

Systematic Review/Meta-analysis

Transcatheter Reduction of Paravalvular Leaks: A Systematic Review and Meta-analysis

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ABSTRACT

Background: Significant paravalvular leak (PVL) after surgical valve replacement can result in intractable congestive heart failure and hemolytic anemia. Because repeat surgery is performed in only few patients, transcatheter reduction of PVL is emerging as an alternative option, but its safety and efficacy remain uncertain. In this study we sought to assess whether a successful transcatheter PVL reduction is associated with an improvement in clinical outcomes.

Methods: We identified 12 clinical studies that compared successful and failed transcatheter PVL reductions in a total of 362 patients. A

RÉSUMÉ

Introduction : Une importante fuite paravalvulaire (PVL) suite à une chirurgie de remplacement valvulaire peut entraîner une insuffisance cardiaque réfractaire et une anémie hémolytique. Comme il est assez rare qu'une réopération soit effectuée, la suppression de PVL par une procédure transcathéter devient une option alternative, mais son innocuité et son efficacité restent incertaines. Dans cette étude, nous avons cherché à déterminer si une réduction d'une PVL par transcathéter est associée à une amélioration des résultats cliniques.

Paravalvular leak (PVL) after surgical valve replacement originates from an incomplete seal between the prosthetic sewing ring and the native valve annulus, related to calcification, infection, or suboptimal surgical technique or prosthetic sizing.¹ PVL of various severities have been detected

in up to 17.6% of the aortic and 22.6% of the mitral valve replacements and patients with symptomatic PVL have a mortality rate comparable with lung cancer.^{2,3} Surgical correction is currently the gold standard therapy for symptomatic PVL and is typically performed in patients with severe congestive heart failure (CHF) and/or refractory hemolytic anemia. Repeated surgeries are associated with a high rate of PVL recurrence and with a higher mortality rate than the index procedure. For this reason, only a minority of patients undergo a surgical correction, leaving a large number of individuals with the need for alternative therapies.⁴⁻⁸

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See page 267 for disclosure information.

Bayesian hierarchical meta-analysis was performed using cardiac mortality as a primary end point. The combined occurrence of improvement in New York Heart Association functional class or hemolytic anemia and the need for repeat surgery, were used as secondary end points.

Results: A successful transcatheter PVL reduction was associated with a lower cardiac mortality rate (odds ratio [OR], 0.08; 95% credible interval [CrI], 0.01-0.90) and with a superior improvement in functional class or hemolytic anemia, compared with a failed intervention (OR, 9.95; 95% CrI, 2.10-66.73). Fewer repeat surgeries were also observed after successful procedures (OR, 0.08; 95% CrI, 0.01-0.40).

Conclusions: A successful transcatheter PVL reduction is associated with reduced all-cause mortality and improved functional class in patients deemed unsuitable for surgical correction.

Méthodes : Nous avons identifié 12 études cliniques qui comparaient les réductions réussies ou infructueuses de PVL par procédure transcathéter sur un total de 362 patients. Une méta-analyse hiérarchique bayésienne a été réalisée en utilisant la mortalité cardiaque comme point d'aboutissement principal. Une amélioration de la classe fonctionnelle de la New York Heart Association ou d'une anémie hémolytique et la nécessité d'une réopération, ont été utilisés comme critères secondaires.

Résultats : Une réduction réussie de PVL par procédure transcathéter a été associée à un taux plus faible de la mortalité cardiaque (ratio d'incidence approché [RIA] 0,08; intervalle de crédibilité [CrI] à 95 %, 0,01 - 0,90) et à une amélioration de la classe fonctionnelle ou d'une anémie hémolytique (RIA 9,95; CrI à 95 %, 2,10 - 66,73). Moins de réopérations ont également été observées après des procédures réussies (RIA 0,08; CrI à 95 %, 0,01 - 0,40).

Conclusions : Une réduction significative de PVL par procédure transcathéter est associée à une mortalité réduite, toutes causes confondues, et à une amélioration de la classe fonctionnelle chez les patients jugés inaptes à une réopération.

