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A meta-analysis and systematic review of transcatheter versus open surgical management of paravalvular leaks

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ADMINISTRATIVE INFORMATION

Support - None reported.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 4 March 2025 and was last updated on 4 March 2025.

INTRODUCTION

Review question / Objective We performed a systematic review and meta-analysis that compared outcomes following transcatheter and surgical management of paravalvular leaks in patients with prosthetic aortic or mitral valves. Primary endpoints included all-cause mortality at 30 days and one year, stroke or transient ischemic attack (TIA) immediately and at 30 days and one year, and life-threatening, disabling, or major bleeding — as defined by the Bleeding Academic Research Consortium — immediately and at 30 days. Secondary endpoints encompassed readmission for heart failure at one year, symptomatic improvement — defined as a reduction of at least one grade in the NYHA functional class and/or improvement in haemodynamic assessment — at one year and long term, device or valve endocarditis at one year, acute kidney injury (AKI) at 30 days, major and minor vascular complications at 30 days, residual PVL (procedural success) immediately and at 30 days, conversion to open surgery at 30 days and one year, and pacemaker insertion at 30 days.

Rationale There is a need within the cardiology and cardio-thoracic community to update the literature regarding the best approach for the treatment of PVL. Owing to a lack of direct comparisons between OSR and transcatheter approaches, it is important to remain up to date with the current literature in order to comment on the superiority of either approach in the short-,medium- and long-run. Although complications from OSR often stem from its invasive nature, a comparison of safety and efficacy with its less invasive counterpart (transcatheter repair) is crucial and will form the basis of a systematic review. Based on the outcome of this review, we are looking to inform the stakeholders (health service providers and patients) and guidelines for the management of PVL.

Condition being studied Haemodynamically significant paravalvular leak is a rare yet progressive and serious complication of heart valve replacement that occurs in 2–10 % and 7–17 % of aortic and mitral valve replacements

respectively, leading to symptomatic heart failure and hemolysis.

METHODS

Search strategy Electronic searches:

We aimed to identify all relevant studies regardless of language, publication year or publication status. The following databases were searched: We aimed to identify all relevant studies regardless of language, publication year, or publication status. To achieve this, we conducted comprehensive searches across multiple databases, including MEDLINE (Ovid MEDLINE Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE Daily, and Ovid MEDLINE), Embase (Ovid), CINAHL (Ebsco), and AMED. A draft search strategy was designed for each of the five databases.

Searching other resources:

For additional reference, we reviewed the reference lists of all relevant studies identified through the electronic search. We also conducted citation searches on relevant review articles. To explore studies that had not yet been published, we searched OpenGrey.

Participant or population Participants aged 18 years or more with echocardiographically diagnosed PVL and indication for intervention (OSR or transcatheter) were included. These indications were either intractable haemolysis and/or HF as per the 2020 ACC/AHA Guideline for the Management of Patients with Valvular Heart Disease.

Intervention Our intervention was transcatheter management (repair and/or ViV procedure) of PVL. Although a range of site-specific devices and techniques were used to manage PVL, we planned to include all types in this review.

Comparator Our comparator was open surgical repair or replacement of PVL.

Study designs to be included We planned to include either randomised controlled trials or quasi-randomised controlled trials that compared transcatheter repair to either OSR or conservative management of PVL. However, due to the relatively small number of PVL cases, we anticipated that the number of such trials would be insufficient. Therefore, we included comparative retrospective observational studies. Only studies with 11 or more participants, as well as those studies published in English or with an available English translation, were considered.

Eligibility criteria None reported.

Information sources Electronic searches:

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Searching other resources:

For additional reference, we reviewed the reference lists of all relevant studies identified through the electronic search. We also conducted citation searches on relevant review articles. To explore studies that had not yet been published, we searched OpenGrey.

