

# Impact of Coronary Artery Disease on 30-Day and 1-Year Mortality in Patients Undergoing Transcatheter Aortic Valve Replacement: A Meta-Analysis

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**Background**—The impact of coronary artery disease (CAD) on outcomes after transcatheter aortic valve replacement (TAVR) is understudied. Literature on the prognostic role of CAD in the survival of patients undergoing TAVR shows conflicting results. This meta-analysis aims to investigate how CAD impacts patient survival following TAVR.

**Methods and Results**—We completed a comprehensive literature search of Embase, MEDLINE, and the Cochrane Library, and included studies reporting outcome of TAVR based on CAD status of patients for the analysis. From the initial 1631 citations, 15 studies reporting on 8013 patients were analyzed using a random-effects model. Of the 8013 patients undergoing TAVR, with a median age of 81.3 years (79–85.1 years), 46.6% (40–55.7) were men and 3899 (48.7%) had CAD (ranging from 30.8% to 78.2% in various studies). Overall, 3121 SAPIEN/SAPIEN XT/SAPIEN 3 (39.6%) and 4763 CoreValve (60.4%) prostheses were implanted, with transfemoral access being the most frequently used approach for the implantation (76.1%). Our analysis showed no significant difference between patients with and without CAD for all-cause mortality at 30 days post TAVR, with a cumulative odds ratio of 1.07 (95% confidence interval, 0.82–1.40;  $P=0.62$ ). However, there was a significant increase in all-cause mortality at 1 year in the CAD group compared with patients without CAD, with a cumulative odds ratio of 1.21 (95% confidence interval, 1.07–1.36;  $P=0.002$ ).

**Conclusions**—Even though coexisting CAD does not impact 30-day mortality, it does have an impact on 1-year mortality in patients undergoing TAVR. Our results highlight a need to revisit the revascularization strategies for concomitant CAD in patients with TAVR. (*J Am Heart Assoc.* 2017;6:e006092. DOI: 10.1161/JAHA.117.006092.)

**Key Words:** coronary artery disease • meta-analysis • revascularization • transcatheter aortic valve implantation • transcatheter aortic valve replacement

Aortic stenosis (AS) and coronary artery disease (CAD) frequently exist together.<sup>1</sup> The coexistence of these 2 entities can be attributed to their similar risk factors and pathophysiology.<sup>2–4</sup> The prevalence of CAD in severe AS ranges from 30% to 50%,<sup>5–8</sup> and increases with age.<sup>9</sup>

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Accompanying Table S1 and Figures S1 through S4 are available at <http://jaha.ahajournals.org/content/6/10/e006092/DC1/embed/inline-supplementary-material-1.pdf>

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Received March 14, 2017; accepted June 28, 2017.

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The presence of CAD has been identified as a negative prognostic indicator for patients undergoing surgical aortic valve replacement (SAVR).<sup>10–12</sup> It is known that addition of coronary artery bypass grafting to SAVR increases the perioperative mortality in patients undergoing SAVR,<sup>13–16</sup> but studies have also reported improved short- and long-term survival in patients with AS and CAD who underwent combined SAVR and coronary artery bypass grafting, compared with those who underwent isolated SAVR.<sup>17,18</sup> Based on these findings, the current guidelines for primary aortic valve disease requiring surgical intervention recommend coronary artery bypass grafting in all patients with significant stenoses at the time of SAVR.<sup>19</sup>

Since the “first-in-man” transcatheter aortic valve replacement (TAVR) in 2002,<sup>20</sup> TAVR has emerged as a reasonable alternative in patients with severe AS who are inoperable or at high risk for SAVR.<sup>21,22</sup> Currently, data are emerging on intermediate-risk patients as well.<sup>23</sup> Because the patients selected to undergo TAVR are typically elderly with multiple comorbid conditions, the prevalence of CAD among them is

## Clinical Perspective

### What Is New?

- Even though prevalence of coronary artery disease (CAD) in patients undergoing transcatheter aortic valve replacement (TAVR) ranges from 40% to 70%, literature regarding the impact of CAD on TAVR outcomes yields conflicting results.
- Coexisting CAD is a negative prognostic indicator with regard to survival of patients undergoing TAVR at 1-year follow-up.
- There were no significant differences between patients with and without CAD for mortality and other Valve Academic Research Consortium outcomes at 30-day follow-up after TAVR.
- Studying the impact of CAD on patient outcomes after TAVR is hindered by nonuniform CAD definitions and infrequent reporting on anatomical and functional assessment of CAD in the published literature.

### What Are the Clinical Implications?

- Since CAD has a negative effect on prognosis at 1-year follow-up, it is important to revisit the revascularization strategies that could be implemented.
- Randomized controlled trials are needed to determine the role of routine revascularization and optimal timing of revascularization in patients with significant CAD undergoing TAVR.
- It is important to find the appropriate management of concomitant CAD as the TAVR population expands to include younger and lower-risk individuals.

generally high. Major randomized controlled trials (RCTs) and registries have demonstrated that the prevalence of CAD in patients undergoing TAVR can range from 40% to 70% or more.<sup>21–27</sup>

The impact of CAD on TAVR outcomes is unclear, as the major RCTs of TAVR, PARTNER (Placement of Aortic Transcatheter Valve Trial) I,<sup>21</sup> and PARTNER II<sup>23</sup> excluded patients with untreated clinically significant CAD requiring revascularization and patients with complex CAD (unprotected left main coronary artery or syntax score >32), respectively. Identifying the optimum revascularization strategy for patients with TAVR who have concomitant CAD is an area of ongoing debate. The few published studies evaluating the impact of CAD on TAVR outcomes and long-term survival show conflicting results.<sup>28–31</sup> The 2 published meta-analyses<sup>32,33</sup> that have attempted to identify the role of CAD in patients undergoing TAVR showed that CAD did not significantly alter the outcomes of TAVR. However, those analyses were limited by small numbers of studies and patients.

Therefore, although the high prevalence of CAD in the TAVR patient population is well documented, the data about the impact of CAD on TAVR outcomes are conflicting and unclear.

The present meta-analysis aims to investigate the impact of CAD on short-term outcomes and follow-up survival after TAVR.

## Methods

### Search Strategy

A systematic review of published literature was conducted following PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) guidelines.<sup>34</sup> A computerized search of all publications in the MEDLINE, Embase, and Cochrane Central databases were searched. Relevant MeSH headings and variations of the words “TAVR,” “coronary artery disease,” and “revascularization” were used. Citations were screened at the title and abstract level and limited to English language and human patients. Full text along with online supplements reporting TAVR outcomes (at least all-cause mortality) based on CAD status of patients were retrieved, and the bibliographies of the relevant articles were searched manually to identify any additional pertinent studies. This was last assessed as up to date on May 15, 2017.

### Study Selection

Two independent reviewers initially screened all possible articles for inclusion at the title and/or abstract level, with the disagreement resolved by consensus. If potentially eligible, the complete article was then reviewed according to the following selection criteria.