In 1992, Hourihan et al. first described the potential of transcatheter PVL reduction to improve survival and quality of life in patients deemed unsuitable for repeat surgery.⁹ The interest for transcatheter PVL reduction is exponentially growing but the global experience remains limited to single-centre experience with varying procedural success rates.¹⁶⁻²⁶

Uncertainties persist on the benefits and risks associated with this technique, which precludes an appropriate case selection. To our knowledge, no group has previously systematically reviewed these data. In the present study we sought to assess the association between transcatheter PVL reduction and clinical outcomes including death, improvement in heart failure or hemolytic anemia, and requirements for repeat surgery. To this end, we systematically reviewed the literature for randomized trials and nonrandomized studies and performed a meta-analysis to appraise the feasibility, efficacy, and safety of transcatheter PVL reduction in symptomatic patients.

Methods

Objective

In this present analysis we sought to evaluate the relationship between a successful transcatheter PVL reduction and clinical outcomes. More specifically, in the present analysis we planned to estimate the odds ratios (ORs) for cardiac mortality (primary end point), for improvement in functional class or hemolytic anemia, and for the reduction in repeat surgery (secondary end points).

Identification of studies

Randomized trials are the preferred source of data for meta-analysis. However, considering the emerging nature of transcatheter PVL reduction and to obtain an appropriate reflection of the global experience we also accounted for nonrandomized studies. Studies that reported immediate and long-term clinical outcomes for successful and failed transcatheter PVL reduction were considered for the systematic

review. No restrictions were applied with regard to language, sample size, technical approach (anterograde/transseptal, retrograde arterial, or transapical), or the type of device used.

Studies were searched (June 2014) using MEDLINE, EMBASE, and CENTRAL. Search strategies included the Medical Subject Heading term and text word searches (Supplemental Table S1). We manually searched reference lists of relevant studies for additional publications and we screened relevant abstracts to see whether they were followed by a complete publication. To this end, the American College of Cardiology, American Heart Association, European Society of Cardiology, Euro-PCR, Transcatheter Cardiovascular Therapeutics, Society for Cardiac Angiography and Interventions, and Canadian Cardiovascular conference proceedings were queried from the years 2008 to 2014. In addition, trial registers including the World Health Organization International Clinical Trial Registry Platform, clinicaltrials.gov, the ISRCTN (International Standard Registered Clinical/Social Study Number) register, and the *MetaRegister* were searched for ongoing or completed studies with potential publication. Preliminary reports were excluded from the systematic review. Relevant studies were reviewed to exclude duplicate reports and selected articles were read entirely. When multiple publications from the same study population were found, the one with the largest sample or the longest follow-up was selected. In case of incomplete data in published studies, authors were contacted and asked for missing information.

Data abstraction and quality assessment

To avoid that knowledge of the results biased the perception of the methods' quality, data from the methods and results sections were abstracted on separate forms. To reduce bias, 2 independent abstractors (X.M. and S.S.) independently extracted variables describing the study population, the procedural characteristics, and clinical outcomes. A third reviewer (E.M.J.) resolved discrepancies between abstractors. At all times, abstractors were blinded to information believed to possibly influence their judgement (authors, titles, journal, institution, or country of origin).

For each selected randomized trial, the general quality of reporting of information was assessed using the validated criteria proposed by Jüni et al.²⁷ For each selected non-randomized study, the general quality of reporting of information was initially assessed using the Strengthening the Reporting of Observational Studies in Epidemiology Consensus Statement.²⁸ The specific risk of bias in non-randomized studies was concomitantly assessed using the Newcastle-Ottawa scale for cohort studies²⁹ and a modification of the validated checklist proposed by Downs and Black³⁰ (Supplemental Table S2). For each study, an independent quality score was given for the assessment of procedural success, death, and clinical improvement.

Data were collected on a customized form adapted from the Cochrane collaboration data collection form for non-randomized studies.³¹ Information included the study design, confounding factors, comparability between groups at baseline, methods used to adjust for confounding, and effect estimate. The quality of studies was not used to adjust their weight in the meta-analysis. Instead, quality is reported as an indicator of external validity.

The reports of the methods presented in this report are compliant with the Meta-analysis Of Observational Studies in Epidemiology consensus statement for nonrandomized studies³² and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses, an update of the **Quality of Reporting of Meta-analyses (QUOROM)** guidelines for reporting systematic reviews and meta-analyses.^{33,34}

Clinical and end point definitions

For the present analysis, a successful PVL reduction was defined as the delivery of a reduction device free of mechanical prosthesis interference and resulting in an immediate ≥ 1 -grade regurgitation reduction. Alternatively, technical success, defined as the successful delivery of a reduction device (irrespective of PVL reduction obtained), was used for sensitivity analyses.

Change in regurgitation grade was quantified using trans-thoracic echocardiography and bi- or tridimensional trans-esophageal echocardiography, as specifically detailed by investigators (see Supplemental Table S3 for study-specific criteria).

