coronary intervention”, “Coronary angiography”, “Coronary intervention”, “End-stage renal disease” “Chronic Renal Failure” (Supplemental S1). Citations of search strategy were downloaded into an EndNote X20 library. Search strategy excluded the use of filters, including time, article type, language, or country. All randomized control trials (R.C.T.), prospective, and retrospective studies were deemed

eligible if they met the inclusion criteria. Two authors (YS and R.S.) performed a phase-I screening, including the exclusion of irrelevant articles based on title and abstract evaluations. Phase II screening included a full-text reading of articles to assess their data for suitability to address the research question.

The studies were eligible to be included in our *meta-analysis* if the study population were age > 18, presence of cardiovascular event data showing a comparison of TR and TF PCI in ESRD or chronic renal failure (CRF). We excluded studies that did not include a comparison of TR PCI and TF PCI, age < 18 years, chronic kidney disease, acute kidney injury, or acute renal failure (ARF). The primary outcome of this *meta-analysis* was to compare the bleeding and in-hospital mortality across TR-PCI and TF-PCI in ESRD patients. The secondary outcomes included cerebrovascular accidents (CVA), Myocardial infarction (MI), Transfusion, and Cardiogenic shock (CS). The common definitions of outcome variables are shown in (Supplemental S2).

Statistical analysis was performed by calculating unadjusted odds ratio (OR) using the random effect model with a ‘test for overall effect’ reported as Z-value, 95 % confidence interval (CI), and probability value (P).[16] Statistical significance was met if 95 % CI does not cross numeric “1” and  $p < 0.05$ . The heterogeneity among studies was assessed by Higgins I-squared ( $I^2$ ) statistical model with  $I^2$  values < 75 % considered mild-moderate and  $\geq 75$  % considered high.[17] For heterogeneity  $I^2 > 75$  %, a leave-one-out (Jack-Knife method) was utilized to explore the cause of heterogeneity and was graphically depicted by the Labbe plot.[18] meta-regression was performed to see any potential effect modifiers for the outcomes using random effect models for study variance and Knapp-Hartung modification. We included demographics, comorbidities, and prior procedural history in effect modifier interrogation. Publication bias was illustrated by the graphical presentation of funnel plot asymmetry and quantitatively assessed by using Harbord’s weighted linear regression [19] The quality of included articles was judged by the Newcastle- Ottawa scale (Supplemental S3). All statistical analyses were performed using S.T.A.T.A. version 17.1 (StataCorp,