Inclusion criteria were:

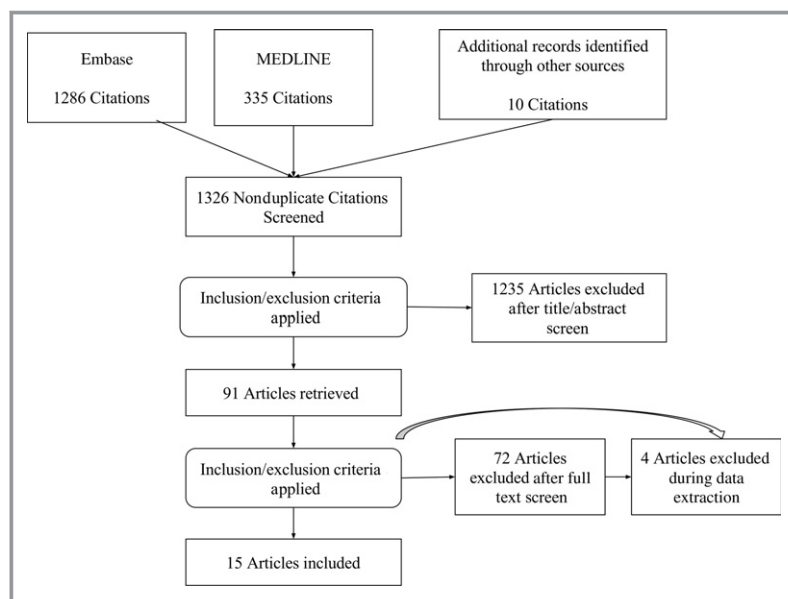
1. Studies that reported primary outcome (all-cause mortality at 30 days and 1 year after TAVR) based on the CAD status of patients.
2. Studies that reported secondary end points at 30 days and/or 1 year after TAVR.

Exclusion criteria were:

1. Duplicate of publication/overlap of patients.
2. Outcomes of the interest (all-cause mortality and/or Valve Academic Research Consortium [VARC] end points following TAVR based on the CAD status of patients) was not clearly reported or was impossible to calculate from published results.
3. Conference presentations, case reports, reviews, and editorials.
4. Studies in languages other than English.

### Study End Points

The primary outcomes of interest for our study were all-cause mortality at 30 days and 1 year after TAVR. Secondary



**Figure 1.** Flow diagram of study selection according to PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) statement.

outcomes included: (1) cardiovascular mortality at 30 days, (2) myocardial infarction at 30 days, (3) stroke at 30 days, (4) major bleeding at 30 days, (5) vascular complications at 30 days, (6) cardiovascular mortality at 1 year, (7) myocardial infarction at 1 year, and (8) stroke at 1 year. Standard definitions, as described by the VARC<sup>35,36</sup> were accepted for all of the outcomes after TAVR. Articles that clearly described their own definition of outcomes were also included. Definitions for CAD used by the included studies are mentioned in Table 1.

### Data Abstraction and Individual Study Quality Appraisal

All data were extracted from article text, tables, figures, and supplementary material. Data on study population, design of study, demographics, procedural details, and outcomes were collected. Two reviewers (K.S. and K.B.) independently conducted the literature searches, study eligibility assessment, and data extraction. Any discrepancies were resolved following discussion and consensus.

Two authors (K.S. and K.B.) independently assessed the risk of bias of included studies using the standardized Newcastle-Ottawa Scale (Table S1). This validated instrument for appraising observational studies measures the risk of bias in 8 categories: representativeness of the exposed cohort (S1); selection of the nonexposed cohort (S2); ascertainment of exposure (S3); demonstration that the outcome of interest was not present at the start of the study (S4); comparability (C1 and C2); assessment of outcome (E1); whether follow-up long enough for outcomes to occur (E2); and adequacy of

follow-up of cohorts (E3). Sensitivity analysis was performed for the primary outcomes.

### Statistical Analysis

Data extracted from the studies were tabulated and analyzed using the “metan” package in STATA 13 (Statacorp). Pooled odds ratios were calculated using a DerSimonian-Laird random-effects model, with inverse variance weights for included studies. Continuous variables were analyzed using a weighted mean and compared with a Student *t* test. Statistical significance was set at  $P=0.05$  (2-tailed). Heterogeneity was assessed by  $I^2$  test. Heterogeneity was considered low if  $I^2 < 25\%$  and significant if  $I^2 > 75\%$ . To address publication bias, we used 2 methods: (1) visual inspection of the funnel plots (Figures S1 and S2) and (2) Egger’s test. We also performed sensitivity analysis (Figures S3 and S4) to evaluate how removal of each study impacts overall outcome.

## Results

### Study Selection

A total of 1631 records were identified in the preliminary search: 1286 from Embase and 335 from MEDLINE. After elimination of duplicates, 1326 records were screened by title and abstract. This excluded 1235 reports. The other 91 articles were retrieved and full texts were reviewed. After applying inclusion and exclusion criteria to the full text articles, 72 articles were removed, while the full text

**Table 1.** Study Characteristics

Author	Year	Design	Country	Total, No.	CAD vs No CAD Comparison
Dewey et al <sup>28</sup>	2010	Retrospective review of data records	12 Centers in North America and Europe	171	Present
Gasparetto et al <sup>29</sup>	2013	Prospective single-center registry	Italy	191	Present
Gautier et al <sup>30</sup>	2011	Retrospective review of data records	France	145	Present
Khawaja et al <sup>38</sup>	2015	Retrospective review of data records	England	271	Present
Linke et al <sup>39</sup>	2014	Prospective multicenter study	44 Centers in 12 countries	1001	Absent; details were extracted
Mancio et al <sup>31</sup>	2015	Prospective single-center registry	Portugal	91	Present
Masson et al <sup>40</sup>	2010	Retrospective review of single-center registry	Canada	136	Present
Muñoz-García et al <sup>41</sup>	2013	Retrospective review of multicenter registry	43 Centers in 9 European and Ibero-American countries	1220	Absent; details were extracted
Panico et al <sup>42</sup>	2012	Prospective single-center registry	Italy	118	Absent; details were extracted
Paradis et al <sup>43</sup>	2017	Retrospective review of data records	North America	377	Present
Rodés-Cabau et al <sup>44</sup>	2010	Retrospective review of multicenter national registry	6 Centers in Canada	339	Absent; Details were extracted
Snow et al <sup>45</sup>	2015	Retrospective review of national registry	31 Centers in the United Kingdom	2562	Present
Stefanini et al <sup>46</sup>	2014	Prospective single-center registry	Switzerland	445	Present
Ussia et al <sup>47</sup>	2013	Prospective multicenter database	14 Centers in Italy	659	Present
Zivelonghi et al <sup>37</sup>	2017	Retrospective review of data records	Italy	287	Present

CAD indicates coronary artery disease.

