ISSN 1949-8462 (online)

World Journal of *Cardiology*

World J Cardiol 2023 February 26; 15(2): 45-75

Published by Baishideng Publishing Group Inc

World Journal of Cardiology

Contents

Monthly Volume 15 Number 2 February 26, 2023

MINIREVIEWS

ORIGINAL ARTICLE

Retrospective Cohort Study

SYSTEMATIC REVIEWS

World Journal of Cardiology

Monthly Volume 15 Number 2 February 26, 2023

Contents

ABOUT COVER

Peer Reviewer of *World Journal of Cardiology*, Turyalai Hakimi, MD, MS, Head department of Pediatric Surgery, Kabul University of Medical Science, Maiwand Teaching Hospital. Kabul city 1006, Kabul, Afghanistan. dr.turyalaihakimi@gmail.com

AIMS AND SCOPE

The primary aim of *World Journal of Cardiology* (*WJC*, *World J Cardiol*) is to provide scholars and readers from various fields of cardiology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJC mainly publishes articles reporting research results and findings obtained in the field of cardiology and covering a wide range of topics including acute coronary syndromes, aneurysm, angina, arrhythmias, atherosclerosis, atrial fibrillation, cardiomyopathy, congenital heart disease, coronary artery disease, heart failure, hypertension, imaging, infection, myocardial infarction, pathology, peripheral vessels, public health, Raynaud's syndrome, stroke, thrombosis, and valvular disease.

INDEXING/ABSTRACTING

The *WJC* is now abstracted and indexed in Emerging Sources Citation Index (Web of Science), PubMed, PubMed Central, Scopus, Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database. The 2022 edition of Journal Citation Reports® cites the 2021 Journal Citation Indicator (JCI) for *WJC* as 0.35. The *WJC*'s CiteScore for 2021 is 0.9, and Scopus CiteScore rank 2021: Cardiology and Cardiovascular Medicine is 260/336.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Hua-Ge Yu*; **Production Department Director:** *Xiang Li*; **Editorial Office Director:** *Yun-Xiaojiao Wu*.

NAME OF JOURNAL
World Journal of Cardiology

ISSN
ISSN 1949-8462 (online)

LAUNCH DATE
December 31, 2009

FREQUENCY
Monthly

EDITORS-IN-CHIEF
Ramdas G Pai, Dimitrios Tousoulis, Marco Matteo Ciccone, Pal Pacher

EDITORIAL BOARD MEMBERS
https://www.wjgnet.com/1949-8462/editorialboard.htm

PUBLICATION DATE
February 26, 2023

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION ETHICS
https://www.wjgnet.com/bpg/GerInfo/288

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
https://www.wjgnet.com/bpg/GerInfo/239

ONLINE SUBMISSION
https://www.f6publishing.com

World Journal of Cardiology

Submit a Manuscript: https://www.f6publishing.com

World J Cardiol 2023 February 26; 15(2): 64-75

DOI: 10.4330/wjc.v15.i2.64

ISSN 1949-8462 (online)

SYSTEMATIC REVIEWS

Safety and efficacy of balloon angioplasty compared to stent-based-strategies with pulmonary vein stenosis: A systematic review and meta-analysis

Pradyumna Agasthi, Srilekha Sridhara, Pattara Rattanawong, Nithin Venepally, Chieh-Ju Chao, Hasan Ashraf, Sai Harika Pujari, Mohamed Allam, Diana Almader-Douglas, Yamini Alla, Amit Kumar, Farouk Mookadam, Douglas L Packer, David R Holmes Jr, Donald J Hagler, Floyd David Fortuin, Reza Arsanjani

Specialty type: Cardiac and cardiovascular systems

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): 0
Grade C (Good): C
Grade D (Fair): D
Grade E (Poor): 0

P-Reviewer: Hu H, China; Ueda H, Japan

Received: September 19, 2022
Peer-review started: September 19, 2022
First decision: November 2, 2022
Revised: November 17, 2022
Accepted: February 8, 2023
Article in press: Feburary 8, 2023
Published online: February 26, 2023

Pradyumna Agasthi, Pattara Rattanawong, Nithin Venepally, Chieh-Ju Chao, Hasan Ashraf, Sai Harika Pujari, Mohamed Allam, Amit Kumar, Farouk Mookadam, Floyd David Fortuin, Reza Arsanjani, Department of Cardiovascular Diseases, Mayo Clinic, Scottsdale, AZ 85259, United States

Srilekha Sridhara, Department of Internal Medicine, Banner Heart Hospital, Mesa, AZ 85054, United States

Diana Almader-Douglas, Library Services, Mayo Clinic, Phoenix, AZ 85054, United States

Yamini Alla, Department of Medicine, Bronx Lebanon Hospital, Bronx, NY 10457, United States

Douglas L Packer, David R Holmes Jr, Donald J Hagler, Department of Cardiovascular Diseases, Mayo Clinic, Rochester, MN 55905, United States

Corresponding author: Nithin Venepally, MD, Academic Research, Department of Cardiovascular Diseases, Mayo Clinic, 5777 E Mayo Blvd, Scottsdale, AZ 85259, United States. nrvenepally@gmail.com

Abstract

BACKGROUND

Pulmonary vein stenosis (PVS) is an uncommon but known cause of morbidity and mortality in adults and children and can be managed with percutaneous re-vascularization strategies of pulmonary vein balloon angioplasty (PBA) or pulmonary vein stent implantation (PSI).

AIM

To study the safety and efficacy outcomes of PBA *vs* PSI in all patient categories with PVS.

METHODS

We performed a literature search of all studies comparing outcomes of patients evaluated by PBA *vs* PSI for PVS. We selected all published studies comparing PBA *vs* PSI for PVS with reported outcomes of restenosis and procedure-related

complications in all patient categories. In adults, PVS following atrial fibrillation ablation and in children PVS related to congenital etiology or post-procedural PVS following total or partial anomalous pulmonary venous return repair were included. The patient-centered outcomes were risk of restenosis requiring re-intervention and procedural-related complications. The meta-analysis was performed by computing odds ratios (ORs) using the random effects model based on underlying statistical heterogeneity.