**Table 1**  
Baseline characteristics of the included studies.

-Year	Total	Age	Male	Female	BMI	DM	HTN	HLD	Smoking	CVA	PAD	Prior MI	Prior HF	Dialysis	Prior PCI	Prior CABG	Multivessel disease
Garg et al. 2020 <sup>8</sup>	270	64.2 ± 10.3/ 67.5 ± 10.9	26 (72.2 %)/156 (66.7 %)	10 (27.8 %)/78 (33.3 %)	32.7 ± 11.0/ 28.3 ± 5.7	21 (58.3 %)/156 (66.7 %)	36 (100.0 %)/231 (98.7 %)	32 (88.9 %)/221 (94.4 %)	2 (5.6 %)/30 (12.8 %)	7 (19.4 %)/56 (23.9 %)	9 (25.0 %)/88 (37.6 %)	19 (52.8 %)/137 (58.5 %)	16 (44.4 %)/135 (57.7 %)	NA	19 (52.8 %)/116 (49.6 %)	3 (8.3 %)/87 (37.2 %)	NA
Kuno et al. 2018 <sup>12</sup>	88	71 (65–80)/65 (62–75)	44(71.0 %)/18 (69.2 %)	18 (29.0 %)/8 (30.8 %)	NA	33 (53.2 %)/19 (73.1 %)	50 (80.6 %)/21 (80.8 %)	24 (38.7 %)/9 (34.6 %)	19 (30.6 %)/9 (34.6 %)	10(16 %)/2 (7.6 %)	9 (14.5 %)/5 (19.2 %)	7(11.2 %)/4 (15.4 %)	12(19.4 %)/10 (38.5 %)	51 (82.2 %)/26 (100 %)	13(21.0 %)/12 (46.2 %)	0(0.0 %)/1 (3.8 %)	NA
Sutton et al. 2020 <sup>7</sup>	6321	NA	486(61 %)/3259 (59 %)	470(59 %)/2264 (41 %)	NA	NA	NA	NA	NA	NA	227 (28.5 %)/2099 (38 %)	344 (43.2 %)/2767 (50.1 %)	416(52.2 %)/3104 (56.2 %)	NA	391(49.1 %)/3043 (55.1 %)	75 (9.5 %)/1242 (22.5 %)	NA
Yashima et al 2020 <sup>10</sup>	398	75.5 ± 9.6 /74.2 ± 10.4	132 (66.30 %)/195 (65.20 %)		23.8 ± 3.9 /23.7 ± 4.2	103 (51.80 %)/183 (61.60 %)	177 (88.9 %)/265 (88.9 %)	139 (69.9 %)/188 (63.1 %)		36 (18.1 %)/48 (16.1 %)	29 (14.6 %)/50 (16.8 %)	58 (29.2 %)/71 (23.8 %)	53 (26.6 %)/95 (31.9 %)	NA	85 (42.7 %)/97 (32.6 %)	10 (5.0 %)/30 (10.1 %)	132 (66.3 %)/205 (68.6 %)
Kuno et al 2019 <sup>11</sup>	306	73.3 ± 9.6/70.0 ± 9.5	67.5 % (77)/77.1 % (148)	32.5 % (37)/22.9 % (44)	23.6 ± 3.8/22.9 ± 3.5	55.2 % (63)/75.5 % (145)	95.6 % (109)/98.4 % (189)	70.2 % (80)/71.9 % (138)	25.4 % (29)/37.5 % (72)	17.5 % (20)/10.4 % (20)	18.4 % (21)/26.6 % (51)	22.8 % (26)/29.7 % (57)	21.9 % (25)/28.1 % (54)	28.9 % (33)/64.0 % (123)	38.6 % (44)/45.3 % (87)	3.5 % (4)/7.8 % (15)	11 (17.7 %)/9 (34.6 %)
Koutozis et al 2018 <sup>9</sup>	124	64.5 ± 12.2/ 63.2 ± 12.9	71 (88.7 %)/36 (81.2 %)	9 (11.3 %)/8 (18.8 %)	NA	29 (36.5 %)/13 (29.5 %)	62 (77.5 %)/31 (70.5 %)	35 (43.8 %)/24 (54.5 %)	32 (40.0 %)/5 (11.4 %)	NA	17 (21.3 %)/17 (38.7 %)	27 (33.7 %)/16 (36.4 %)	NA	NA	26 (32.5 %)/17 (38.6 %)	9 (11.3 %)/21 (47.7 %)	NA

Abbreviation: BMI = Body mass index; DM = Diabetes mellitus; HTN = Hypertension; HLD = Hyperlipidemia; CVA = Cerebrovascular accident; PAD = Peripheral arterial Disease; MI = Myocardial infarction; HF = Heart failure; PCI = Percutaneous coronary intervention; CABG = Coronary artery bypass grafting.