**Table 2.** Baseline Features of Patients and CAD Definition Used in Included Studies

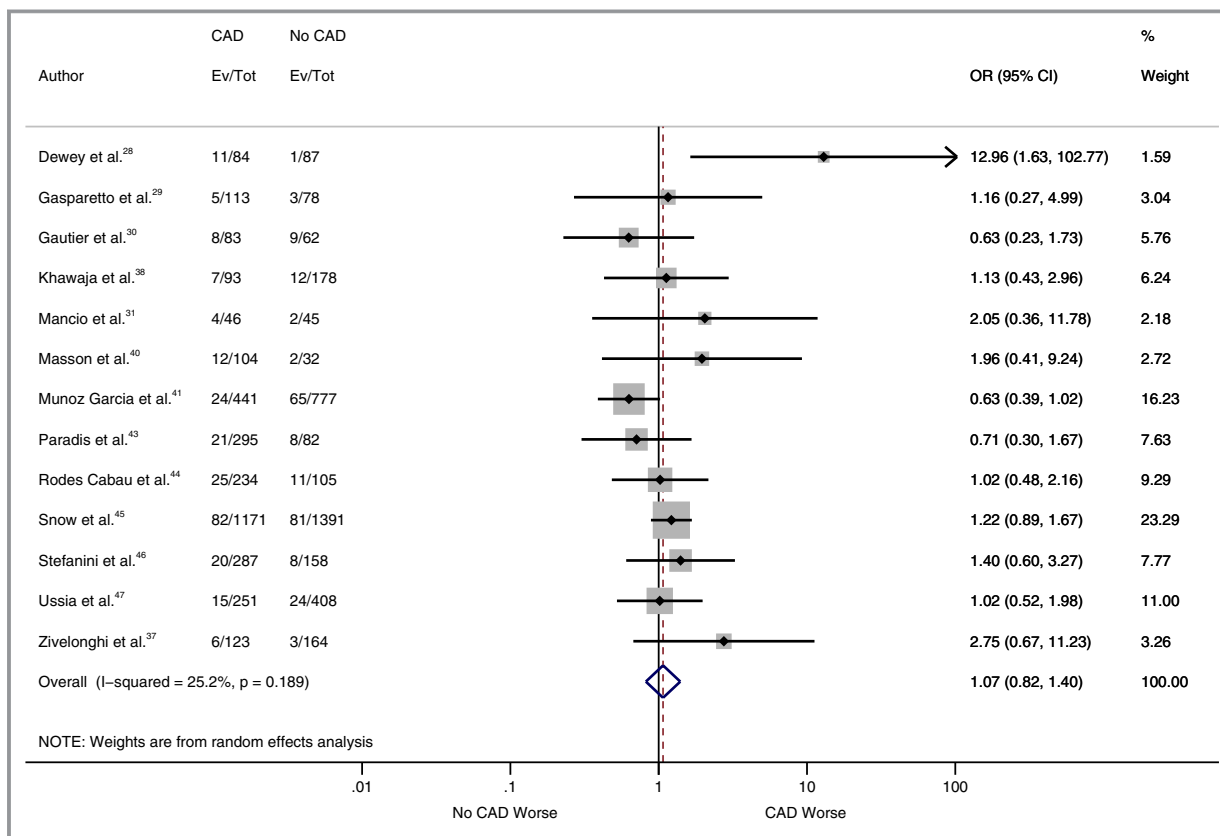
Study	Mean Age, y	Men, %	STS (Mean)	EuroSCORE (Mean)	CAD, %	CAD Definition
Dewey et al <sup>28</sup>	83.8	49.1	12.06	30.86	49.1	Prior CABG/PCI
Gasparetto et al <sup>29</sup>	80.5	42.4	NA	21.4	59.2	Prior CABG/PCI and/or presence of any coronary stenosis of at least 50%
Gautier et al <sup>30</sup>	82	52.7	16	28	57.2	Prior CABG/PCI or >70% stenosis (>50% for left main)
Khawaja et al <sup>38</sup>	82.5	55.7	6.14	21.46	34.3	>70% stenosis (>50% for left main)
Linke et al <sup>39</sup>	81.1	49	5.3	16	57.8	Not specified
Mancio et al <sup>31</sup>	79	52	6	NA	50.5	Prior CABG/PCI and/or presence of any coronary stenosis of at least 50%
Masson et al <sup>40</sup>	85.1	50.7	9.1	21	30.8	Prior CABG/PCI or >50% stenosis (extent was assessed by DMJS)
Muñoz-García et al <sup>41</sup>	80.7	45.3	NA	17.8	36.1	Not specified
Panico et al <sup>42</sup>	82.5	46.6	NA	25.8	51.7	Not specified
Paradis et al <sup>43</sup>	82.5	51.9	8.5	25.4	78.2	>50% stenosis in vessels >1.5 mm in diameter
Rodés-Cabau et al <sup>44</sup>	81	44.8	9.8	NA	69	Not specified
Snow et al <sup>45</sup>	81.3	46.3	NA	18.06	45.7	>50% stenosis of the left main or 3 main coronaries or their major epicardial branches
Stefanini et al <sup>46</sup>	82.5	44	6.9	23.4	64.5	>50% stenosis in vessels $\geq$ 1.5 mm in diameter
Ussia et al <sup>47</sup>	81.2	40	NA	23.1	38.1	Prior CABG/PCI
Zivelonghi et al <sup>37</sup>	81.2	43.2	NA	28.6	42.9	>50% Stenosis

CABG indicates coronary artery bypass grafting; CAD, coronary artery disease; DMJS, Duke Myocardial Jeopardy Score; EuroSCORE, European system for cardiac operative risk evaluation; NA, not available; PCI, percutaneous coronary intervention; STS, the Society of Thoracic Surgeons risk score.

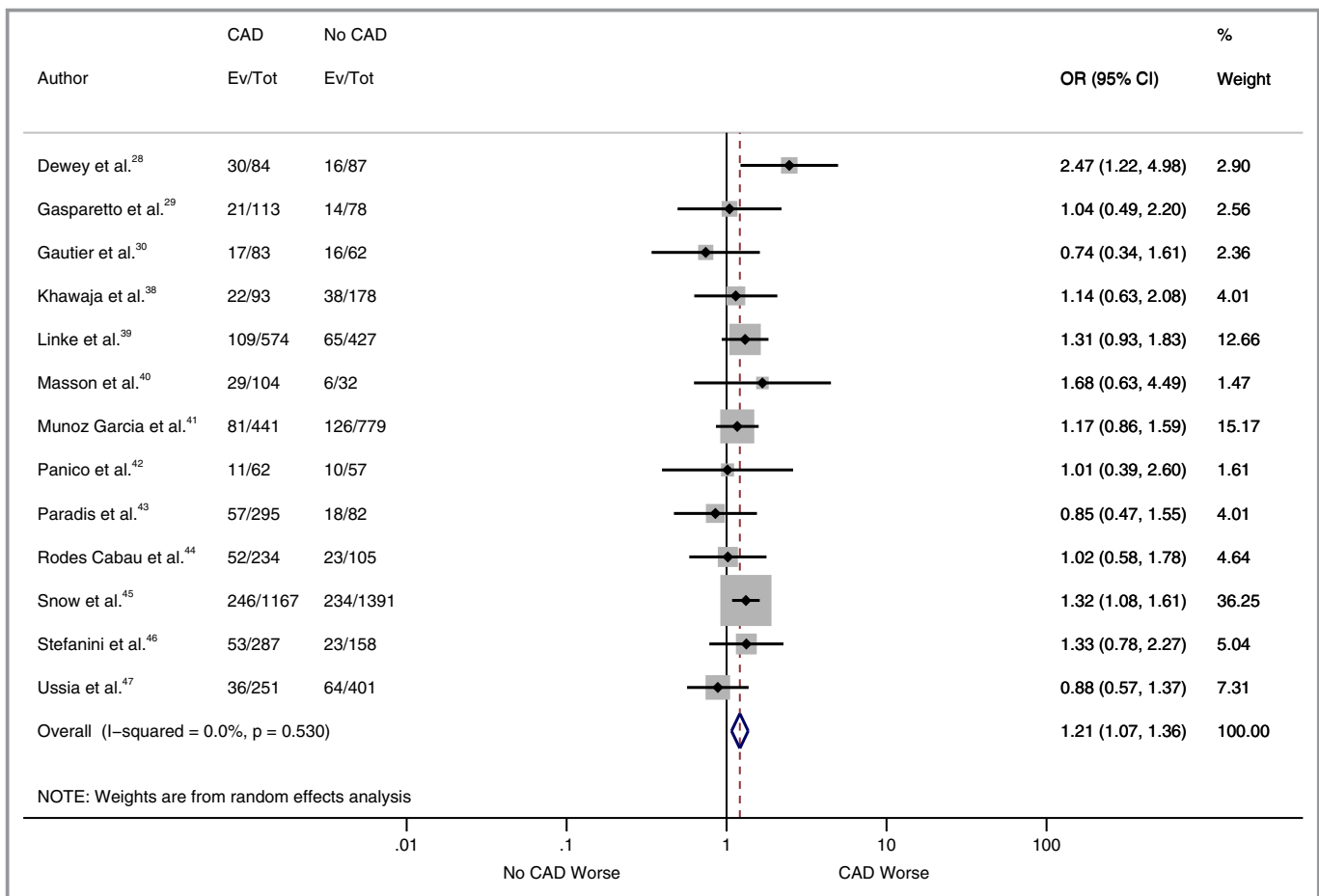
**Table 3.** Procedural (TAVR) and Revascularization Details of Included Studies