RESULTS

Eight observational studies treating 768 severe PVS in 487 patients met our inclusion criteria. The age range of patients was 6 months to 70 years and 67% were males. The primary outcome of the re-stenosis requiring re-intervention occurred in 196 of 325 veins in the PBA group and 111 of 443 veins in the PSI group. Compared to PSI, PBA was associated with a significantly increased risk of re-stenosis (OR 2.91, 95%CI: 1.15-7.37, P = 0.025, I^2 = 79.2%). Secondary outcomes of the procedure-related complications occurred in 7 of 122 patients in the PBA group and 6 of 69 in the PSI group. There were no statistically significant differences in the safety outcomes between the two groups (OR: 0.94, 95%CI: 0.23-3.76, P = 0.929), I^2 = 0.0%).

CONCLUSION

Across all patient categories with PVS, PSI is associated with reduced risk of re-intervention and is as safe as PBA and should be considered first-line therapy for PVS.

Key Words: Pulmonary veins; Pulmonary vein stenosis; Constriction; Balloon angioplasty; Stents; Drug-eluting stents

Core Tip: 81.5% of patients with pulmonary vein stenosis undergoing a transcatheter intervention reported symptom of dyspnea. Pulmonary vein stent implantation (PSI) was superior to pulmonary vein balloon angioplasty (PBA) in preventing restenosis of the pulmonary vein. No difference in procedural related complications was noted between PSI and PBA. Differences in peri-procedural anticoagulation strategies between studies could have affected the outcome.

Citation: Agasthi P, Sridhara S, Rattanawong P, Venepally N, Chao CJ, Ashraf H, Pujari SH, Allam M, Almader-Douglas D, Alla Y, Kumar A, Mookadam F, Packer DL, Holmes DR Jr, Hagler DJ, Fortuin FD, Arsanjani R. Safety and efficacy of balloon angioplasty compared to stent-based-strategies with pulmonary vein stenosis: A systematic review and meta-analysis. *World J Cardiol* 2023; 15(2): 64-75
URL: https://www.wjgnet.com/1949-8462/full/v15/i2/64.htm
DOI: https://dx.doi.org/10.4330/wjc.v15.i2.64

INTRODUCTION

Catheter ablation for atrial fibrillation in adults involves the use of radiofrequency energy to electrically isolate the pulmonary vein[1]. As injured tissue heals scar tissue extends deeper into vein from the ostium leading to pulmonary vein stenosis (PVS). Cryoballoon ablation therapy for atrial fibrillation can have similar consequences[2]. With increased utilization of techniques aimed to reduce PVS such as antral isolation, 3-dimensional mapping and use of intra-cardiac ultrasound, the incidence of PVS has declined substantially from 20%-40% to 1%-1.5% currently[3]. In children, PVS can be primary (idiopathic) or secondary (post-surgical) following repair of total or partial anomalous pulmonary venous return[4], post pulmonary vein isolation and in Fibrosing Mediastinitis, where the patients develop severe pulmonary vein stenosis which is challenging to treat. Patients with severe PVS report symptoms of pleuritic chest pain, cough, hemoptysis and dyspnea on exertion. Untreated severe PVS can be progressive leading to irreversible lung parenchymal damage, pulmonary hypertension, heart failure and death[5].

Percutaneous intervention with balloon angioplasty (PBA) or pulmonary vein stent implantation (PSI) is the current treatment modality in adults. Re-stenosis risk after percutaneous interventions is higher in all patient categories and there is increasing adoption of stent-based strategies[6]. Available literature on this topic reports risk of restenosis with balloon angioplasty in the range of 44%-73%[6-8] and risk of re-stenosis of stent-based strategies over 16 years is 18%[8]. PVS confers poor prognosis in children and is conventionally treated with catheter intervention including PBA/PSI and/or surgery.

The former has been considered as a palliative approach. The mortality rate is as high as 47% at a median follow-up of 2 mo and re-intervention appeared to improve survival[5] and children with bare metal stents had better survival compared to drug-eluting stents (DES) and biliary atresia (BA)[9]. This may be dependent on the vessel size and on adjunctive therapy. The aim of this study is to perform a comprehensive analysis of safety and efficacy outcomes of percutaneous re-vascularization strategies of BA *vs* stent-based strategies for PVS in all patient categories.

MATERIALS AND METHODS

Protocol and registration

The protocol detailing the methods of the systematic review and meta-analysis was registered on the International Prospective Register of Systematic Reviews. The current meta-analysis was performed using the guidelines set by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[10]. Ethical review and approval were waived for this study, as our study is a meta-analysis and involves no interaction with human subjects and access to any subject identifiers.

Study identification and search strategy

We performed a comprehensive search for studies comparing PBA *vs* PSI in patient with PVSs using scientific databases (PubMed, EMBASE, Cochrane, Web of science, Scopus) from inception to December 2019. The search terms were pulmonary vein stenosis, balloon angioplasty, pulmonary balloon angioplasty, stents. The last search was run on December 31st, 2019. The authors (PA and SS) developed the search strategy along with a clinical information specialist (DA–D). The authors have read the PRISMA 2009 Checklist, and the manuscript was prepared and revised according to the PRISMA 2009 Checklist. Details of the search strategy are provided in the Supplementary Table 1-PRISMA checklist.

Study selection

Initial screening of the search results was performed by two reviewers (PA and SS). Title and abstract screening were first performed followed by comprehensive review of the entire manuscripts. When inconsistencies in screening were found and no consensus was reached a third reviewer (RA) casted the deciding vote.

Eligibility criteria

We selected all published studies comparing PBA *vs* PSI for PVS with reported outcomes of re-stenosis and procedure-related complications in all patient categories. In adults, PVS following atrial fibrillation ablation and in children PVS related to congenital etiology or post-procedural PVS following total or partial anomalous pulmonary venous return repair are included. All types of stents are included. No restrictions on study selection based on outcomes were used. Studies which assessed stent-based strategies without PBA group, abstracts which are published without full text publications and studies lacking endpoint measures were excluded.