Death was abstracted as cardiac vs noncardiac. Cardiac death included causes such as tamponade, cardiogenic shock, CHF, transplantation, myocardial infarction, prosthesis endocarditis, vascular access site complication, malignant ventricular arrhythmias, and sudden death.

Improvement in CHF was defined as a reduction of ≥ 1 grade on the New York Heart Association (NYHA) functional class scale and improvement in hemolytic anemia was defined as a decrease of transfusion requirements or significant improvement on hemolytic parameters, quantified according to hemoglobin/hematocrit, lactate dehydrogenase, reticulocyte/schistocyte count, or bilirubin.

Statistical analysis

We used a Bayesian hierarchical meta-analysis model to account for possible variations in methods, patient characteristics, and other differences that are likely to occur especially across nonrandomized studies, which might affect the

ORs estimated.³⁵ At the first level of the hierarchical model, the probability of an event varies within each group and across studies. To model this between-study variability, the logarithms of the ORs of each outcome were assumed to follow a normal distribution. The mean of the normal distribution of log ORs across studies represents the average effect within each study, and the variance represents the degree to which the ORs vary across studies. Diffuse previous distributions were used throughout, so that the data drove the final inferences. Specifically, we used normal densities with mean zero and variance of 100,000 or larger for all mean parameters, and a uniform distribution with range (0-5) for the between study standard deviation, measured on a log scale. This latter parameter implies that the 95% range of the ORs (approximately 4 times the SD) is 20 on a log scale, meaning that ORs from $\exp(-20)$ to $\exp(20)$ are accommodated; an extremely wide range. We report the posterior median and 95% credible interval (CrI) for this between-study standard deviation on the log odds scale. A posterior density concentrating near zero would be evidence that a fixed model might suffice, and any other posterior density indicates important heterogeneity is likely present and hence a random effects model is to be preferred. A particular study did not account for an outcome when no events were possible in either the successful or the failure group. For this reason, variable group sizes were obtained for each outcome. WinBUGS software (version 1.4.3, MRC Biostatistics Unit, Cambridge, UK) was used for analyses. We ran 5000 burn-in iterations to ensure convergence of the Markov chains and a further 50,000 iterations to obtain highly accurate posterior estimates. No convergence problems were detected in any of the analyses. Forest plots were produced to display the ORs and 95% CrIs for all major outcomes considered in our meta-analysis. CrIs are the Bayesian analogues to frequentist confidence intervals. Our Bayesian hierarchical model is similar in nature to a frequentist random effects meta-analysis model, and with our use of the factors already mentioned herein, should return numerically similar interval estimates.

Sensitivity analyses

For the primary analysis, procedural success (device delivery and reduction in regurgitation volume) was used to dichotomize patients between successful vs failed PVL reduction. Because the delivery procedure itself bears a significant risk, we also performed a sensitivity analysis in which technical success (device delivery vs no device delivery) was used to dichotomize patients into treatment groups. This analysis was believed necessary to better reflect the risk to benefit ratio conferred by the attempted intervention alone.

Results

Search results

Initial searches of randomized controlled trials and non-randomized studies retrieved 58 and 553 reports respectively, most of which were on nonrelated topics. As shown in Figure 1, the initial screening retrieved 68 unique reports. A manual search of conference proceedings retrieved 1 additional report.¹¹ An important proportion of excluded reports