Study	Transfemoral	Transapical	Trans-Subclavian	Transaortic	Edwards SAPIEN	Core Valve	PCI (Staged/Concomitant) Prior to TAVR, No. (%)
Dewey et al <sup>28</sup>	136	35	0	0	171	0	0/84 (0)
Gasparetto et al <sup>29</sup>	128	58	5	0	104	87	39/113 (34.5)
Gautier et al <sup>30</sup>	NA	NA	NA	NA	NA	NA	11/83 (13.3)
Khawaja et al <sup>38</sup>	124	96	0	51	271	0	25/93 (26.9)
Linke et al <sup>39</sup>	880	0	95	21	0	996	Not specified
Mancio et al <sup>31</sup>	87	4	0	0	12	79	13/46 (28.3)
Masson et al <sup>40</sup>	93	43	0	0	0	136	15/104 (14.4)
Muñoz-García et al <sup>41</sup>	1155	0	65	0	0	1220	Not specified
Panico et al <sup>42</sup>	116	0	2	0	82	36	Not specified
Paradis et al <sup>43</sup>	182	195	0	0	377	0	54/295 (18.3)
Rodés-Cabau et al <sup>44</sup>	167	172	0	0	339	0	Not specified
Snow et al <sup>45</sup>	1749	NA	NA	NA	1345	1243	172/1171 (14.7)
Stefanini et al <sup>46</sup>	348	92	5	0	202	240	139/287 (48.4)
Ussia et al <sup>47</sup>	595	0	64	0	0	659	Not specified
Zivelonghi et al <sup>37</sup>	240	44	3	0	218	67	56/123 (45.5)

NA indicates not available; PCI, percutaneous coronary intervention; TAVR, transcatheter aortic valve replacement.



**Figure 2.** Forest plot comparing risk of 30-day all-cause mortality between patients with and without coronary artery disease (CAD). The diamond indicates the overall summary estimate for the analysis. The center of the diamond represents the point estimate and the width represents 95% confidence interval (CI). OR indicates odds ratio.



**Figure 3.** Forest plot comparing risk of all-cause mortality at 1 year between patients with and without coronary artery disease (CAD). The diamond indicates the overall summary estimate for the analysis. The center of the diamond represents the point estimate and the width represents 95% confidence interval (CI). OR indicates odds ratio.

screening and 4 articles were removed during data extraction. Finally, 15 publications were selected for the present study.<sup>28–30,37–47</sup> The study selection process is presented in Figure 1. According to the PRISMA statement.<sup>34</sup>

### Study Characteristics

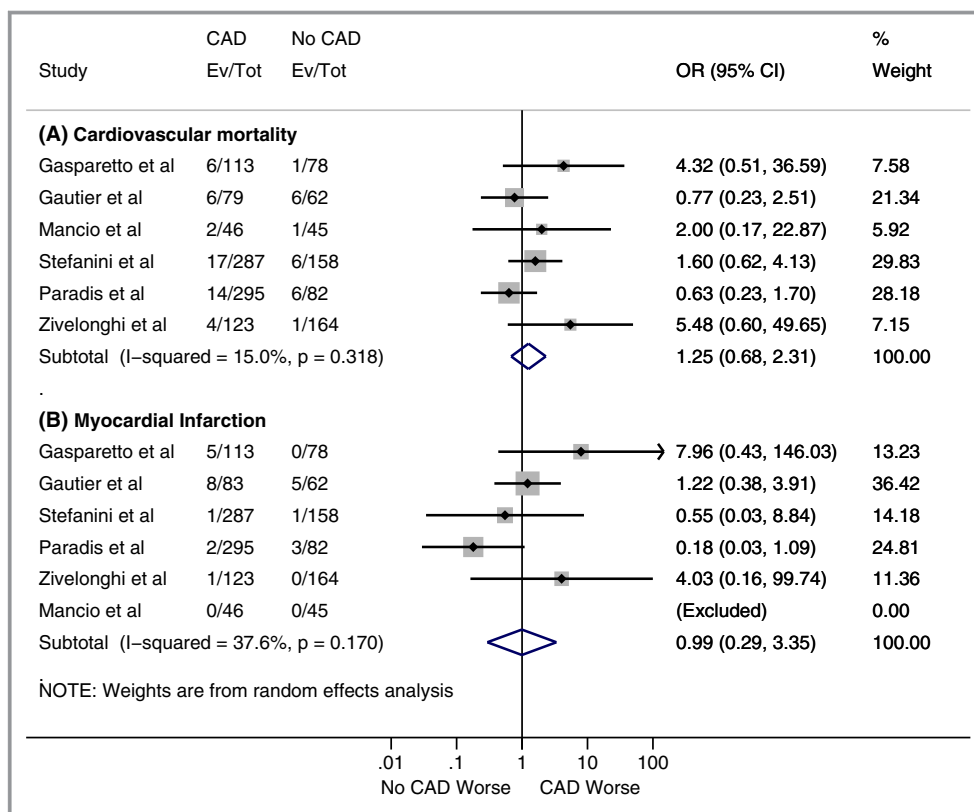
Among the included studies, the majority (9 studies) were retrospective in design. All included studies were published between 2010 and 2017. The CAD status–based comparisons were present in 11 studies, and CAD status–based outcome details were extracted in the remaining 4 studies.<sup>39,41,42,44</sup> The details of the included studies such as study design, year of publication, country of origin, and sample size are given in Table 1.

### Baseline Characteristics and Procedural Details

Table 2 shows the baseline characteristics of patients in the included studies. A total of 8013 patients who underwent

TAVR were included, with a median age of 81.3 years (79–85.1 years), and 46.6% (40–55.7%) were men. The mean logistic EuroSCORE (European system for cardiac operative risk evaluation) was >20% in 10 studies (among 13 studies that reported it). The mean Society of Thoracic Surgeons risk score was >5% in all 9 studies that reported it. Of the total of 8013 patients, 3899 (48.7%) had CAD (ranging from 30.8% to 78.2% in various studies). Even though there were slight variations in the definition of CAD among the included studies, the majority used prior coronary artery bypass grafting/percutaneous coronary intervention (PCI) or >70% stenosis (>50% for left main) as the indicator of CAD status.

Apart from Gautier et al,<sup>30</sup> all of the studies reported the procedural details of TAVR such as different valve types and the approaches used. Overall, 3121 Edwards SAPIEN/SAPIEN XT/SAPIEN 3 (39.6%) and 4763 Medtronic CoreValve (60.4%) prostheses were implanted. A total of 6000 (76.1%) prostheses were implanted via the transfemoral approach, and the remainder were implanted via the transapical/transaortic/trans-subclavian route, with transaortic delivery being the



**Figure 4.** Forest plots comparing risk of (A) 30-day cardiovascular mortality and (B) 30-day myocardial infarction between patients with and without coronary artery disease (CAD). The diamond indicates the overall summary estimate for the analysis. The center of the diamond represents the point estimate and the width represents 95% confidence interval. OR indicates odds ratio.

least followed approach among the 3 procedures. Ten of 15 studies reported the revascularization strategies used for patients with CAD. Of the total 4676 patients in those 10 studies, 2399 (51.3%) had CAD, and among those 2399 patients with CAD, 524 patients (21.8%) underwent PCI prior to TAVR. Table 3 shows the TAVR procedural details of the included studies.