Data extraction and quality assessment

For all the studies included, we extracted: (1) Study participants characteristics including age, gender, imaging modality after ablation, frequency of clinical symptoms related to PVS, study's inclusion criteria; (2) types of intervention- PBA *vs* PSI, stent size, post-intervention antiplatelet therapy and follow up imaging; and (3) outcome measures including re-stenosis requiring re-intervention and procedure-related complications. Cochrane Consumers and Communication Review Group's data extraction template was used to develop a standardized data extraction sheet for screening studies. The two authors independently collected the data and kappa values were used to report agreement measures. The primary outcome was re-stenosis requiring re-intervention and the secondary outcome was major complications related to procedures including death, major adverse cardiac and cerebrovascular events, major in-hospital complications requiring prolonged hospitalization or additional therapy (*i.e.* major bleeding or vascular complication, cardiac tamponade)

Quality assessment of studies, risk of bias

The study quality of included studies was assessed using the Newcastle-Ottawa Quality Assessment Scale for Cohort Studies as shown in Supplementary Table 2 (http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm). Briefly, studies were quoted using prespecified items on patients' selection (representativeness and selection of patients, ascertainment of exposure, demonstration that outcome of interest was not present at the start of the study), comparability of cohorts based on the design or analysis, and assessment of outcomes (recording, adequacy of follow-up including length of follow up). Ratings for each item were added to provide a study quality score (maximal score, 9). Two independent reviewers (PA and SS) performed the Newcastle-Ottawa Scale grading. Discrepancies were resolved by consensus.

Method of analysis

The meta-analysis was performed by computing odds ratios (ORs) using the random effects model based on underlying statistical heterogeneity. A biomedical statistician performed the statistical review of the study. We calculated the OR and 95% confidence intervals (CIs) for each treatment effect for each study and pooled the point estimates of OR from each study using the generic inverse-variance method of Der Simonian and Laird[10,11]. Stata SE Statistical Software: Release 14.1, College Station, TX: StataCorp LP, StataCorp 2015. I^2 statistics were used to test statistical heterogeneity. The I^2 statistics describes the percentage of variation across studies that is because of heterogeneity rather than those expected by random chance [$I^2 = 100\% \times (Q\text{-}df)/Q$].

A CI for I^2 was constructed using either (1) noncentral chi-squared distribution method of Hedges and Piggott (2001) or (2) test-based method of Higgins and Thompson. The heterogeneity of effect size estimates across these studies was quantified using the I^2 statistic. The I^2 statistic ranges in value from 0 to 100% (I^2 < 25%, low heterogeneity; I^2 = 25%–50%, moderate heterogeneity; and I^2 > 50%, substantial heterogeneity)[12]. Publication bias was assessed using a funnel plot and Egger's regression test[13] (P < 0.05 was considered significant). A summary of evidence table was created to summarize the main results (patient-centered outcomes) using the GRADE Pro tool [Guideline Development Tool (Software), McMaster University, 2015 (developed by Evidence Prime, Inc)][14]. Sensitivity analysis was performed for primary analysis through an influence analysis by omitting one study at a time.

RESULTS

Study selection

A total of 856 Citations were identified using Pubmed, EMBASE, Scopus, Web of Science, and Cochrane databases. We excluded 415 studies based on the title and abstracts. After these exclusions and screening rest of the studies in detail we found eight studies that met the inclusion criteria mentioned above. The PRISMA diagram was created for the systematic review Figure 1. Kappa for agreement on full text, and abstract inclusion was 0.89 (95%CI: 0.86-0.94).

Study and patient characteristics

Table 1 and 2 summarizes the study characteristics. The trials that were included were published between 2003 and 2019. Studies were observational prospective and retrospective cohort studies and had a follow-up duration of 6 mo to 48 mo. A total of 487 patients were included in this meta-analysis. Study population included children and adults; the age range of patients was 6 mo to 70 years. 67% of the study population were males, 81.5% of the study population reported symptoms of dyspnea and 8.4% of patients were asymptomatic. 768 severe PVS lesions were included from all studies. Severe pulmonary vein was defined as > 70% luminal stenosis of the pulmonary vein based on computed tomography (CT) imaging. For adults with PVS, the time between atrial fibrillation ablation/pulmonary vein isolation to the development of clinical symptoms ranged from 1 mo to 18 mo. The imaging protocols used to diagnose PVS were contrast-enhanced spiral CT scans, magnetic resonance imaging, lung perfusion scans. PVS was confirmed by invasive angiography. Procedural aspects consisted of right heart hemodynamic monitoring, selective pulmonary angiography, and access of left atrium by transseptal puncture. Interventions performed were predilation, gradual balloon dilation, stenting in a stepwise manner or primary stenting. Pulmonary vein surgery was required in 5 children in reintervention group with pericardial well procedure[5] and hybrid stenting was performed after cardiac arrest in the operating room in some children with precluding anatomic factors, difficult vascular access, multiple closely spaced ostium[9]. Post-procedural antiplatelet and anticoagulant therapy was employed to ensure vessel patency. CT imaging and other imaging modalities were employed to follow up patients (Table 3).

Structure of the meta-analysis

The study compared PBA with PSI for patients with PVS. Bare metal stents, DES and hybrid stents placed surgically in children were included in this meta-analysis.

Patient-centered outcomes

Risk of re-stenosis requiring re-intervention: The data were available for all the 8 studies including 487 patients. 196 events occurred in 325 PBA interventions and 111 events occurred in 443 PSI interventions. Results show that PBA is associated with a significantly higher risk of re-stenosis compared to PSI (OR 2.91, 95%CI: 1.15-7.37, P = 0.025). A high degree of heterogeneity was noted (I^2 = 79.2%). Figure 2 shows the forest plots analysis for this outcome.

Risk of procedure-related complications: The data was available for 3 studies, 7 events occurred in 122 PBA interventions and 6 in 69 PSI interventions. Overall results show that there is no difference in procedure-related complications between PBA *vs* PSI for PVS (OR: 0.94, 95%CI: 0.23-3.76, P = 0.929),

Table 1 Main demographics of patients treated with either balloon angioplasty or stenting included in meta-analysis

Ref.	Patients (*n*)	Mean age (yr)	Males (%)	Frequency of clinical symptoms; Dyspnea (%)	Hemoptysis (%)	Asymptomatic (%)	Severe PVS treated (*n*)
Qureshi *et al* [19]	19	51 ± 13	NA	95	63	5	37
Prieto *et al*[7]	44	53 ± 11	70	88	23	7	68
Neumann *et al* [6]	12	58	70	77	8	17	15
Fender *et al* [20]	113	50	77	67	27	0	178
Cory *et al*[5]	30	Median age-6.4 m	50	NA	NA	NA	58
Schoene *et al* [15]	39	62.1 ± 9.0	60	79	26	NA	61
Kurita *et al*[9]	31	7 mo	65	NA	NA	NA	53
Suntharos *et al* [8]	199	55 ± 12	78	83	13	13	319

NA: Not available; PVS: Pulmonary vein stenosis.