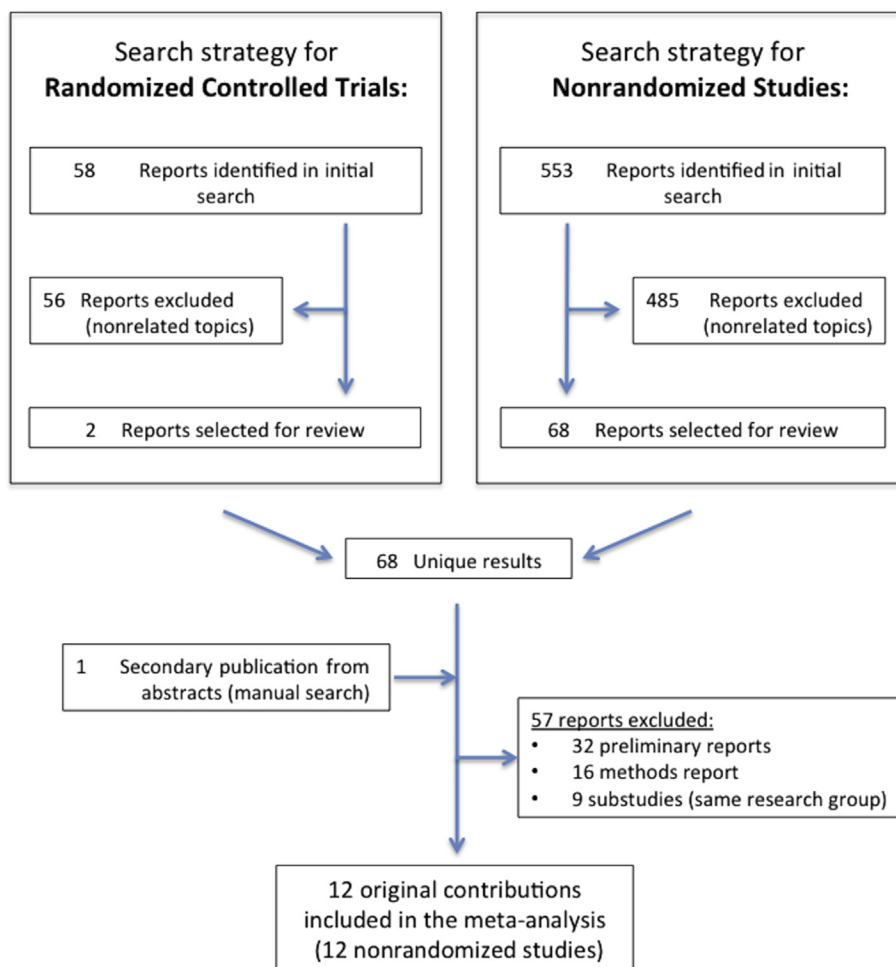


Figure 1. Flow diagram of eligible studies that compared successful vs failed procedures of transcatheter paravalvular leak reduction.

were abstracts. Additional reports were excluded because procedural details and follow-up information were not available ($n = 16$). A total of 12 nonrandomized studies were included in the systematic review. No randomized trials were retrieved. The interabstracter agreement on study eligibility was 100%.

Study characteristics

The characteristics of the study populations are shown in [Table 1](#). A total of 362 patients were included in the analysis, with 213 men (59%) and 149 women (41%). The mean age varied from 62 to 75 years. The primary indications for PVL reduction were CHF (51%), hemolytic anemia (10%), or both (39%). As shown by Society of Thoracic Surgeons scores and logistic Euroscores, most patients were deemed poor candidates for repeat surgery because of numerous previous open-chest surgeries and multiple comorbid conditions (see [Supplemental Table S4](#) for study-specific inclusion/exclusion criteria and surgical risk assessment). Despite the eventual severity of symptoms, all procedures were performed electively, with no emergent interventions described.

Technical and procedural characteristics are summarized in [Table 2](#). PVLs were most frequently located at the mitral

position (70%). Mechanical and biological prostheses were similarly represented. Aortic PVL reductions were most frequently attempted using a retrograde approach (via the femoral arteries), and the mitral PVL reductions were most frequently attempted using an anterograde approach (via transseptal puncture). In 31 patients with mitral PVL, the reduction procedure was attempted using a transapical approach. Globally, procedural success was achieved in 76.5% of cases, ranging from 29.6% to 100%. Likewise, technical success was achieved in 86.5% of cases, ranging from 62.5% to 100% ([Fig. 2A](#)).

With respect to leak position, mitral transcatheter PVL reduction was performed in 274 patients with a technical success rate of 82.3% and a procedural success rate of 73.3%. When information was available, authors reported success rates of 100% in mitral leaks attempted via a transapical approach, compared with technical and procedural success rates of 78.4% and 66.4%, respectively, obtained in the classical anterograde or retrograde approaches. Eighty-eight patients underwent aortic procedures, with technical and procedural success rates of 86.9% and 84.1%, respectively ([Fig. 2B](#)).