**Outcomes**

The 30-day all-cause mortality was reported in 13 studies, and 1-year all-cause mortality was reported in all of the studies except Mancio et al<sup>31</sup> (reported 30-day and 2-year outcomes only) and Zivelonghi et al<sup>37</sup> (30-day outcomes only). Six studies<sup>29–31,37,43,46</sup> reported 30-day VARC end points (cardiovascular death, myocardial infarction, stroke, major bleeding, and vascular complications) based on the CAD status of patients, whereas VARC end points (cardiovascular death, myocardial infarction, and stroke) at 1 year based on the CAD status of patients were present in only 3 studies.<sup>29,43,46</sup>

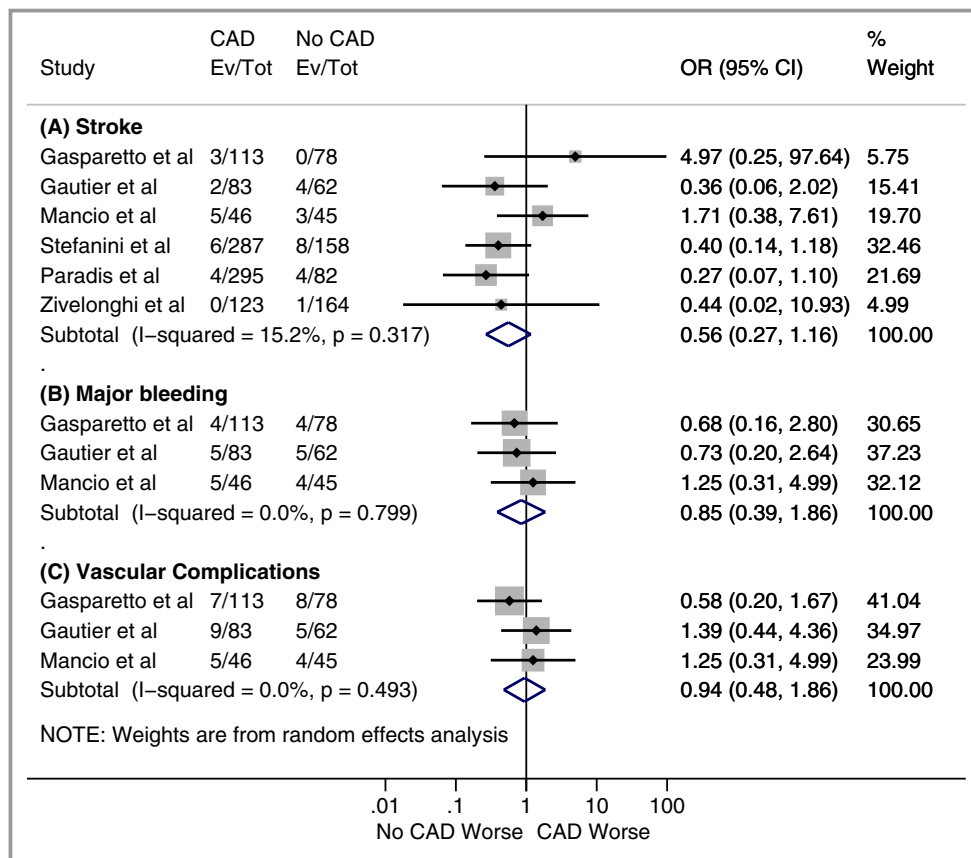
While the median 30-day all-cause mortality for CAD patients post TAVR was 7.1% (ranging from 4.4% to 13.1%), that of patients post TAVR without CAD was 5.9% (1.2–14.5%).

The median 1-year all-cause mortality for patients with CAD post TAVR was 19.75% (14.5–35.7%) and that of patients without CAD was 17.75% (14.6–25.8%).

As shown in Figure 2, our analysis showed no statistically significant difference for all-cause mortality at 30 days between patients with and without CAD, with a cumulative odds ratio of 1.07 (95% confidence interval, 0.82–1.40; *P*=0.62). However, there was a statistically significant increase in all-cause mortality at 1 year in the CAD cohort compared with the patients without CAD (Figure 3), with a cumulative odds ratio of 1.21 (95% confidence interval, 1.07–1.36; *P*=0.002). No statistically significant difference was found among patients with and without CAD in the analysis of studies, which reported other VARC end points in separate cohorts (CAD versus no CAD) at 30 days and 1 year (Figures 4 through 6).

**Publication Bias**

Publication bias in the primary outcome of interest (all-cause mortality at 30 days and 1 year) was initially evaluated graphically with funnel plots (Figures S1 and S2), which showed some asymmetry in both outcomes. Egger’s



**Figure 5.** Forest plots comparing (A) 30-day risk of stroke, (B) 30-day risk of major bleeding, and (C) 30-day risk of vascular complications between patients with and without coronary artery disease (CAD). The diamond indicates the overall summary estimate for the analysis. The center of the diamond represents the point estimate and the width represents 95% confidence interval (CI). OR indicates odds ratio.

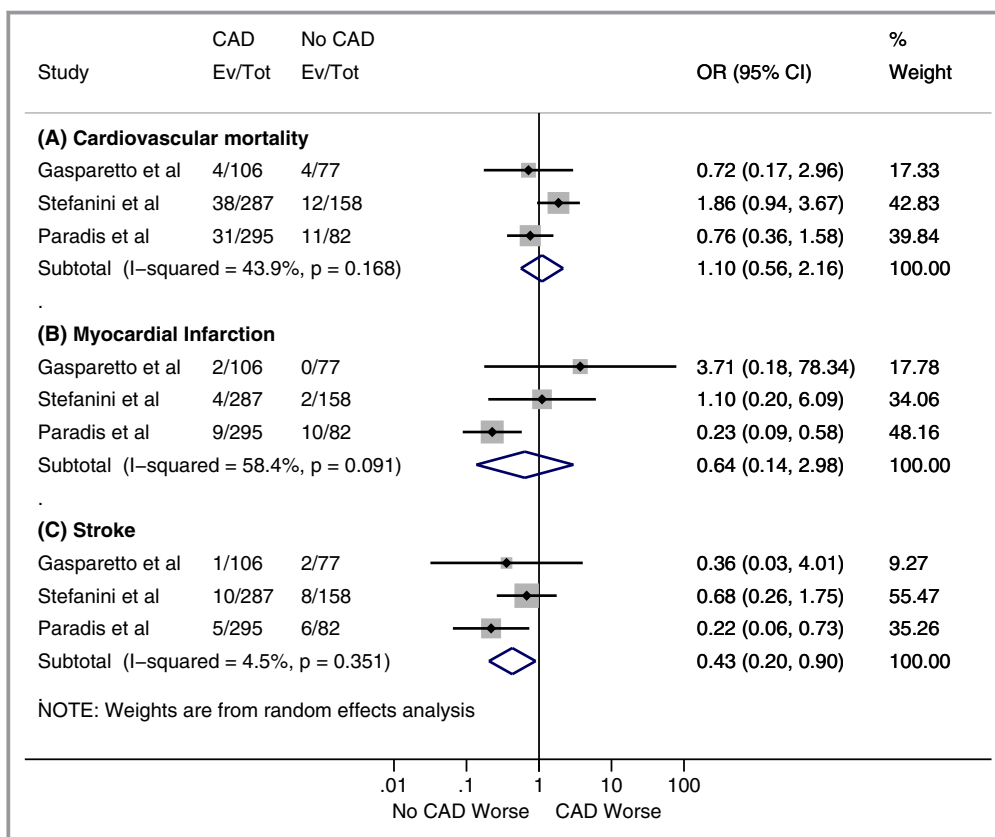
regression asymmetry was applied for quantitative assessment and generated *P* values of 0.21 (30-day all-cause mortality) and 0.44 (1-year all-cause mortality), indicating that conclusions were not altered because of publication bias.