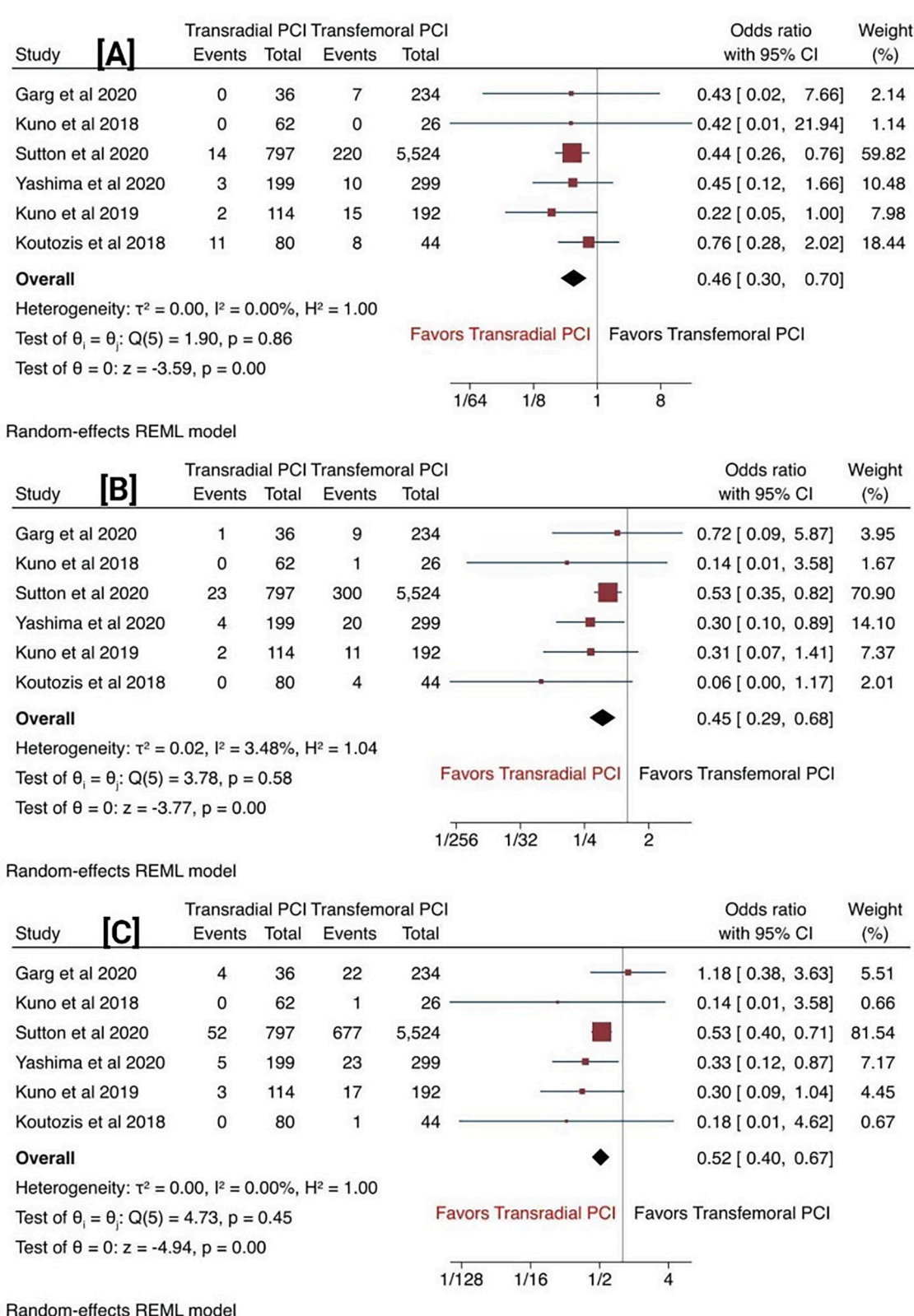


Fig. 2. Forest plot showing odds of mortality, bleeding and transfusion between TR-PCI and TF-PCI in ESRD.

College Station, Texas) [20].

### 3. Results

Our search included articles from inception up to 30th May 2021 and

resulted in 141 articles. Duplicate ( $n = 27$ ), not in English ( $n = 5$ ), and lack of available data for comparison of TR and TF ( $n = 104$ ) studies were excluded. A total of 6 studies were reviewed in full text form (retrospective = 5, prospective = 1) (Supplemental S1). [6–11] Four studies included patients who underwent both PCI and PCA [8,11] and