without heterogeneity (I^2 = 0.0%). The forest plot analysis for this outcome is shown in Figure 3. In a study by Prieto *et al*[7], one patient in PBA group while undergoing pulmonary vein (PV) dilation developed an intimal flap needing stenting and had a transient ischemic event without permanent debility. Two patients in the stenting group developed tamponade requiring evacuation of pericardial space but there was no mortality. In a study by Neumann *et al*[6], there were 3 adverse events- one patient developed hemoptysis immediately after dilation of the left upper PV which stopped 10 min after protamine administration, one patient developed small dissection of the left upper PV during dilation before stenting distally with clinical hemoptysis which resolved by additional stenting of the vein distal to the original stenosis and allergic reaction to the contrast agent used was seen in one patient. In a study by Schoene *et al*[15], major events in PBA group were 2 wire-induced PV perforations with tamponade managed by pericardiocentesis and 2 balloon-induced PV ruptures with tamponade managed by urgent surgical repair in one and emergency stenting and pericardiocentesis in another. In the stent group, an acute stent thrombosis resulting in a stroke occurred which was complicated by intracerebral bleeding with thrombolytic therapy use but there was no mortality. Supplementary Tables provide further information regarding outcomes in the included studies (Supplementary Tables 3 and 4).

Sensitivity analysis: The funnel plot distribution of outcomes was derived from the standard error of the logarithm OR plotted against the OR of re-stenosis and procedure-related complications, respectively (Supplementary Figures 1 and 2). Influence analysis demonstrated that no single study significantly altered the summary ORs for the primary or secondary outcome, because the exclusion of each study did not alter the point estimate outside the 95%CI (Figure 4 and 5).

DISCUSSION

The analysis examines the safety and efficacy of intervention with PBA *vs* PSI in patients with PVS. The principal findings of our study include (1) Similar safety profile of PBA *vs* PSI in the management of PVS; and (2) A higher risk of re-stenosis with PBA in comparison to PSI in patients with PVS. The PSI demonstrated a lower risk of re-stenosis can be attributed to the use of stents in patients with higher risk and the use of devices not particularly designed for PVS intervention. A follow-up with cardiac imaging every 3-6 mo is usually done in patients with asymptomatic PVS with about 50%-70% stenosis, particularly with ipsilateral PVS, and revascularization is considered when the PVS progress to severe grade defined as luminal stenosis > 70% by CT imaging[16]. Intervention needs to be performed urgently in patients with concomitant ipsilateral PVS in order to prevent potential progressive vascular fibrosis, occlusion, atrophy, and congestion with consequent lung infarction[17].

In the advent of suboptimal results of angiography and the occurrence of complications post-dilation, an acute mechanical benefit is provided well by stents compared to PBA. In addition, it is suggested that there is a time-dependent reduction in patency of the vessel post-PBA, making stenting favored in terms of long-term advantages[18]. This can be ascribed to the pathophysiological mechanisms of the venous

Table 2 Clinical characteristics of patients treated with either balloon angioplasty or stenting included in meta-analysis

Ref.	Study type	Enrolment Period	Main inclusion criteria	Imaging after ablation	Mean time between PVI and clinical symptoms	Revascularization approach	Stent size	Acute angiographic success	Primary outcome at follow-up	Follow-up
Qureshi *et al*[19], 2003	*Observational retrospective study*	2000-2002	Severe PVS with clinical symptoms	CT-scans in symptomatic patients	4 mo	Stepwise	4-10 mm	NA	Freedom of reinter-vention	10 ± 9 mo
Prieto *et al* [7], 2008	*Observational retrospective study*	2000-2007	Severe PVS with clinical symptoms	CT-scans, lung perfusion scans in symptomatic patients	11.5 mo	Stepwise/primary stenting	8-10 mm	Residual stenosis ≤ 30%	Recurrence of symptoms requiring reintervention	25 ± 21 mo
Neumann *et al*[6], 2009	*Observational prospective study*	2003-2005	Severe PVS (> 70%) with clinical symptoms and/or significant perfusion defect	Surveillance imaging with MRI, lung perfusion scans, CT scans, TTE every 3 mo	NA	Stepwise (if rebound stenosis was observed after balloon dilatation)/primary stenting	8-12 mm	NA	Clinically symptomatic restenosis	48 mo
Fender *et al* [20], 2016	*Observational prospective study*	2000-2014	Severe PVS (> 75%) with clinical symptoms	Surveillance imaging with CT-scans at 3 mo + CT-scans and lung perfusion scans in symptomatic patients	4.0 ± 3.0 mo	Stepwise	6-10 mm + DES 4 mm	Residual stenosis < 20%	Clinically symptomatic restenosis	48 mo
Cory *et al* [5], 2017	*Observational retrospective study*	2005-2016	Catheter intervention for PVS for patients < 18 yr	NA	NA	Stepwise/primary stenting	Median-DES 4 mm, BMS 5 mm	NA	Mortality following transcatheter PV intervention	Median of 30.6 mo
Schoene *et al*[15], 2018	*Observational retrospective study*	2004-2017	Symptomatic PVS with > 70% in a single stenosis or > 60% in multiple ipsilateral stenosis	Initial screening process from 2004-2007- TEE 6-12 mo after PVI or when symptomatic, subsequent CT or MRI. Screening terminated in 2008, symptomatic patients underwent CT, MRI and/or PV angiography	10.2 ± 8.0 mo	Stepwise/primary stenting	Median stent- 7 mm × 20 mm, DES 5 mm	Residual stenosis < 10%-20%	Restenosis rate following transcatheter intervention	Median of 6 mo
Kurita *et al* [9], 2019	*Observational retrospective study*	2001-2017	PVS associated with total anomalous pulmonary venous connection and isolated congenital PVS	Combination of ultrasound, CT and angiography	Median 7 from birth	Stepwise/primary stenting-PCI/hybrid surgery	3-8 mm	NA	In-stent restenosis following stent placement using CT or angiography ≥ 50% higher stenosis of stent size	19 mo
Suntharos *et al*[8], 2019	*Observational retrospective study*	2000-2016	PVS after PVI undergoing PCI	CT-scan pulmonary vein protocol, quantitative lung perfusion scan	NA	Stepwise/primary stenting	3-16 mm	NA	Freedom of reinrevention	Median follow up-17 mo