## Discussion

To our knowledge, this is the first meta-analysis with more than 5000 patients to examine the impact of CAD on TAVR outcomes. This meta-analysis has 2 main findings. First, although there was no significant difference for all-cause mortality at 30 days, there was a significant increase in all-cause mortality at 1 year in the CAD group, compared with patients without CAD. Second, procedural complications including cardiovascular mortality, myocardial infarction, stroke, bleeding, and vascular complications are no different based on CAD status. Notably, we identified important limitations of the data, which are nonuniformity in the CAD definitions used in RCTs, registries, and large observational studies and absence of stratified TAVR outcomes based on the CAD status of patients in RCTs and major registries.

The first published study on the impact of CAD in TAVR outcomes was by Dewey et al<sup>28</sup> in 2010. They reported the outcomes on 171 patients based on CAD status and found that presence of CAD was the most significant factor associated with 30-day mortality with an odds ratio of 10.1%. Since then, most other studies have failed to show any statistically significant difference between the cohorts for 30-day mortality. With 1-year follow-up, reports of mortality varied widely. Dewey et al<sup>28</sup> and Mancio et al<sup>31</sup> found significantly higher mortality in the CAD cohort. On the contrary, many other studies did not show any statistically significant difference between the groups. One approach was to classify patients with CAD according to Syntax scores. Based on this stratification, Stefanini et al<sup>46</sup> and Khawaja et al<sup>38</sup> showed that it is the complexity and severity of CAD (higher Syntax scores) that have more prognostic implications in the TAVR outcomes rather than the mere presence of CAD. While both studies showed higher mortality at 1 year, only Khawaja et al demonstrated higher mortality at 30 days as well. These results were condensed into a meta-analysis by Taha et al,<sup>33</sup> which showed that a residual or baseline Syntax





**Figure 6.** Forest plots comparing (A) 1-year risk of cardiovascular mortality, (B) 1-year risk of myocardial infarction, and (C) 1-year risk of stroke between patients with and without coronary artery disease (CAD). The diamond indicates the overall summary estimate for the analysis. The center of the diamond represents the point estimate and the width represents 95% confidence interval (CI). OR indicates odds ratio.

score  $\leq 10$  does not affect the clinical outcomes after TAVR. D’Ascenzo et al<sup>32</sup> were the first to perform a pooled analysis on the prognostic role of CAD in TAVR outcomes. Their analysis revealed that even though CAD represented a common amnestic finding in patients undergoing TAVR, it does not affect the midterm outcomes after TAVR procedures.

The benefits of revascularization and the impact of nonrevascularized myocardium in TAVR outcomes is an ongoing debate. Kleczynski et al<sup>48</sup> showed that incomplete coronary revascularization may be an independent predictor of all-cause mortality after TAVR; however, on the contrary, Van Meighem et al<sup>49</sup> state that complete revascularization is not a prerequisite for success in current TAVR practice. Even though Goel et al<sup>50</sup> showed that PCI can be performed in patients with severe symptomatic AS and CAD without an increased risk of short-term mortality, considerable uncertainty persists regarding the timing of revascularization (concomitant versus staged). This meta-analysis highlights the need for further randomized studies to find the optimal revascularization strategy for CAD in TAVR candidates and to ascertain the impact of nonrevascularized myocardium in TAVR outcomes. The results of the ongoing ACTIVATION

(Percutaneous Coronary Intervention Prior to Transcatheter Aortic Valve Implantation) RCT<sup>51</sup> (PCI prior to transcatheter aortic valve implantation) in this regard are anxiously awaited.

**Limitations**

Even though our large meta-analysis is able to provide some indications regarding the impact of CAD on TAVR outcomes, there are a few limitations to our analysis. First, this was a meta-analysis performed on study-level data and it lacks individual patient-level data. Second, there was nonuniformity of CAD definitions among the included studies. Third, only limited studies reported all of the VARC or secondary end points at 30 days (6 studies) and 1 year (3 studies) based on the CAD status of the patients and, hence, results from these analyses should be extrapolated with caution. In addition, we do not have sufficient granular data to study other details such as how the impact of syntax scores might vary or how unprotected left main coronary artery disease (and/or ostial disease of the left anterior descending coronary artery) might impact the outcomes separately compared with other types of CAD.

## Conclusions

The present meta-analysis of 15 studies comparing mortality in patients with and without CAD undergoing TAVR did not find a statistically significant difference in mortality at 30 days. However, there was a significant increase in mortality at 1 year in the patients with CAD undergoing TAVR, compared with patients who did not have concomitant CAD. There are a few directions we can take from here. First, since CAD has a prognostic role in the survival of patients, it is important to revisit revascularization strategies that could be implemented. However, data are limited on the safety and efficacy of revascularization in these patients and further prospective research is needed to validate these conclusions. Second, there is need for additional randomized studies to investigate the impact of pre-TAVR PCI in the outcomes after TAVR. Third, more data are needed to determine whether a staged or simultaneous PCI prior to TAVR is preferable. Finally, if the studies show favorable results with staged PCI, further studies will be required to elucidate the optimal time gap between PCI and TAVR.

## Disclosures

None.

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# **SUPPLEMENTAL MATERIAL**

**Table S1. Assessment of study quality using the New-castle Ottawa scale.**

Author(s)	Selection				Comparability		Exposure			Total stars
	S1	S2	S3	S4	C1	C2	E1	E2	E3	
<i>Carlo Zivelonghi et al<sup>1</sup></i>	*	*	*	*	*	*	*	-	-	7
<i>Dewey et al<sup>2</sup></i>	*	*	*	*	*	*	*	*	*	9
<i>Gasparetto et al<sup>3</sup></i>	*	*	*	*	*	*	*	*	*	9
<i>Gautier et al<sup>4</sup></i>	*	*	*	*	*	*	*	*	*	9
<i>Khawaja et al<sup>5</sup></i>	*	*	*	*	*	*	*	*	*	9
<i>Linke et al<sup>6</sup></i>	*	*	-	*	-	-	*	*	*	6
<i>Mancio et al<sup>7</sup></i>	*	*	*	*	*	*	*	*	-	8
<i>Masson et al<sup>8</sup></i>	*	*	*	*	*	*	*	*	*	9
<i>Munoz Garcia et al<sup>9</sup></i>	*	*	-	*	-	-	*	*	*	6
<i>Panico et al<sup>10</sup></i>	*	*	-	*	-	-	*	*	*	6
<i>Paradis et al<sup>11</sup></i>	*	*	*	*	*	*	*	*	*	9
<i>Rodes-Cabau et al<sup>12</sup></i>	*	*	-	*	-	-	*	*	*	6
<i>Snow et al<sup>13</sup></i>	*	*	*	*	*	*	*	*	*	9
<i>Stefanini et al<sup>14</sup></i>	*	*	*	*	*	*	*	*	*	9
<i>Ussia et al<sup>15</sup></i>	*	*	*	*	*	*	*	*	*	9

Representativeness of the exposed cohort (S1); selection of the non-exposed cohort (S2); ascertainment of exposure (S3); demonstration that the outcome of interest was not present at the start of the study (S4); comparability (C1 and C2); assessment of outcome (E1); was follow-up long enough for outcomes to occur (E2); adequacy of follow-up of cohorts (E3)

Figure S1. Funnel plot for all-cause mortality at 30-day after TAVR.