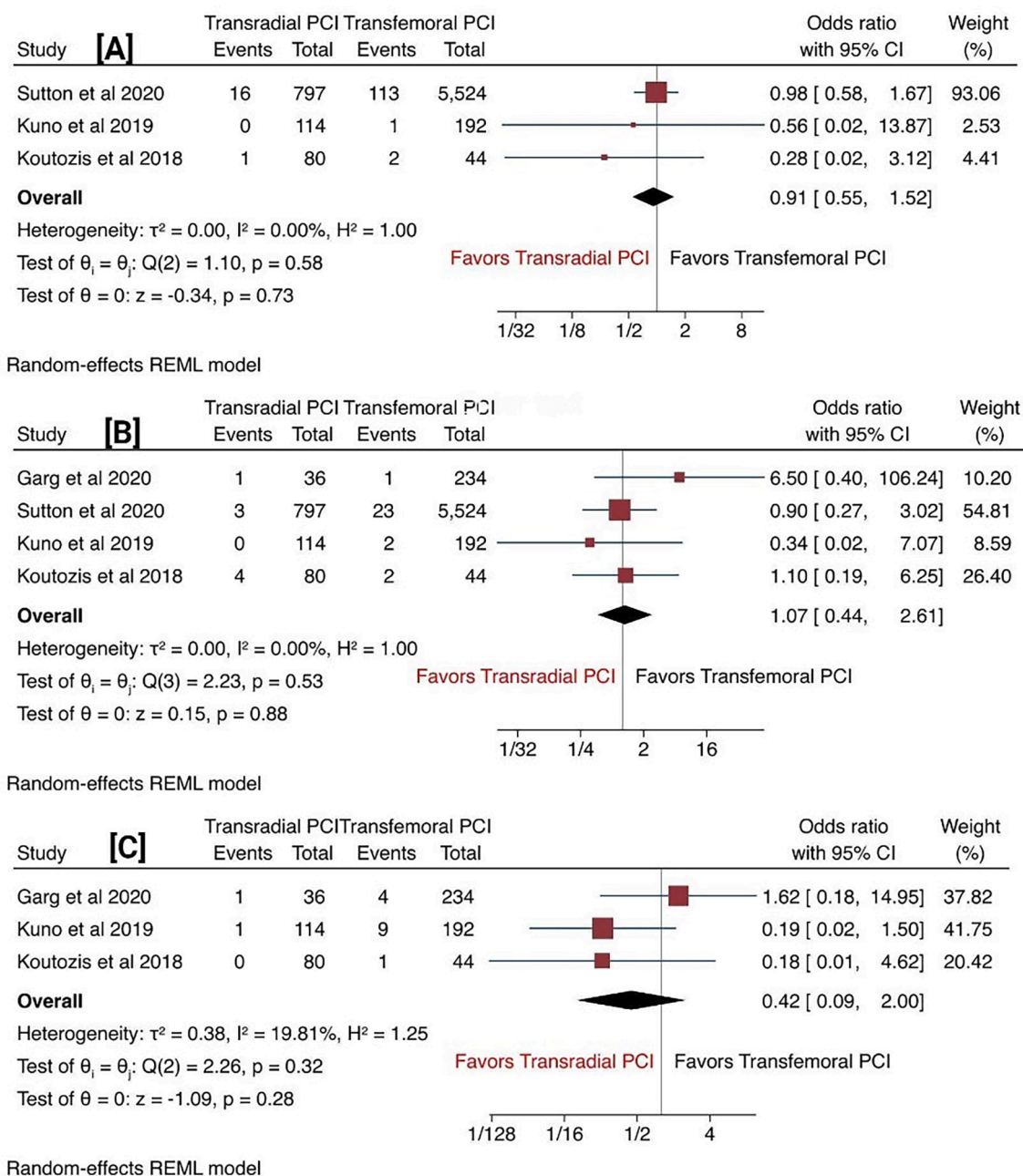


Fig. 3. Forest plot showing the odds of cerebrovascular accident, myocardial infarction, and cardiogenic shock.

two studies had only PCI patients.[6,7,9,10] Moreover, the studies we included had patients with both stable and unstable angina. The detailed Preferred Reporting Items for Systematic Reviews and meta-Analyses (P. R.I.S.M.A.) flow diagram is given in Fig. 1.

A total of 7507 patients (TR-PCI = 1288 (16.9 %); TF-PCI = 6319 (83.1 %) were included in the analysis. (Table 1 and S. Table 3) The overall mean age was 67.75 years, while the mean age for TR-PCI and TF-PCI was 69.7 and 67.9 years, respectively. Among the study population, the female gender constituted up to 25.7 %. Baseline comorbidities included diabetes mellitus (51 % vs 56.4 %), hypertension 88.52 % vs 87.46 %), dyslipidemia (62.3 % vs 63.7 %), cerebrovascular disease (17.75 % vs 14.5 %), peripheral arterial disease (18.76 % vs 27.78 %) and prior history of Myocardial Infarction (29 % vs 31.85), Heart Failure (28.07 % vs 39.05 %) PCI (37.52 % vs 42.46 %) and coronary artery bypass graft (CABG) (5.6 % vs 21.32 %) in TR-PCI versus TF-PCI, respectively.