Because no specific device is formally labelled for PVL reduction, many devices of the Amplatzer occluders/plugs

Table 1. Study characteristics

Characteristic	Study											
	Hein 2006 ¹⁵ (n = 21)	Corres 2008 ¹² (n = 27)	Garcia-Borbolla Fernandez 2009 ¹⁴ (n = 8)	Nietlispach 2010 ¹⁸ (n = 5)	Ruiz 2011 ²¹ (n = 43)	Sorajja 2011 ²⁵ (n = 126)	Swaans 2012 ²⁶ (n = 7)	Bocuzzi 2013 ¹¹ (n = 12)	Noble 2013 ¹⁹ (n = 56)	Smolka 2013 ²³ (n = 7)	Smolka 2013 ²⁴ (n = 7)	Cruz 2014 ¹³ (n = 33)
Mean age, y	65.5	63	63.7	75	69.4	67	72.8	68.3	64.9	62.5	73	71
Male sex, %	62	81	75	40	67	53	71	67	52	71	71	45
Indication for intervention, n (%)												
CHF	8 (38)	9 (33)	5 (63)	0 (0)	9 (16)	89 (71)	1 (1)	5 (42)	34 (61)	10 (59)	7	7 (21)
Hemolysis	2 (10)	3 (11)	1 (13)	1 (20)	8 (14)	9 (7)	3 (4)	2 (17)	5 (9)	0 (0)	NR	1 (3)
Both	11 (52)	15 (56)	2 (25)	4 (80)	26 (60)	28 (22)	3 (4)	5 (42)	17 (30)	7 (41)	NR	25 (76)
NYHA dyspnea class	3	NR	NR	4	3	3	3.4	2.9	3	3	3.3	3
Procedural risk for cardiac surgery	NR	NR	NR	NR	NR	6.7	NR	NR	NR	NR	7.1	20
STS	23.7	NR	NR	NR	NR	NR	28.5	20.2	18.8	NR	15.0*	NR
Euroscore (logistic)	13.5	3	15	6.3	42	11 [†]	3	NR	30 [†]	6	1	3
Mean follow-up, mo	NR	NR	36	NR	42	85	NR	20	NR	6	NR	3
Longest follow-up, mo	NR	NR	NR	NR	NR	NR	NR	20	NR	6	NR	3

CHF, congestive heart failure; NR, not reported; NYHA, New York Heart Association; STS, Society of Thoracic Surgeons.

*Euroscore II.

[†]Median.

family currently used for the closure of other anatomical defects were used. The device most commonly used was the Amplatzer Duct Occluder, in 26% of the procedures. However, in the most recent publications, the Amplatzer Vascular Plug III was the most used device. More than 1 device was required in 66 patients (18%).

According to the high mortality risk of the global cohort, 22.7% (72 patients) died during a variable follow-up, of whom 18 patients died from cardiac causes. Twelve per cent of patients (6 of 50 patients) presented cardiac death after a failed procedure but only 5.7% (12 of 210) died after a successful procedure.

The combined end point of improvement in NYHA functional class or hemolytic anemia was achieved in 71.0% of patients (137 of 193) with a successful procedure and in 28.4% of patients (21 of 74) after a suboptimal transcatheter PVL reduction.

When data were reported, 6.8% of patients with successful procedures (17 of 250 patients) required surgical reintervention during follow-up, compared with 31.8% of patients (21 of 66 patients) after a failed procedure.

Results of the meta-analysis

A successful PVL reduction was associated with a lower cardiac mortality rate compared with a failed reduction (260 patients; OR, 0.08; 95% CrI, 0.01-0.90; Fig. 3A). A positive tendency toward lower all-cause mortality was also observed in successful procedures (311 patients; OR, 0.52; 95% CrI, 0.09-1.74). The posterior standard deviation was estimated to be 0.79 (95% CrI, 0.04-3.79), indicating a high probability of clinically important between-study variability.

A superior functional class improvement or improved hemolytic anemia was observed in successful compared with failed PVL reductions (267 patients; OR, 9.95; 95% CrI, 2.10-66.73; Fig. 3B). This effect was mostly driven by an improvement in NYHA functional class (192 patients; OR, 72.24; 95% CrI, 5.09-693). Wide CrIs for the estimated effect of PVL reduction on hemolysis alone (35 patients; OR, 2.22; 95% CrI, 0.06-194) preclude definitive conclusions.

Procedurally successful transcatheter PVL reduction was also associated with fewer surgical reinterventions (316 patients; OR, 0.08; 95% CrI, 0.01-0.40; Fig. 3C).

The results of the sensitivity analysis showed that technical success (appropriate device delivery regardless of the grade of PVL reduction) was also associated with a combined improvement in functional class or hemolytic anemia (162 patients; OR, 30.96; 95% CrI, 5.31-224). Nevertheless, technical success was not associated with a significantly lower rate of cardiac mortality (132 patients; OR, 0.08; 95% CrI, 0.003-1.91).