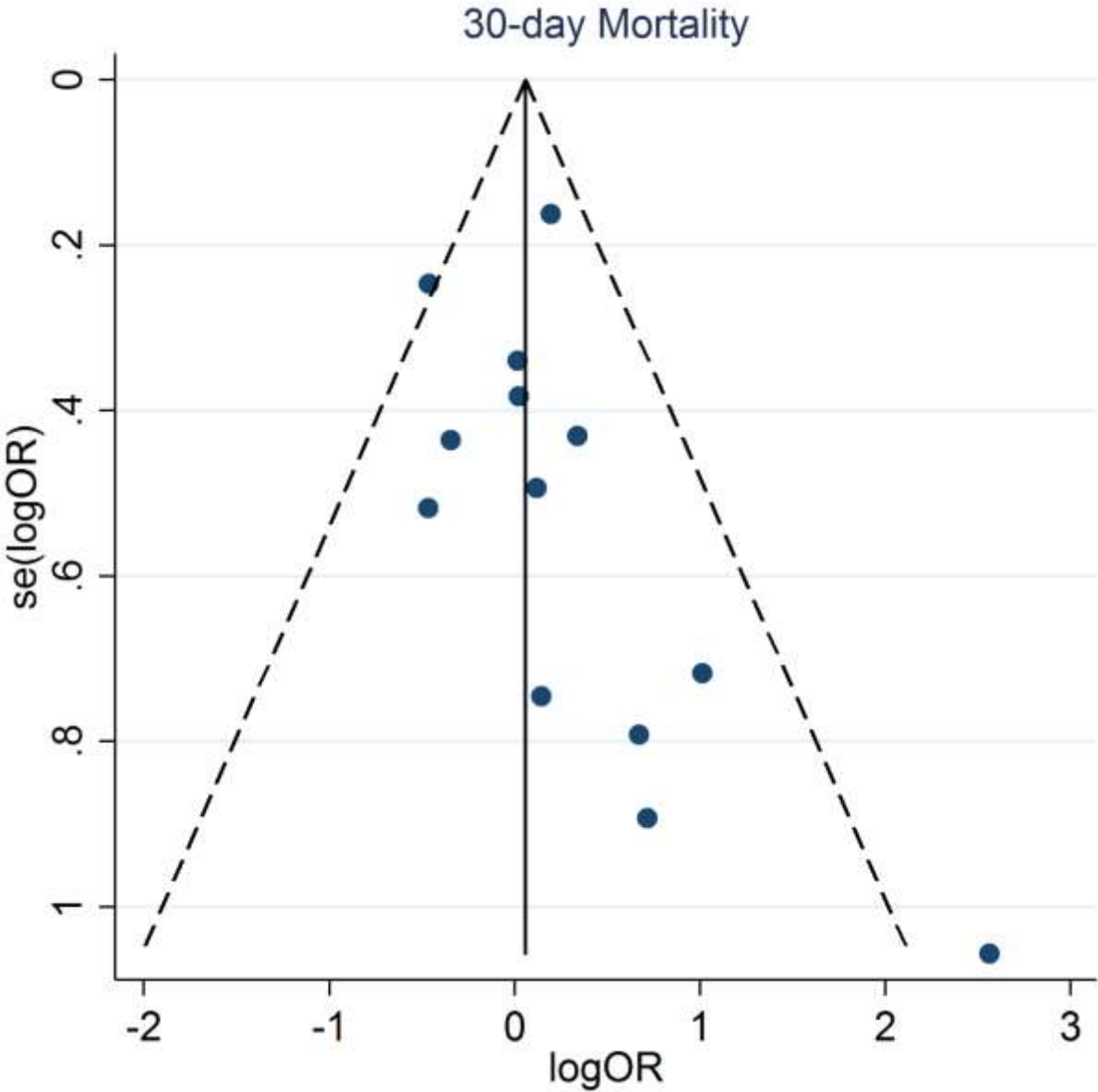


Figure S2. Funnel plot for all-cause mortality at 1-year after TAVR.