On pooled analysis, TR-PCI was associated with lower odds of primary outcomes, including mortality (OR 0.46 95 % CI 0.30–0.70,  $p < 0.05$ ,  $I^2$  0.00 %), and bleeding (OR 0.45 95 % CI 0.29, 0.68,  $p < 0.05$ ,  $I^2$  3.48 %). Among secondary outcomes, TR-PCI was associated with lower odds of transfusion requirements (OR 0.52 95 % CI 0.40, 0.67,  $p < 0.05$ ,  $I^2$  0.00 %) (Fig. 2). We did not find any statistically significant difference in CVA (OR 1.07 95 % CI 0.44, 2.61  $p > 0.05$ ,  $I^2$  0.00 %) and cardiogenic shock (OR 0.42 95 % CI 0.09, 2.00,  $p > 0.05$ ,  $I^2$  19.81 %) between TR and TF PCI in ESRD population but was not statistically significant (Fig. 3). The visual summary of the results is shown in (Fig. 4).

On visual assessment, our funnel plot was symmetrical with an equal number of studies on each side of the vertical axis (S. Figure 10–15). The line graph harbored regression and egger regression excluded any presence of small-study effects ( $P > 0.05$ ) as shown in (S. Figures 16–21)

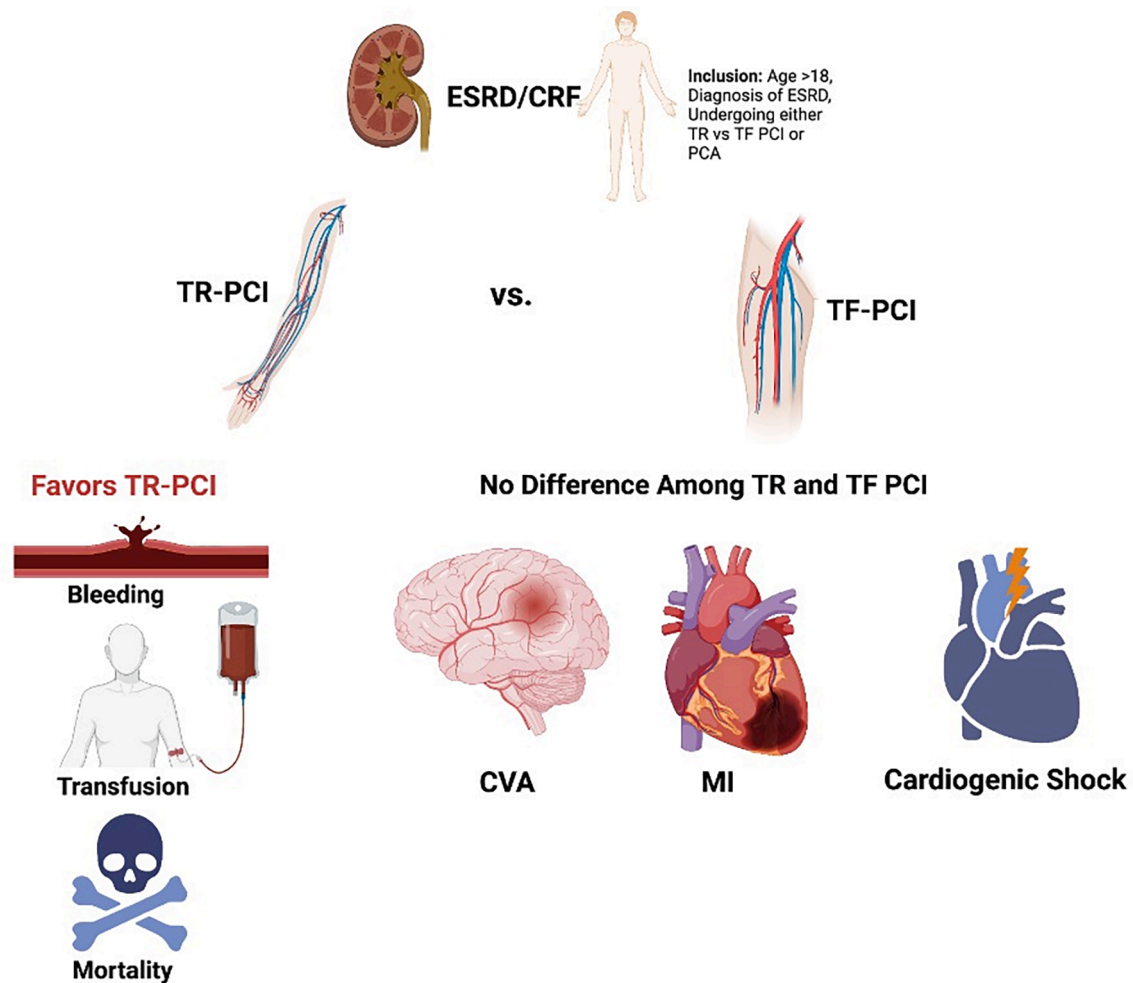


Fig. 4. Summary of pooled results and visual abstract.

**Table 2**  
meta-regression of potential effect modifiers for all study outcomes\*\*.

Meta-Regression Variables	Mortality		Bleeding		Transfusion	
	Coefficient	p	Coefficient	p	Coefficient	p
<b>Demographic</b>						
Age	-0.023	0.743			-0.072	0.198
Male	-0.100	0.511	0.010	0.943	-0.002	0.989
Female	0.240	0.652	0.191	0.664	0.431	0.245