Discussion

Results of the present analysis suggest that a successful transcatheter PVL reduction reduces cardiac mortality and improves functional class in highly symptomatic patients deemed unsuitable for surgical correction. In appropriately selected cases, transcatheter reduction of PVL can be attempted safely and with a technical success rate of 86.5% (and improvement in regurgitation grade in > 75% of patients).

Table 2. Technical and procedural characteristics

Characteristic	Study											
	Hein 2006 ¹⁵ (n = 21)	Cortes 2008 ¹² (n = 27)	Garcia-Borbolla Fernandez 2009 ¹⁴ (n = 8)	Nietlispach 2010 ¹⁸ (n = 5)	Ruiz 2011 ²¹ (n = 43)	Sorajja 2011 ²⁵ (n = 126)	Swaans 2012 ²⁶ (n = 7)	Bocuzzi 2013 ¹¹ (n = 12)	Noble 2013 ¹⁹ (n = 56)	Smolka 2013 ²³ (n = 7)	Smolka 2013 ²⁴ (n = 7)	Cruz 2014 ¹³ (n = 33)
Technical successes vs failures (n)	20 vs 1	17 vs 10	5 vs 3	5 vs 0	37 vs 6	115 vs 11	7 vs 0	12 vs 0	42 vs 14	15 vs 2	7 vs 0	31 vs 2
Procedural successes vs failures (n)	19 vs 2	8 vs 19	4 vs 4	5 vs 0	35 vs 8	96 vs 30	7 vs 0	11 vs 1	40 vs 16	15 vs 2	7 vs 0	30 vs 3
Prosthesis position, n												
Aortic	8	0	0	1	10	27	1	5	12	17	0	7
Mitral	13	27	8	4	33	99	6	7	44	0	7	26
Prosthesis type, n												
Mechanical	NR	27	7	1	15	49	4	2	50	11	4	32
Bioprosthesis		0	1	4	28	77	3	10	6	6	3	1
Total number of devices implanted	26	17	7	6	57	156	7	NR	53	24	20	34
Device type												
AVP-III	0	0	0	5	0	0	7	11	7	17	20	34
AVP-II	0	0	0	0	5	77	0	0	0	7	0	0
ADO	8	17	7	1	39	20	0	0	18	0	0	0
mVSD	13	0	0	0	11	10	0	0	28	0	0	0
ASO	5	0	0	0	2	12	0	1	0	0	0	0
Patients with ≥1 device implanted, n	5	0	1	1	12	20	0	6	5	8	7	1
Approach, n												
Retrograde	NR	0	2	2	NR	32	0	NR	12	17	0	26
Anterograde		17	5	0		100	0		44	0	0	7
Transapical		0	0	4		13	7		0	0	7	0

ADO, Amplatzer Duct Occluder; ASO, Amplatzer Septum Occluder; AVP, Amplatzer Vascular Plug Occluder; mVSD, Amplatzer Muscular Ventricular Septum Defect Occluder; NR, not reported.

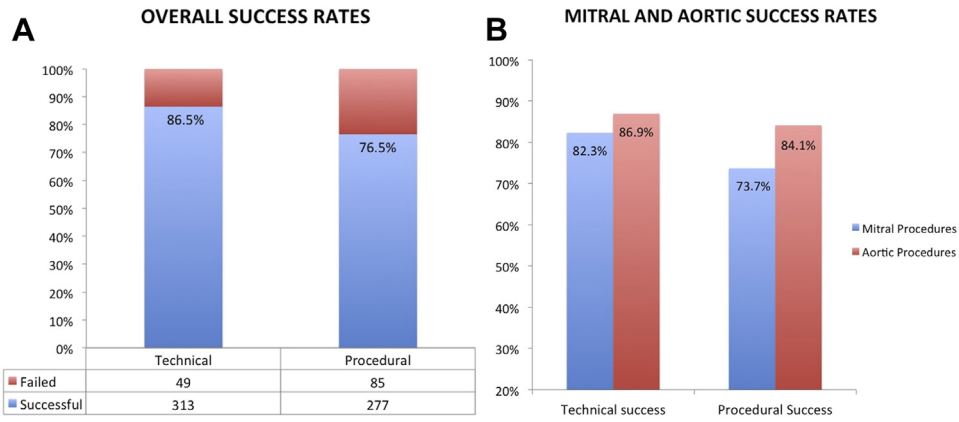


Figure 2. (A) Overall procedural and technical success rates. (B) Procedural and technical success rates in mitral and aortic paravalvular leaks. Technical success is defined as successful delivery of a reduction device (irrespective of paravalvular leak reduction obtained); procedural success is defined as delivery of a reduction device free of mechanical prosthesis interference and resulting in an immediate grade ≥ 1 regurgitation reduction.

