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Thirty-day readmissions in surgical and transcatheter aortic valve replacement: A systematic review and meta-analysis

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ABSTRACT

Background: The 30-day all-cause readmission rate after surgical aortic valve replacement (SAVR) and transcatheter aortic valve replacement (TAVR) vary substantially. We conducted a systematic review and meta-analysis to examine the overall incidence, causes, and risk factors of 30-day all-cause readmission rate after SAVR and TAVR.
Methods: Eight medical research databases were searched; Cochrane, Medline, Embase, UpToDate, PROSPERO, National Guideline Clearinghouse, SweMed and Oria. We followed The Preferred Reporting Items for Systematic reviews and Meta-analysis (PRISMA) for this study.
Results: Thirty-three articles were included in the systematic review, 32 of which were appropriate for the meta-analysis. Overall, 17% (95% CI: 16–18%) of patients in the SAVR group, and 16% (95% CI: 15–18%) in the TAVR groups were readmitted within 30 days. Heart failure, arrhythmia, infection, and respiratory problems were the most frequent causes of all-cause readmission after SAVR and TAVR. Most frequent reported prior risk factors for all-cause readmission following TAVR were diabetes, chronic lung disease/chronic obstructive pulmonary disease, atrial fibrillation, kidney problems, and transapical approach/nonfemoral access. For SAVR, no risk factors for 30-day all-cause readmission were reported in the literature to date.
Conclusion: In conclusion, the overall proportion of 30-day all-cause readmission after SAVR and TAVR are high. Interventions to prevent avoidable readmissions ought to be developed and implemented.

1. Introduction

Today, surgical aortic valve replacement (SAVR) is the standard treatment for patients with operable severe aortic stenosis (AS) [1,2]. Surgical treatment for AS improves survival and enhances patients' quality of life [3–5]. In older patients (>75 years) with symptomatic severe AS and who are at high surgical risk, transcatheter aortic valve replacement (TAVR) is the established alternative to SAVR [1,6,7]. TAVR yields favorable outcomes compared to medical treatment [8].

Arrhythmias, infections, or other complications after SAVR and TAVR are relatively frequent [9] and often require readmission to the hospital. Unplanned readmissions are costly for individuals and the public and negatively affect patients' quality of life and rehabilitation [10]. Furthermore, it increases the risk for hospital-acquired complications [10]. In the literature, it is reported that the incidence of 30-day all-cause readmissions after SAVR and TAVR is about one out of every four discharges results in a readmission [9,11,12]. However, reported readmission rates vary substantially. Hence, the precise estimation of the magnitude of the problem remains unaddressed. Moreover, risk factors for and causes of readmissions following SAVR and TAVR have not yet been systematically scrutinized. This information is important, because it can guide clinicians, hospital administrators, and policy-makers in developing and implementing programs to improve the quality of care for SAVR and TAVR patients following hospital discharge. This will be even more important in the coming years, as the increasing trend in

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life expectancy translates to more SAVR and TAVR procedures [5,13–15]. An accurate estimation of readmission rates and risk factors leading up to them is also relevant for researchers in the area of valve replacement, because resulting data could be used for benchmarking and would enable researchers to calculate the sample sizes needed for future trials that assess interventions to reduce readmissions.

These issues prompted us to conduct a systematic literature review and meta-analysis. Our aims were (i) to estimate the overall 30-day all-cause readmission rate in patients following SAVR and TAVR, and (ii) to identify risk factors for and causes of 30-day all-cause readmissions after discharge of these patients.

2. Methods

The protocol for this systematic literature review and meta-analysis was prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO; no. 42016032670). The Preferred Reporting Items for Systematic reviews and Meta-analysis (PRISMA) guidelines were used. [16].

2.1. Literature search

The first author (SOD) developed the search strategy in collaboration with an experienced research librarian. The following databases were consulted: Cochrane (Cochrane database of Systematic Reviews, Cochrane Central Register of Controlled Trials, Cochrane Methodology Register, NHS Economic Evaluation Database, Health Technology Assessment Database and Other Reviews); Medline (accessed through PubMed; http://www.ncbi.nlm.nih.gov/pubmed); Embase; UpToDate; PROSPERO; National Guideline Clearinghouse; SveMed; and Oria.no. In addition, reference lists of candidate articles were screened to find additional references missed by our search strings (i.e., snowball method). Details on the search terms and the search strings can be found in online Table 2. Publication date limits were set from database inception to October 8, 2017. Language search was limited to English, and the Scandinavian languages. If necessary information was missing, we emailed the authors to obtain additional information.

Articles were eligible for inclusion if they reported study results on 30-day all-cause readmission following SAVR and TAVR procedures. For the present review, we defined 30-day all-cause readmission as an unplanned readmission for any reason within 30 days after discharge [17]. We excluded articles that reported results from studies dealing with multiple valves or specific diseases/conditions related to the SAVR and TAVR treatment. We also excluded articles that reported results from studies dealing with procedural or cardiac-related causes or other specific causes for readmissions, because they did not address all-cause readmissions. One researcher (SOD) screened all the records identified by title, and two researchers (SOD/IL) assessed the full-text candidate articles of the first screening using the inclusion criteria listed above. Before our review was completed, we consulted the databases several more times to check whether we had missed any eligible articles (Online Table 2).