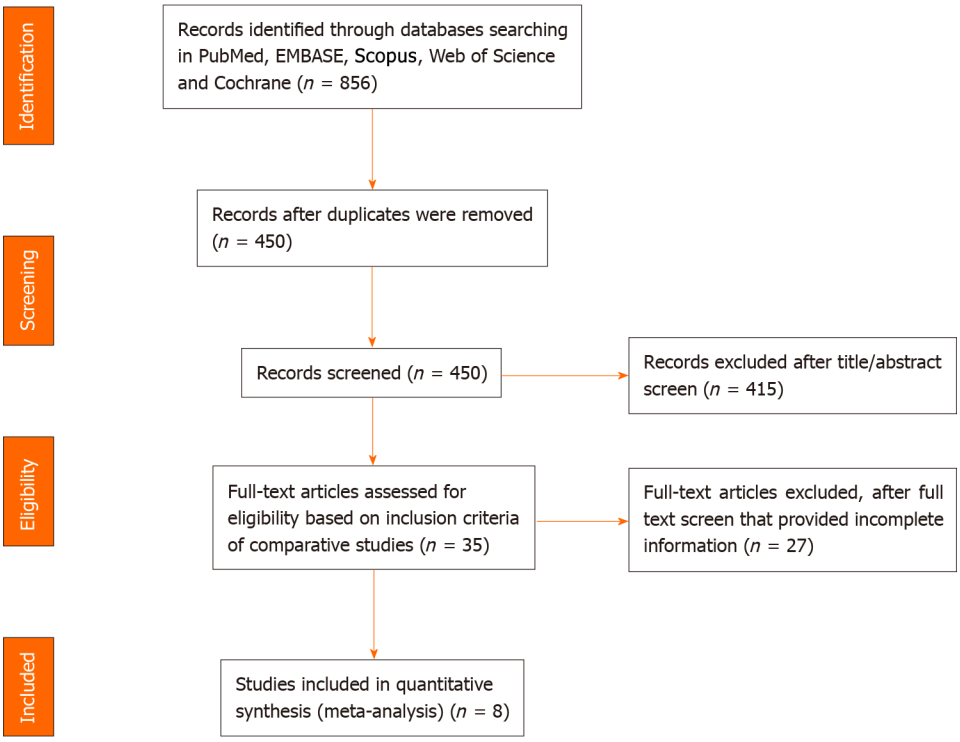
CT: Computed tomography; DES: Drug-eluting stents; NA: Not available; PVI: Pulmonary vein isolation; PVS: Pulmonary vein stenosis; PV: Pulmonary vein; TEE: Transesophageal echocardiography; MRI: Magnetic resonance imaging; PCI: Percutaneous interventions.

system as well as the histological features. This ensues from post-thrombotic fibrosis inside and around the vein, with extravenous compressive bands and accompanying perivenous fibrosis leading to the obstructive processes in intima at ablation sites, which also involves the distal sites to PV ostia. Stenting

Table 3 Follow up characteristics after revascularization

Ref.	Antiplatelet therapy	Imaging modalities	Restenosis definition
Qureshi *et al* [19], 2003	NR	CT-scans every 3 mo	PV narrowing > 70% of the original PV lumina
Prieto *et al*[7], 2008	NR	CT-scans, lung perfusion scans at 3-12-24 mo	NR
Neumann *et al* [8], 2009	ASA+Clopidogrel+Coumadin for 3 mo	CT-scans, lung perfusion scans every 3 mo	PV narrowing > 70%of the original PV lumina before PVI
Fender *et al* [20], 2016	Coumadin+Clopidogrel	CT-scans, lung perfusion scans at 3-12-24 mo	PV narrowing > 75% in the previously treated PV
Cory *et al*[5], 2017	NA	Angiography	Vein loss defined as PV atresia or PVs of uncertain status in deceased patients
Schoene *et al* [15], 2018	ASA 4 weeks+Clopidogrel 6 mo+Coumadin or DOACs	CT-scans, MR imaging	PV narrowing > 70% in the previously treated PV
Kurita *et al*[9], 2019	ASA, Ticlopidin, Warfarin	CT or angiography	In stent restenosis: ≥ 50% luminal narrowing
Suntharos *et al* [8], 2019	Anticoagulation followed by low-dose aspirin	CT-scans, lung perfusion scans, angiography based on intervention-3 mo, 6 mo, 1yr	Severe restenosis/concern for progression to total occlusion

ASA: Acetyl salicylic acid; CT: Computed tomography; NA: Not available; NR: Not reported; PV: Pulmonary vein; PVI: Pulmonary vein isolation.



DOI: 10.4330/wjc.v15.i2.64

Figure 1 PRISMA flow diagram for clinical study selection for meta-analysis.

may be able to provide an advantage against these pathophysiological mechanisms.

Studies show a high success rate and low re-stenosis rates of PSI compared to PBA, with longer freedom from re-stenosis[6]. Hence, stenting can be considered a first-line strategy. Studies have also consistently shown that large stent sizes, have excellent clinical outcomes and long-term patencies. Meta-analyses showed that long-term patency is better with large stent sizes of 9-10 mm[6,7]. The incidence of in-stent re-stenosis is shown to be less in large stents, as opposed to small stents[17,19,20]. Although stenting is widely used in the pulmonary vein, the operator needs to be careful due to the risk of protruding into the LA, jailing PV side branches, and crossing a low-flow distal side branch[18]. Other frequent complications, such as hemoptysis and self-limiting hemorrhages, have been found to be similar between the two groups. Revascularization is indicated in the advent of elevated PA pressure

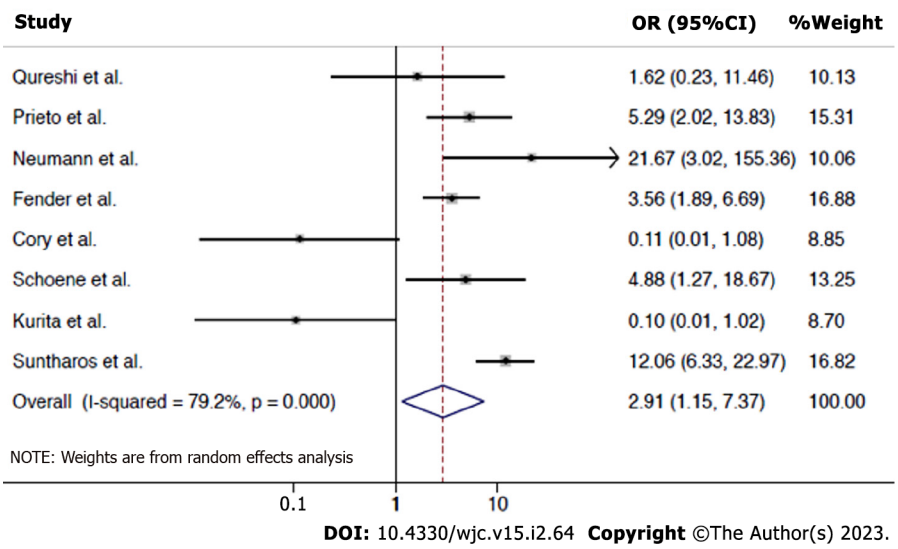


Figure 2 Forest plot for recurrent pulmonary vein stenosis in pulmonary vein balloon angioplasty group compared to pulmonary vein stent implantation group.