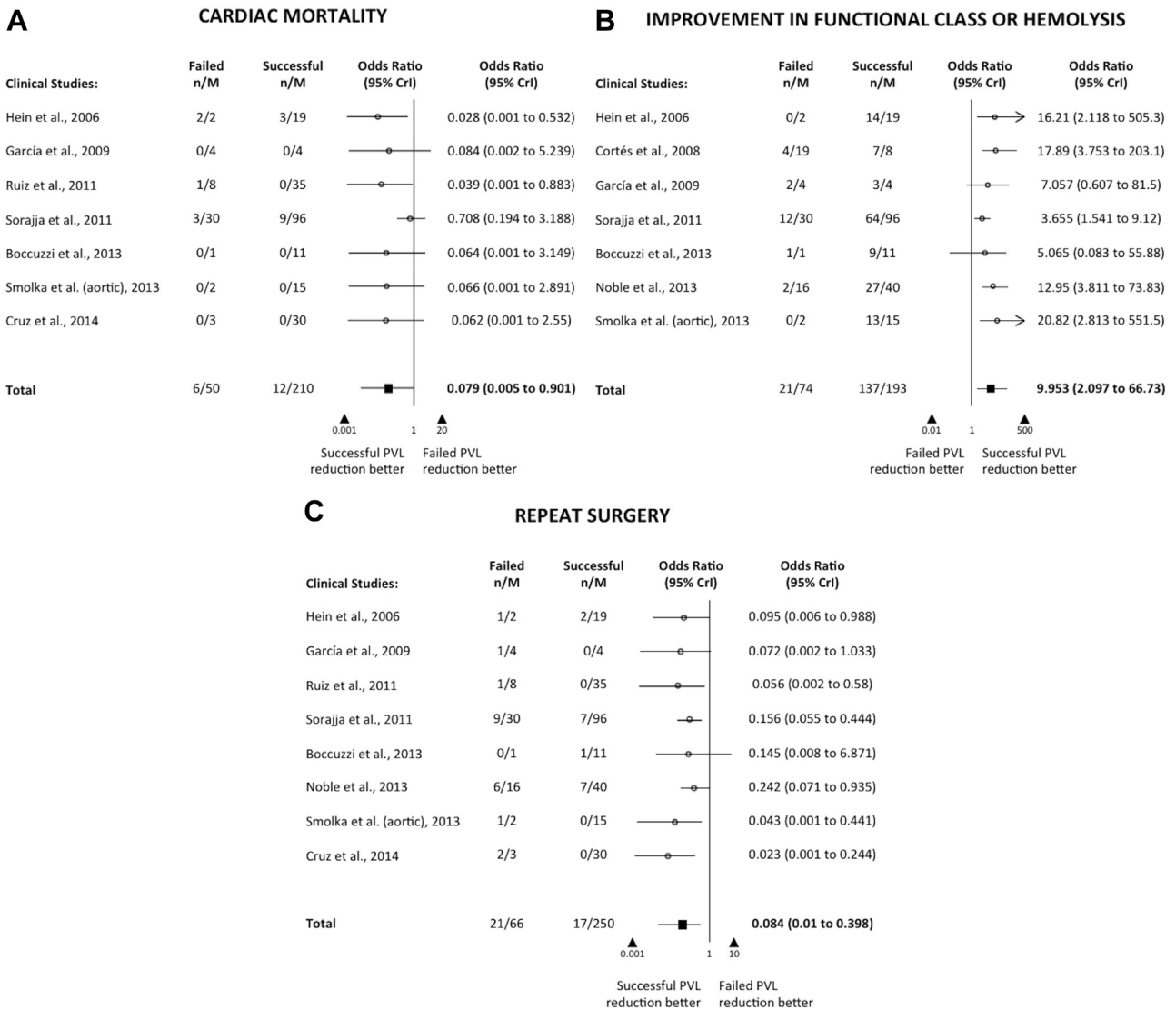


Figure 3. Forest plot for (A) cardiac mortality in a comparison of successful vs failed transcatheter paravalvular leak (PVL) reductions; (B) functional class or hemolysis improvement in a comparison of successful vs failed transcatheter PVL reductions; and (C) repeat surgery requirements in a comparison of successful vs failed transcatheter PVL reductions. CrI, credible interval; M, number of possible events.

