INPLASY PROTOCOL

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None declared.

Transcatheter Mitral Valve Replacement for Degenerated Mitral Valve Bioprostheses, Failure of Mitral Valvuloplasty and Native Valve with Severe Mitral Annulus Calcification: A Systematic Review and Meta-Analysis

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Review question / Objective: P: Patients with degenerated mitral valve bioprostheses, failure of mitral valvuloplasty and native valve with severe mitral annulus calcification requiring transcatheter mitral valve replacement. I / C: Compare the feasibility of applying TMVR to patients with degenerated mitral valve bioprostheses (valve-in-valve, ViV), failure of mitral valvuloplasty (valve-in-ring, ViR), and serious mitral annulus calcification (vale-in-MAC, ViMAC). O: All-cause Mortality within 30 days, Bleeding, Bleeding, Conversion to Cardiac surgery, LVOT obstruction, Stroke, Vascular complication, Vascular complication, Need for second valve implantation, Postprocedural Mitral Regurgitation [Trace / None, 1 (+), 2 (+) or greater]. S: Controlled Trial (RCT) or cohort study. Objective: We conducted a systematic review and meta-analysis to evaluate the feasibility of TMViV, TMViR, and TMViMAC, and suggest the outcomes that require attention in clinical treatment. At the same time, some possible solutions to complications are summarized to provide new treatment ideas for the clinic.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 31 March 2021 and was last updated on 31 March 2021 (registration number INPLASY202130113).

INTRODUCTION

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C: Compare the feasibility of applying TMVR to patients with degenerated mitral valve bioprostheses (valve-in-valve, ViV), failure of mitral valvuloplasty (valve-in-ring, ViR), and serious mitral annulus calcification (vale-in-MAC, ViMAC). O: All-cause Mortality within 30 days, Bleeding, Bleeding, Conversion to Cardiac surgery, LVOT obstruction, Stroke, Vascular complication, Vascular complication, Need for second valve implantation, Postprocedural Mitral Regurgitation [Trace / None, 1 (+), 2 (+) or greater]. S: Controlled Trial (RCT) or cohort study. Objective: We conducted a systematic review and meta-analysis to evaluate the feasibility of TMViV, TMViR, and TMViMAC, and suggest the outcomes that require attention in clinical treatment. At the same time, some possible solutions to complications are summarized to provide new treatment ideas for the clinic.

Rationale: The degenerative changes of the mitral valve bioprosthesis (valve-in-valve, ViV) and the failure of surgical rings (valve-in-ring, ViR) were largely due to the rise in life expectancy of the elderly and the short-term durability of bioprostheses compared to the mechanical mitral valve. After Cheung first reported transcatheter mitral valve-in-valve (TMViV) implantation in 2009 and De Weger performed transcatheter mitral valve-in-ring (TMViR) replacement for the first time in 2011, more and more patients have received these two types of surgery and benefited from them. Although compared with traditional surgery, patients have achieved some efficacy after using TMVR, the ultimate results were still unsatisfactory due to the patients' relatively poor baseline characteristics and various comorbidities, especially patients who received transcatheter mitral valve-in-mitral annulus calcification (TMViMAC). At one time, some clinicians doubted the feasibility of TMVR. The earliest experience of TMVR with severe mitral annulus calcification (MAC) was collected in the TMVR of the MAC Global Registry, reporting a mortality rate of 25% at 30 days. A follow-up study from the multicenter TMVR registry reported a 30-day mortality rate of 34.5%. In the existing reports, we found that the relatively high mortality rate was due to severe comorbidities and technical challenges related to calcium load. Although the use of transcatheter mitral valve replacement for patients with severe mitral valve ring calcification still had a high mortality rate, it must be admitted that compared with traditional mitral valve surgery, TMVR had become an urgent and preferred treatment for high-risk severe mitral valve disease.

Condition being studied: Mitral valve disease is abnormal valve structure or function caused by mucoid degeneration, congenital, degenerative disease and inflammation. And from the latest AHA (American Heart Association) statistics, the incidence and mortality of mitral valve disease are increasing year by year. Patients suffering from severe mitral valve disease (insufficiency, regurgitation, etc.) were increasingly repairing with annuloplasty rings or using prosthetic biological valves for treatment. By analyzing the data of heart valve replacement patients in California, USA from 1996 to 2013, it was found that during this period, the utilization rate of bioprosthesis during mitral valve replacement increased from 16.8% to 53.7%. Due to tissue degeneration and disease progression, bioprosthetic tissue valves and natural valves that have undergone surgical repair were prone to degenerate and form lesions over time, and the vast majority of patients were most likely to need another operation. From the current point of view, the number of repeated mitral valve operations in various heart centers around the world was increasing, and with the addition of experience, various postoperative Curative effect was constantly improving. But it was undeniable that the risk of repeated mitral valve surgery was still higher than that of the first mitral valve surgery. Several reports have shown that the risk of repeated mitral valve surgery was very high. The 30-day mortality rate for elective mitral valve surgery was between 6.3% and 15%, and the mortality rate for emergency surgery was 17.8%. When the third or fourth operation was required, the 30-day

mortality rate for elective operations was 17.3% and 40%, respectively, while emergency operations were 40% and 44%. In recent years, transcatheter mitral valve replacement (TMVR) had become an alternative to traditional cardiac surgery, and it was often used in patients with severe mitral valve disease such as severe mitral valve bioprosthesis degradation, failure of valvuloplasty surgery, or severe mitral valve natural annulus calcification. Recent studies showed that TMVR was the first choice of treatment for patients with repeated mitral valve surgery and high-risk mitral valve disease who were not suitable for traditional surgery.