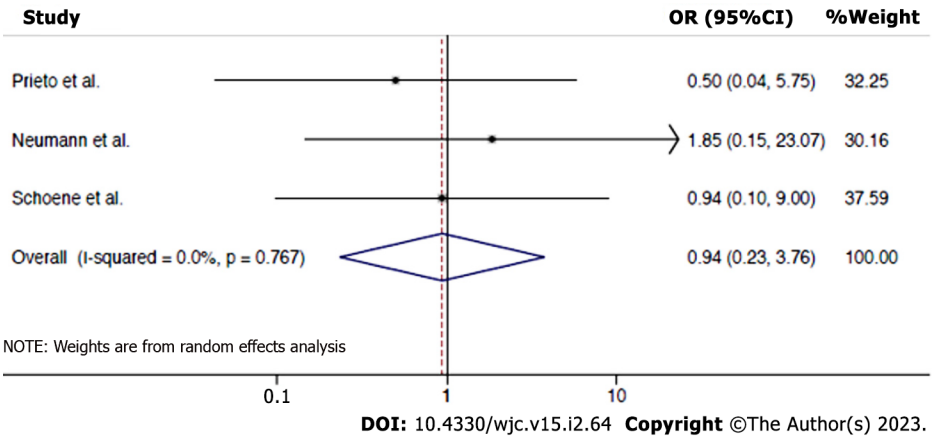


Figure 3 Forest plot for procedure related complications in pulmonary vein balloon angioplasty group versus pulmonary vein stent implantation group.

levels or the presence of typical symptoms. There is a chance of missing the diagnosis as the progression is unpredictable, and clinical symptoms may be atypical and can appear late. But early diagnosis and intervention are essential to prevent irreversible pulmonary damage.

Limitations of the study need to be acknowledged. The present study analyzes data comparing PBA and PSI from observational studies, but not randomized controlled trials. The analysis tends to be challenging to interpret when patients are treated with stenting after trial and failure of BA, as observed in some studies. In addition, procedural success and severe PVS definitions differ widely in studies, subsequently causing substantial heterogeneity. Also, the follow-up imaging techniques and protocols vary widely in the studies, which come into play when diagnosing post-procedural re-stenosis. Lastly, the antiplatelet/anticoagulation regimens post-procedure varies considerably in studies which might have possibly modified the treatment effect. The regimens were not consistently reported among different studies (Cory *et al*[5], Prieto *et al*[7], and Qureshi *et al*[19] didn't mention their regimens). The reported antiplatelet/anticoagulation regimens were also various, including 3 mo of dual-antiplatelet therapy[6], warfarin and aspirin/ticlopidine[9], and at least 6 mo of anticoagulation followed by long term aspirin[8]. Interestingly, the re-stenosis rates varied between the two studies included an anticoagulation agent (70% at 5 years, and 27% at 5 years), whereas the dual-antiplatelet regimen was associated with a 23% restenosis at about 4 years. This observation implies the post-procedural antiplatelet/anticoagulation regimens may have a minor role for restenosis.

Summary of evidence

The current analysis updates the summary of evidence by incorporating two recent observational

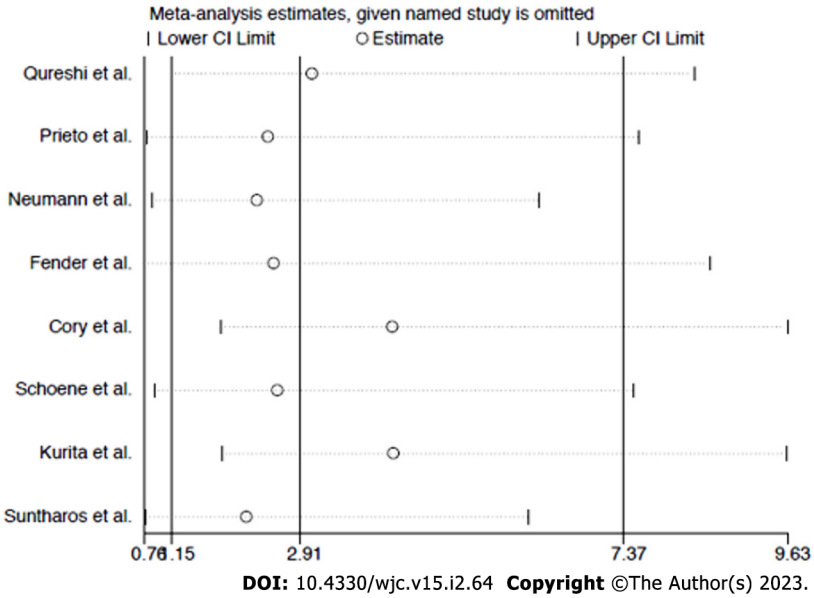


Figure 4 Sensitivity analysis for recurrent pulmonary vein stenosis.

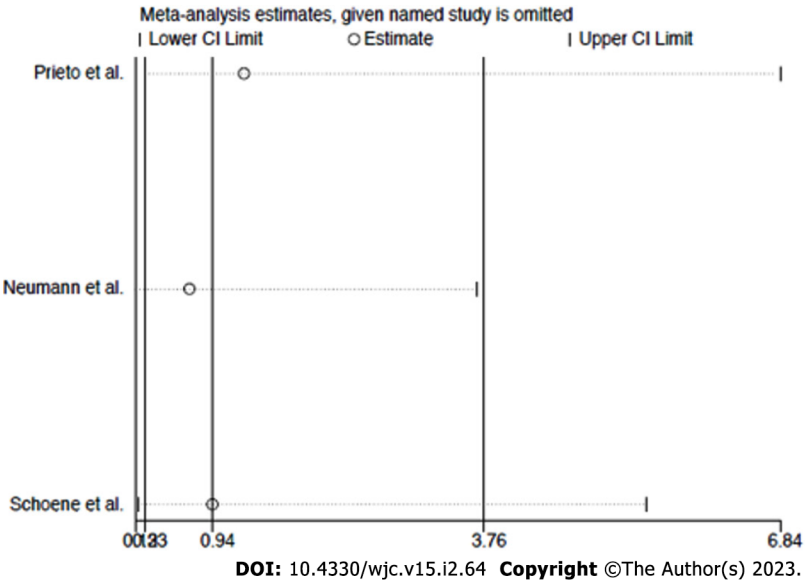


Figure 5 Sensitivity analysis for procedure related complications.

studies. Overall, we found sufficient evidence evaluating the comparative efficacy of pulmonary vein isolation (PVI) and PBA in treating patients with PVS. The outcomes with a moderate grade of certainty of evidence include pulmonary restenosis and procedure-related complications (Table 4).