2.2. Data abstraction

Data from included articles were extracted onto a standard form according to an a priori protocol. Extracted data included information on study-related characteristics, patient-related characteristics, and main findings. The study-related variables included the article's year of publication; country where the study took place; representativeness of the cohort (single-center, multicenter, or nationwide data); whether the cohort was prospectively or retrospectively studied; and whether 30-day all-cause readmission was reported as a primary or secondary endpoint. Patient-related variables included mean age and proportion of the study population that were males. The results we were interested in, and what we extracted, pertained to the total sample size reported in the article and the number of events (30-day all-cause readmission).

2.3. Quality of the studies

Two researchers independently assessed the quality of the studies (SOD/IL) using the Newcastle-Ottawa Scale (NOS). NOS is an established scale for assessment of cohort studies [18]. For studies with no relevant data accordingly to NOS items for appraisal, we noted them as "not relevant" (NR). Consensus by discourse resolved disagreements.

2.4. Statistical analysis

To calculate an overall incidence of 30-day all-cause readmission, we used a random effects meta-analysis of single proportions according to the DerSimonian-Laird method [19]. We used the Freeman-Turkey double arcsine transformation to stabilize the variance [20]. Heterogeneity between studies was assessed with the Cochran's Q test, and its magnitude was evaluated by the I^2 statistic. This describes the proportion of total variation due to heterogeneity rather than chance [21]. To investigate possible sources of heterogeneity, we performed analyses stratified by the study characteristic, prospective versus retrospective timing of the study, representativeness of the cohort (single- versus multi-center), country where the study took place (USA versus others), and whether or not 30-day all-cause readmission was reported as the primary endpoint. Further univariable random effects meta-regression analyses were used to examine whether estimates were affected by the study-level covariates. Source of heterogeneity was considered to be important if the covariate decreased between-study variance. The estimate of $\tau 2$ in the presence of a covariate versus its omission allows the proportion of the heterogeneity variance explained by the covariate to be calculated. For power consideration, we determined that a minimum of 10 studies per covariate was required in a single model of meta-regression [22]. An additional sensitivity analysis was conducted by iteratively omitting one study at a time from the meta-analysis and assessing its influence on the overall results [23]. Publication bias was evaluated visually by funnel plots and further assessed using a test of asymmetry (Egger's test of the intercept) applied to funnel plots [24].

All statistical analyses were performed with STATA 14.0 (STATA Data Analysis and Statistical Software; StataCorp LP, College Station, TX, USA.)

3. Results

3.1. Included articles

One article was excluded because it reported results from another article we had already included. Another article was excluded because the mean age of participants in the study was >80 years. We identified a total of 6867 candidate articles (Fig. 1). After duplicates were removed, we reviewed the title and abstract of 6848 articles, 6588 of which were not relevant for our purposes. The remaining 260 articles were assessed for eligibility based on full-text review; 227 were deemed ineligible. We included 33 articles in the systematic review and 32 in the meta-analysis, 12 on the SAVR population and 20 on the TAVR population.

3.2. Study characteristics in included articles

The characteristics of the studies included are presented in Online Table 1. We identified 12 cohort studies [14,25–35] on SAVR, all of which were published from 2008 to 2017. Ten studies used a retrospective design, 8 studies were conducted in the USA, and 7 designated 30-day all-cause readmission as the primary endpoint. Overall, 558,396 patients were included in our review of SAVR studies, yielding 111,909 readmissions. Mean age of the included patients ranged from 61 to 81 years; the proportion of males ranged from 48% to 71%.

For articles reporting TAVR results, we identified 20 cohort studies [6,7,11–13,28,34–47], which were published from 2015 to2017. Sixteen studies employed a retrospective design; 11 studies were performed in the USA; and 11 studies had 30-day all-cause readmission as a primary endpoint. In these 20 studies, 109,730 patients were included, yielding 21,192 readmissions. Mean age ranged from 80.7 to 84.3 years; the proportion of males ranged from 34% to 57%.

3.3. Quality assessment and publication bias

The overall quality of studies in the included articles was moderate on the NOS. Many of these retrospective studies failed to provide descriptions of how the outcome was derived and how it was validated. Thus, this produced an overall assessment of moderate quality (online Table 3). We found no publication bias, neither in SAVR studies (Egger test, $p = 0.255$) nor in TAVR studies (Egger test, $p = 0.140$). Funnel plots are presented in online material (Online Fig. 1).

3.4. Incidence of 30-day all-cause readmission rate following SAVR or TAVR

The incidence of 30-day all-cause readmission rate for SAVR ranged from 7 to 23%, and for TAVR, from 5 to 27%. The pooled estimated proportion of the 30-day all-cause readmission after SAVR was 17% (95% CI: 16–18), with substantial heterogeneity ($I^2 = 98.44\%$) (Fig. 2). Subgroup analysis of heterogeneity in the SAVR population revealed a significantly higher readmission rate in multicenter studies (20%) compared to single-center studies (12%) (Table 1). Regional differences were also observed, with higher readmission rates in the USA (18%) compared to other countries (14%). A lower incidence of readmissions

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