Main outcome(s) The selection of outcomes was guided by the document entitled 'Clinical Trial Principles and Endpoint Definitions for Paravalvular Leaks in Surgical Prosthesis' by the PVL Academic Research Consortium(6). Primary endpoints included all-cause mortality at 30 days and one year, stroke or transient ischemic attack (TIA) immediately and at 30 days and one year, and life-threatening, disabling, or major bleeding — as defined by the Bleeding Academic Research Consortium — immediately and at 30 days. Secondary endpoints encompassed readmission for heart failure at one year, symptomatic improvement — defined as a reduction of at least one grade in the NYHA functional class and/or improvement in haemodynamic assessment — at one year and long term, device or valve endocarditis at one year, acute kidney injury (AKI) at 30 days, major and minor vascular complications at 30 days, residual PVL (procedural success) immediately and at 30 days, conversion to open surgery at 30 days and one year, and pacemaker insertion at 30 days.

Additional outcome(s) We assessed heterogeneity through visual inspection of forest plots and the Chi² test for heterogeneity. The heterogeneity of the overall results for outcomes

was evaluated using Chi^2, I^2, and Tau^2 statistics, in line with the Cochrane Handbook for Systematic Reviews of Interventions. The Handbook suggests that 30% to 60% may indicate moderate heterogeneity, 50% to 90% may suggest substantial heterogeneity, and 75% to 100% may indicate considerable heterogeneity(33). If clinical heterogeneity was significant enough to suggest differing treatment effects across studies, or if substantial statistical heterogeneity was identified, we planned to use a random-effects meta-analysis to provide an overall summary where the mean treatment effect would be clinically relevant.

Data management Selection of studies

Two review authors (SH and ME) independently screened all titles and abstracts identified from the literature searches to identify studies that potentially met the inclusion criteria. The full texts of all studies selected by at least one review author were subsequently retrieved. The same review authors independently screened the full-text articles for inclusion or exclusion. We resolved any differences in study selection by discussion or, when necessary, by consulting a third review author (WT). A list of all studies excluded at the full-text review stage, along with reasons for exclusion, are presented in Table 1 in the supplementary material. The screening and selection processes are described using the adapted PRISMA flow diagram(28,29).

Data extraction and management

Two reviewers (SH and ME) independently extracted data from eligible studies using the 'Data Extraction and Assessment Form' provided by Cochrane(30). Any discrepancies were resolved through discussion or, if needed, by consulting a third review author (WT). One review author (SH) entered all extracted data into Review Manager 5, while a second reviewer (ME) verified the accuracy and consistency of the data against the extraction sheets(31). The baseline characteristics of participants, methods — including the type of intervention (open surgical repair and/or transcatheter management) — and primary and secondary outcomes are summarised in Table 2 of the supplementary material.

Quality assessment / Risk of bias analysis Two review authors (SH and ME) separately evaluated the quality of risk of bias for all included studies through use of the Newcastle-Ottawa Scale (NOS) (32). This scoring system assesses studies based on three main criteria: study group selection, comparability of groups, and outcome of interest. Each study is awarded a number of stars for each criterion, with a higher total star count representing higher methodological quality (see Table 3 in the supplementary material). In our analysis, NOS scores were classified according to the total number of stars as low (1-3), moderate (4-6) or high (7-9) quality.

Strategy of data synthesis We performed statistical analyses using Review Manager 5, by adopting a fixed-effect meta-analysis for synthesising data where it was reasonable to assume that studies were estimating the same underlying treatment effect(31).

Subgroup analysis None reported.

Sensitivity analysis A sensitivity analysis was performed to investigate potential sources of inconsistency for procedural success, by only including studies that used endpoints as defined by the "Clinical Trial Principles and Endpoint Definitions for Paravalvular Leaks in Surgical Prosthesis: An Expert Statement" from the Journal of the American College of Cardiology.

Language restriction Only studies published in English or with an available English translation, were considered.

Country(ies) involved United Kingdom.

Keywords paravalvular leak, closure devices, transcatheter, surgical repair, surgical replacement.

Dissemination plans We aim to publish this research and present it at relevant conference(s).

Contributions of each author

Author 1 - Syedah Aleena Haider - Author 1 designed and drafted the paper, screened abstracts and full-text articles and performed statistical analysis.
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