CONCLUSION

Percutaneous re-vascularization with stents appears to be superior to PBA, in regard to re-stenosis and the need for re-intervention. Hence, stenting should be considered as the first line of choice over BA. A further follow-up to ascertain the real success of the intervention and the re-stenosis patterns is crucial.

Table 4 Summary of evidence

Outcomes	Anticipated absolute effects[a] (95%CI)		Relative effect (95%CI)	No. of participants (studies)	Certainty of the evidence (GRADE)[b]
	Risk with PSI	Risk with PBA			
Restenosis	251 per 1000	493 per 1000 (278 to 711)	OR 2.91 (1.15 to 7.37)	487 (8 observational studies)	⊕ ⊕ ⊕ ◯ MODERATE[c]
Procedure related complications	87 per 1000	82 per 1000 (21 to 264)	OR 0.94 (0.23 to 3.76)	191 (3 observational studies)	⊕ ⊕ ⊕ ◯ MODERATE[c]

[a]The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95%CI).

[b]GRADE Working Group grades of evidence: (1) High certainty: We are very confident that the true effect lies close to that of the estimate of the effect; (2) Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different; (3) Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect; and (4) Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

[c]Rated down for imprecision as the 95% confidence interval overlaps with no effect and fails to exclude important benefit or important harm. PBA: Pulmonary vein balloon angioplasty; PSI: Pulmonary vein stent implantation.

ARTICLE HIGHLIGHTS

Research background

Pulmonary vein balloon angioplasty (PBA) and pulmonary vein stent implantation (PSI) are the two re-vascularization strategies used to manage pulmonary vein stenosis.

Research motivation

Both these strategies are widely used to treat pulmonary vein stenosis. Our study tends to explore outcomes and complications with each of these strategies

Research objectives

Our study tried to explore the safety and efficacy outcomes of two re-vascularization strategies Pulmonary vein balloon angioplasty *vs* pulmonary vein stent implantation in the management of pulmonary vein stenosis.

Research methods

The meta-analysis was performed by computing odds ratios using the random effects model based on underlying statistical heterogeneity.

Research results

The primary outcome of the re-stenosis requiring re-intervention occurred in 196 of 325 veins in the PBA group and 111 of 443 veins in the PSI group. Compared to PSI, PBA was associated with a significantly increased risk of restenosis (OR 2.91, 95%CI: 1.15-7.37, $P = 0.025$, $I^2 = 79.2\%$).

Research conclusions

Percutaneous re-vascularization with stents appears to be superior to PBA, in regard to re-stenosis and the need for re-intervention. Hence, stenting should be considered as the first line of choice over balloon angioplasty.

Research perspectives

A further follow-up to ascertain the real success of the intervention and the re-stenosis patterns is crucial.

FOOTNOTES

Author contributions: Agasthi P and Sridhara S contributed equally to this work; Agasthi P, Sridhara S, Mookadam F, Fortuin FD and Arsanjani R, designed the research study; Agasthi P, Sridhara S, Rattanawong P, Venepally NR, Chao C, Ashraf H and Pujari S performed the research; Douglas DA, Allam Mohamed, Alla Y, Kumar A contributed new reagents and analytic tools; Agasthi P, Sridhara S, Rattanawong P, Venepally NR, Chao C, Ashraf H, Pujari S and Allam M analyzed the data and wrote the manuscript; Mookadam F, Packer DL, Holmes DR Jr, Hagler DJ, Fortuin FD and Arsanjani R reviewed the manuscript before submission; All authors have read and approved the final

manuscript.

Conflict-of-interest statement: All the authors received no financial support for the research, authorship, and/or publication of this article.

PRISMA 2009 Checklist statement: The authors have read the PRISMA 2009 Checklist, and the manuscript was prepared and revised according to the PRISMA 2009 Checklist.

Country/Territory of origin: United States

ORCID number: Pradyumna Agasthi 0000-0003-3067-6979; Srilekha Sridhara 0000-0002-7216-9716; Pattara Rattanawong 0000-0001-9419-5854; Nithin Venepally 0000-0002-7156-1927; Chieh-Ju Chao 0000-0001-6155-0266; Hasan Ashraf 0000-0002-2820-6735; Sai Harika Pujari 0000-0002-1073-7482; Mohamed Allam 0000-0002-3915-5187; Diana Almader-Douglas 0000-0001-6538-666X; Yamini Alla 0000-0002-4007-4616; Farouk Mookadam 0000-0002-9056-8956; Douglas L Packer 0000-0003-2060-869X; David R Holmes Jr 0000-0002-0037-0373; Donald J Hagler 0000-0002-0331-3294; Floyd David Fortuin 0000-0003-2820-6839; Reza Arsanjani 0000-0001-7081-4286.