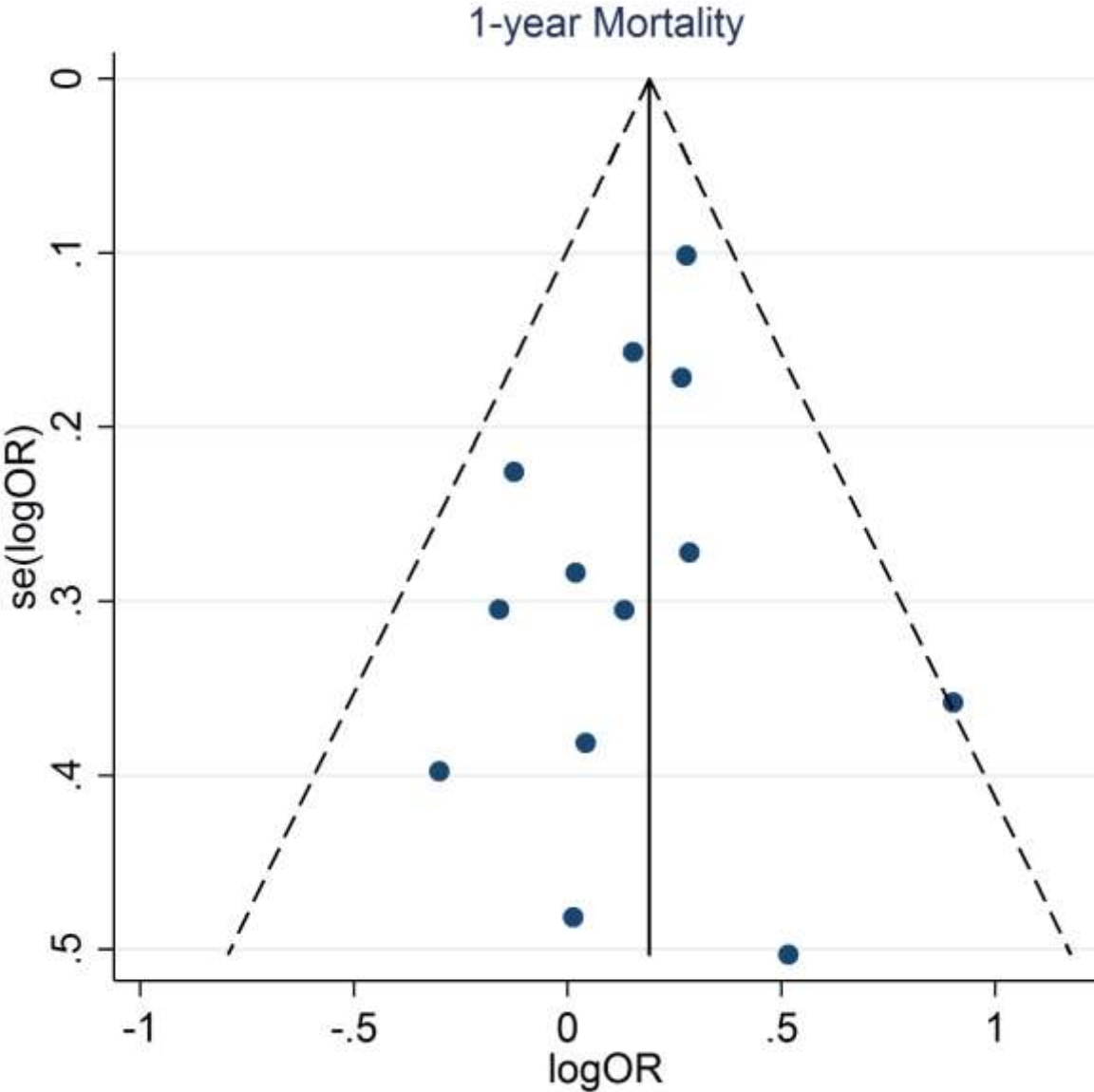


Figure S3. Sensitivity analysis for all-cause mortality at 30-day

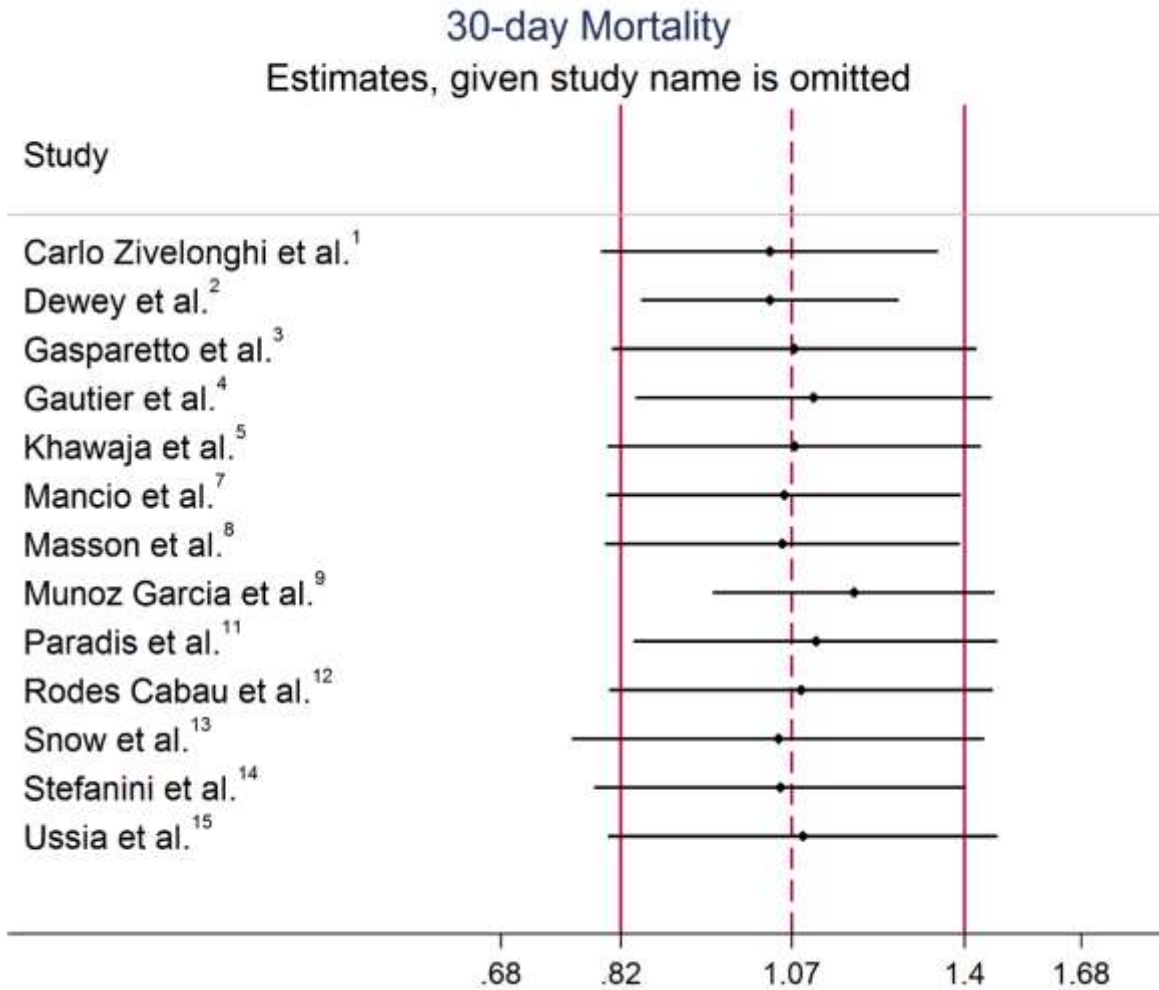
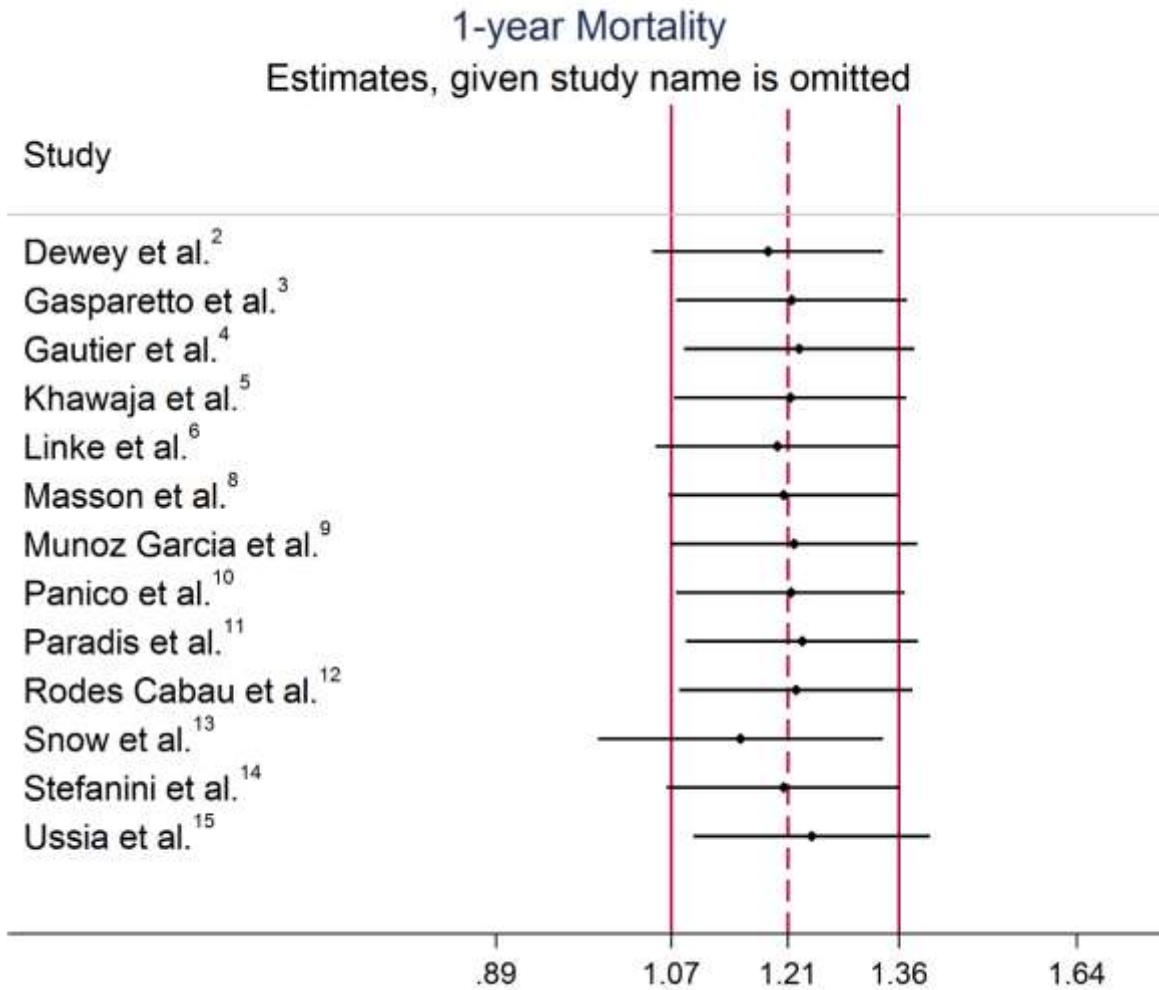




Figure S4. Sensitivity analysis for all-cause mortality at 1-year



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