METHODS

Search strategy: # 1 TS = (Valve-in-Ring) OR TS = ("Valve in Ring") OR TS = (ViR) # 2 TS = (Valve-in-Valve) OR TS = ("Valve in Valve") OR TS = (ViV) # 3 TS = (Valve-in-Mitral Annular Calcification) OR TS = ("Valve in Mitral Annular Calcification") OR TS = (ViMAC) # 4 #2 AND #1 # 5 #3 AND #1 # 6 #3 AND #2 # 7 #4 OR #5 OR #6.

Participant or population: Patients with degenerated mitral valve bioprostheses, failure of mitral valvuloplasty and native valve with severe mitral annulus calcification requiring transcatheter mitral valve replacement.

Intervention: Compare the feasibility of applying TMVR to patients with degenerated mitral valve bioprostheses (valve-in-valve, ViV), failure of mitral valvuloplasty (valve-in-ring, ViR), and serious mitral annulus calcification (vale-in-MAC, ViMAC).

Comparator: Compare the feasibility of applying TMVR to patients with degenerated mitral valve bioprostheses (valve-in-valve, ViV), failure of mitral valvuloplasty (valve-in-ring, ViR), and serious mitral annulus calcification (vale-in-MAC, ViMAC).

Study designs to be included: Randomized Controlled Trial (RCT) or cohort study.

Eligibility criteria: 1. Articles written in English. 2. Minimum of 30 days follow up post-procedure. 3. The subject of the study was the outcomes of transcatheter mitral valve replacement (TMVR) for patients with degenerated bioprostheses [valve-in-valve (ViV)], failed annuloplasty rings [valve-in-ring (ViR)], and severe mitral annular calcification [valve-in-mitral annular calcification (ViMAC)]. 4. The research included ≥10 patients undergoing either ViV-ViR, ViR -ViMAC or ViV-ViR-ViMAC.

Information sources: Determine the search terms through the "PICO" principle, conducted systematic electronic searches on Pubmed, Embase, Web of Science, Cochrane Library, and manually searched the references of the included documents to identify other publications. The time was from the establishment of the database to December 5, 2020. The purpose was to find all relevant documents on transcatheter mitral ViV, ViR and ViMAC.

Main outcome(s): All-cause Mortality within 30 days, Bleeding, Bleeding, Conversion to Cardiac surgery, LVOT obstruction, Stroke, Vascular complication.

Additional outcome(s): Vascular complication, Need for second valve implantation, Postprocedural Mitral Regurgitation [Trace / None, 1 (+), 2 (+) or greater]. S: Controlled Trial (RCT) or cohort study.

Data management: The retrieved articles from the databases were exported to EndNote X9 for duplicate removal and further categorization. The full text of reviews will also be uploaded and attached to EndNote X9. We shall perform predevelopment Microsoft Excel 2019 spreadsheets to extract data and later export into tables and figures.

Quality assessment / Risk of bias analysis: All the included literature was evaluated from three aspects through the Newcastle-Ottawa Scale (NOS) scoring standard: population selection, comparability and outcome. There are 8 questions in total, and the highest score is 9 points. It was

generally believed that when the score was ≥7, the study was considered high quality. Among scoring items, except for the fifth scoring standard, which could be up to two points, the other items were all one point.

Strategy of data synthesis: All analyses were conducted using Revman 5.4 (http://ims.cochrane.org/revman) [Computer program]. We chose unadjusted raw data because various researches have not adjusted for the same set of confounding factors. Categorical variables are expressed as the number of occurrences, and the Effect Measure was the Odds Ratio (OR). Continuous variables are expressed as mean ± SD. When the unit of measurement was consistent, Mean Difference (MD) was used, otherwise, Std. Mean Difference (SMD) was used. A standard confidence interval of 95%(95%CI) was applied in all analyses. Q test and I2 test were used for statistical heterogeneity analysis. When I2>50% or P<0.1, the random effects model was adopted, if not, the fixed effects model was adopted. The test level α = 0.05, which means that when the P-value < 0.05, it was considered statistically significant.

Subgroup analysis: If there were identified single factors that influenced heterogeneity between included studies, we would perform a subgroup analysis.

Sensitivity analysis: For studies with significant heterogeneity or high risk of bias, sensitivity analysis will be used to verify the stability of the combined effect.

Language: Articles written in English.

Country(ies) involved: China.

Keywords: Mitral valve, TMVR, Valve-in-Valve, Valve-in-Ring, Valve-in-MAC.

Dissemination plans: The full article will be published in the public journal as a paper.

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