S-Editor: Liu JH
L-Editor: A
P-Editor: Liu JH

REFERENCES

1 **Cappato R**, Calkins H, Chen SA, Davies W, Iesaka Y, Kalman J, Kim YH, Klein G, Packer D, Skanes A. Worldwide survey on the methods, efficacy, and safety of catheter ablation for human atrial fibrillation. *Circulation* 2005; **111**: 1100-1105 [PMID: 15723973 DOI: 10.1161/01.CIR.0000157153.30978.67]

2 **Kuck KH**, Fürnkranz A. Cryoballoon ablation of atrial fibrillation. *J Cardiovasc Electrophysiol* 2010; **21**: 1427-1431 [PMID: 21091966 DOI: 10.1111/j.1540-8167.2010.01944.x]

3 **Marrouche NF**, Martin DO, Wazni O, Gillinov AM, Klein A, Bhargava M, Saad E, Bash D, Yamada H, Jaber W, Schweikert R, Tchou P, Abdul-Karim A, Saliba W, Natale A. Phased-array intracardiac echocardiography monitoring during pulmonary vein isolation in patients with atrial fibrillation: impact on outcome and complications. *Circulation* 2003; **107**: 2710-2716 [PMID: 12756153 DOI: 10.1161/01.CIR.0000070541.83326.15]

4 **Seale AN**, Webber SA, Uemura H, Partridge J, Roughton M, Ho SY, McCarthy KP, Jones S, Shaughnessy L, Sunnegardh J, Hanseus K, Rigby ML, Keeton BR, Daubeney PE; British Congenital Cardiac Association. Pulmonary vein stenosis: the UK, Ireland and Sweden collaborative study. *Heart* 2009; **95**: 1944-1949 [PMID: 19737738 DOI: 10.1136/hrt.2008.161356]

5 **Cory MJ**, Ooi YK, Kelleman MS, Vincent RN, Kim DW, Petit CJ. Reintervention Is Associated With Improved Survival in Pediatric Patients With Pulmonary Vein Stenosis. *JACC Cardiovasc Interv* 2017; **10**: 1788-1798 [PMID: 28823777 DOI: 10.1016/j.jcin.2017.05.052]

6 **Neumann T**, Kuniss M, Conradi G, Sperzel J, Berkowitsch A, Zaltsberg S, Wojcik M, Erkapic D, Dill T, Hamm CW, Pitschner HF. Pulmonary vein stenting for the treatment of acquired severe pulmonary vein stenosis after pulmonary vein isolation: clinical implications after long-term follow-up of 4 years. *J Cardiovasc Electrophysiol* 2009; **20**: 251-257 [PMID: 19261037 DOI: 10.1111/j.1540-8167.2008.01316.x]

7 **Prieto LR**, Schoenhagen P, Arruda MJ, Natale A, Worley SE. Comparison of stent versus balloon angioplasty for pulmonary vein stenosis complicating pulmonary vein isolation. *J Cardiovasc Electrophysiol* 2008; **19**: 673-678 [PMID: 18284494 DOI: 10.1111/j.1540-8167.2008.01110.x]

8 **Suntharos P**, Worley SE, Liu W, Siperstein M, Prieto LR. Long-term outcome of percutaneous intervention for pulmonary vein stenosis after pulmonary vein isolation procedure. *Catheter Cardiovasc Interv* 2020; **95**: 389-397 [PMID: 31778024 DOI: 10.1002/ccd.28628]

9 **Kurita Y**, Baba K, Kondo M, Eitoku T, Kasahara S, Iwasaki T, Ohtsuki S, Tsukahara H. Clinical outcomes after the endovascular treatments of pulmonary vein stenosis in patients with congenital heart disease. *Cardiol Young* 2019; **29**: 1057-1065 [PMID: 31287033 DOI: 10.1017/S1047951119001495]

10 **DerSimonian R**, Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986; **7**: 177-188 [PMID: 3802833 DOI: 10.1016/0197-2456(86)90046-2]

11 **Moher D**, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009; **6**: e1000097 [PMID: 19621072 DOI: 10.1371/journal.pmed.1000097]

12 **Higgins JP**, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003; **327**: 557-560 [PMID: 12958120 DOI: 10.1136/bmj.327.7414.557]

13 **Sterne JA**, Egger M. Funnel plots for detecting bias in meta-analysis: guidelines on choice of axis. *J Clin Epidemiol* 2001; **54**: 1046-1055 [PMID: 11576817 DOI: 10.1016/s0895-4356(01)00377-8]

14 **GS HJ**. Cochrane Handbook for Systematic Reviews of Interventions. Hoboken, NJ: John Wiley & Sons; 2011 [DOI: 10.1111/1556-4029.12195]

15 **Schoene K**, Arya A, Jahnke C, Paetsch I, Nedios S, Hilbert S, Bollmann A, Hindricks G, Sommer P. Acquired Pulmonary Vein Stenosis After Radiofrequency Ablation for Atrial Fibrillation: Single-Center Experience in Catheter Interventional Treatment. *JACC Cardiovasc Interv* 2018; **11**: 1626-1632 [PMID: 30139470 DOI: 10.1016/j.jcin.2018.05.016]

16 **Rostamian A**, Narayan SM, Thomson L, Fishbein M, Siegel RJ. The incidence, diagnosis, and management of pulmonary vein stenosis as a complication of atrial fibrillation ablation. *J Interv Card Electrophysiol* 2014; **40**: 63-74 [PMID: 24626996 DOI: 10.1007/s10840-014-9885-z]

17 **Di Biase L**, Fahmy TS, Wazni OM, Bai R, Patel D, Lakkireddy D, Cummings JE, Schweikert RA, Burkhardt JD, Elayi CS, Kanj M, Popova L, Prasad S, Martin DO, Prieto L, Saliba W, Tchou P, Arruda M, Natale A. Pulmonary vein total occlusion following catheter ablation for atrial fibrillation: clinical implications after long-term follow-up. *J Am Coll Cardiol* 2006; **48**: 2493-2499 [PMID: 17174188 DOI: 10.1016/j.jacc.2006.08.038]

18 **Buiatti A**, von Olshausen G, Martens E, Schinke K, Laugwitz KL, Hoppmann P, Ibrahim T. Balloon angioplasty versus stenting for pulmonary vein stenosis after pulmonary vein isolation for atrial fibrillation: A meta-analysis. *Int J Cardiol* 2018; **254**: 146-150 [PMID: 29273240 DOI: 10.1016/j.ijcard.2017.11.100]

19 **Qureshi AM**, Prieto LR, Latson LA, Lane GK, Mesia CI, Radvansky P, White RD, Marrouche NF, Saad EB, Bash DL, Natale A, Rhodes JF. Transcatheter angioplasty for acquired pulmonary vein stenosis after radiofrequency ablation. *Circulation* 2003; **108**: 1336-1342 [PMID: 12952852 DOI: 10.1161/01.CIR.0000086322.21781.6A]

20 **Fender EA**, Packer DL, Holmes DR Jr. Pulmonary vein stenosis after atrial fibrillation ablation. *EuroIntervention* 2016; **12** Suppl X: X31-X34 [PMID: 27174109 DOI: 10.4244/EIJV12SXA7]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: bpgoffice@wjgnet.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com