<b>Comorbidities</b>						
BMI	0.012	0.854	0.037	0.454	0.056	0.057
HTN	-0.045	0.621	0.053	0.491	0.089	0.183
DM	-0.072	0.525	0.011	0.910	0.014	0.923
HLD	-0.004	0.915	0.030	0.373	0.047	0.052
Smoking	-0.024	0.738	-0.045	0.427	-0.066	0.072
Prior MI	0.005	0.907	0.032	0.372	0.046	0.042
PAD	-0.0345	0.725	0.0542	0.484	0.090	0.079
Prior HF	0.023	0.729	0.039	0.448	0.061	0.050
CVD	0.0872	0.638	0.118	0.435	0.195	0.055
<b>Procedures</b>						
Prior PCI	-0.024	0.823	0.068	0.402	0.102	0.055
Prior CABG	0.023	0.799	0.059	0.401	0.085	0.044

\*\*p- >0.05 shows that our study had no effect modifiers in our studied outcomes. HTN- Hypertension, DM- Diabetes mellitus, HLD- hyperlipidemia.

meta-regression ruled out effect modifiers including demographics (age, male, female), comorbidities (B.M.I., cardiovascular disease, Diabetes Mellitus, smoking, hyperlipidemia, hypertension, prior H.F., peripheral artery disease) and prior procedures (PCI, CABG) (Table 2) and (S. Figs. 1-9).

#### 4. Discussion

Our analysis showed the following findings: [1] TR-PCI is associated with significantly lower in-hospital 30-day mortality risk, reduced rate of bleeding complications, and transfusion requirement when compared



to TF-PCI, and [2] There was no statistically significant difference in the risk of in-hospital CVA, MI and CS post-PCI between TR and TF groups with ESRD. Our findings demonstrate that the TR approach in patients with ESRD who need PCI is feasible and safe.