These results have important research and clinical applications because of the increasing use of this procedure, nowadays applicable to even the highest-risk patients. In the following years, the success rates associated with percutaneous PVL reduction rates are expected to improve thanks to operators beyond their learning curve with more developed techniques available. Several studies included in this meta-analysis support the transapical approach as an alternative access method when anterograde transseptal or retrograde transaortic approaches are unsuccessful or technically challenging (eg, septal or posterior locations for mitral PVL). However, it is multimodality imaging and the possibility to fuse different imaging techniques that make transcatheter PVL reduction a safer and more successful procedure.³⁶ The lack of devices specifically designed for this purpose has been repeatedly mentioned, but the use of more appropriate appliances as the Amplatzer Vascular Plug III, with its capability to fit elliptical-shaped vascular structures, has allowed recent success rates as high as 94%.¹³ Overall, the continuous development of transcatheter PVL reduction provides the potential to further advance this procedure.

The systematic review of the literature has highlighted important disparities in the practice of this intervention on a global scale: (1) the disagreement on the definition of success, for which many studies focused on technical feasibility regardless of the grade of PVL reduction achieved; (2) the absence of standardized methods to quantify the severity of PVL-related regurgitation with imaging; and (3) the variability on outcomes assessment proven by the multiple definitions of hemolysis improvement found among different studies. These disparities would be best served by the creation of an academic research consortium on the topic.

The incidence of PVL after surgical prosthesis implantation has been known for years. Additionally, with the recent surge in transcatheter aortic valve replacement and the upcoming transcatheter mitral replacement,³⁷ PVL is likely to reach epidemic proportions in the years to come. Therefore, transcatheter PVL reduction could expand importantly in settings after the transcatheter procedure. In the **Placement of Aortic Transcatheter Valves (PARTNER)** trial, for instance, significant PVLs were present in 12% of patients and its presence independently predicted long-term mortality.³⁸⁻⁴⁰

Limitations and future directions

Information on transcatheter PVL reduction is limited because of small sample sizes, lack of randomized data, variable report rates, incomplete follow-up, and single-centre retrospective nature of the data. This meta-analysis was performed by abstracting data at the group level not at a patient level. However, authors were contacted for clarification when important data could not be abstracted directly from the report. Besides, reports regarding success rates and follow-up outcomes depending on the principal indication intervention (heart failure or hemolysis) were incomplete, and the available data did not allow a description of clinical end points according to the prosthetic valve attempted (aortic vs mitral) or its approach (anterograde transseptal, retrograde transaortic, or transapical). Because the procedural risk is low, technical failure (addressed in the sensitivity analysis) would be theoretically comparable with medical treatment, but this option

was not included in the current study design and has not been specifically assessed.

The small numbers of studies precluded accurate estimation of the between-study variance, which led to wide CrIs across most of the outcomes, reflecting the probabilistic uncertainty of the point estimates reported. Our results should be taken with caution and are not meant to direct medical practice.

Results of the present study demonstrate the need for additional research to expand the emerging techniques of PVL reduction. Our data offer an unprecedented insight into the possible benefits and risks associated with this intervention, and raises several unanswered questions, such as the differential effect of PVL reduction in mitral vs aortic position and the appropriate case selection or timing for intervention.

To further the PVL reduction, these important questions must be addressed by the creation of a patient-level data register and a PVL academic research consortium. An international patient-level data register would allow a better understanding of the patient population, including the development of a risk score specific to patients with PVL. Such consortium would permit the unification on reporting of outcomes and clinical assessment and the design of future clinical investigations.

Conclusions

Results of the current study suggest that successful transcatheter PVL reduction is associated with a reduction in cardiac mortality and functional class improvement in patients unsuitable for surgical correction. An appropriately designed multicentre trial is needed to confirm our findings regarding this technique and to evaluate its efficacy in other subsets of patients, especially in high surgical risk patients, compared with surgical correction or medical treatment.

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Disclosures

Dr Ibrahim, Dr Arzamendi, and Dr Cruz-González report to be consultants for St Jude Medical. St Jude Medical had no role in the design, subject recruitment, or preparation of this report. The remaining authors have no conflicts of interest to disclose.

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Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Cardiology* at www.onlinecjc.ca and at <http://dx.doi.org/10.1016/j.cjca.2014.12.012>.