Prior studies demonstrated a mortality benefit with trans radial access in various subgroups of patients undergoing PCI.[12] We demonstrate a similar benefit in the ESRD population. The decrease in the mortality rates among the TR-PCI group could be related to lower rates of vascular complications, including bleeding, stroke, and site-related complications, as reported by Koutouzis et al.[8] In addition, ESRD patients are at increased risk for periprocedural bleeding due to platelet dysfunction. Nevertheless, our study found a lower incidence of bleeding among TR-PCI patients compared to TF-PCI, which is consistent with the findings of the major clinical trial and meta-analyses. [21–26] Agostoni et al and Jolly et al showed reduced incidence of access site bleeding events among TR-PCI (0.3 % vs 2.8 %;  $P = 0.0001$ ; and 0.05 % vs 2.3 %;  $P = 0.001$ , respectively) compared to TF-PCI. [25,26] One of the reasons for the lower bleeding among TR-PCI can be operator-dependent with a higher frequency of use of TR-PCI. Another possible explanation is that the radial artery is both superficial and easily compressible and hence the lower bleeding complications. In addition, major bleeding has been reported to cause an increased incidence of nonfatal myocardial infarction, stroke, and both early and late mortality.[27] Therefore, bleeding risk should be balanced with the other complications, including MI, mortality, and stroke, in considering PCI approach, especially in ESRD patients given their increased risk of bleeding. Furthermore, we found lower incidences of blood transfusions needed among TR-PCI patients consistent with findings of the MORTAL study, which reported halving of the transfusion rate and a reduction in 30-day and 1-year mortality with the TR-PCI approach.[28].

In our analysis, there was no difference in stroke incidence among both groups. Our findings are similar to meta-analyses which showed no difference in the stroke rates between TR-PCI and TF-PCI.

PCI.[29,30] Furthermore, our study also showed non-significant lower odds of MI and cardiogenic shock in both groups. Moreover, vascular complications, including bleeding, have been reported to have caused cardiogenic shock.[31] Due to heterogeneity in the studies included in our study, we performed a meta-regression analysis to know the influence of several comorbidities on the outcomes. The effects of age, sex, BMI, diabetes mellitus, hypertension, hyperlipidemia, smoking, CVD, PAD, and prior history of MI, HF, PCI, and CABG were assessed sequentially on the procedural mortality, bleeding, transfusion. None of the covariates were found to influence any of the short-term outcomes assessed ( $p > 0.05$ ) (S. Figures 10–21). Although TR-PCI is not as common as TF, the use of TR, in general, has increased tremendously over the past several years.[32] Our study demonstrates the short-term safety and feasibility of this approach for PCI in patients with ESRD. Studies have not reported the patency rates of radial arteries after TR PCI. It is crucial to understand the risk of loss of radial artery patency that will devoid the patient of ideal dialysis access. Further studies are needed to assess the long-term impact of transradial access on arterial patency and the success rate of radio-cephalic AVF surgery after prior TR PCI.

## 5. Limitations

The studies included in our analysis were observational, and therefore the limitations related to these studies, including selection bias, should be considered. Subgroup analysis for the type of studies was not performed given all studies were observational and no availability of R. C.T. The follow-up duration for the short or long term was also not available, and we included all outcomes as an in-hospital follow-up that can have selection bias. Moreover, we could not include data regarding anticoagulants, hydration status, catheter size, stents per patient, access time duration, use of ultrasound, and the size of sheath were not considered, which could have been an important impact on the

outcomes, especially for the bleeding risks in the TF-PCI group. In addition, we were unable to report outcomes among different anginal patients due to the unavailability of the separate data in the included studies. Furthermore, univariate meta-regression was not possible for C. V.A., MI, and C.S. given the sparsity of data, the statistical software could not apply a regression module due to convergence not being achieved. We also would consider the outcomes to be related to individual experience.

## 6. Conclusion

In conclusion, among ESRD patients undergoing PCI, the TR approach is associated with a lower risk of all-cause mortality and lower bleeding complications and blood transfusion requirement compared to the TF approach. However, we found no significant difference in cardiovascular outcomes of CS and stroke between the two approaches. Prospective randomized trials in this vulnerable population are needed to confirm the safety and risk of complications. The impact of trans radial access on the success of a future radio cephalic AVF surgery needs further study.

Clinical Perspective:

- Transradial (TR) approach is the standard for percutaneous coronary intervention (PCI) and has been associated with a lower risk of bleeding, vascular complications, shorter hospital stay, and overall lower healthcare costs compared with the transfemoral (TF) approach.
- TR-PCI is a less common approach in ESRD patients due to arteriovenous fistula (AVF) or the need to preserve radial artery.
- Data on the comparison of clinical outcomes between TR and TF approach in ESRD population is limited.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijcha.2022.101110>.

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