Characteristics and Outcomes of Pulmonary Angioplasty With or Without Stenting for Sarcoidosis-Associated Pulmonary Hypertension: Systematic Review and Individual Participant Data Meta-Analysis

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Abstract: ***Background:*** **Pulmonary angioplasty has been performed in patients with sarcoidosis-associated pulmonary hypertension (SAPH) but most evidence comes from case reports and small case series. Overall outcomes remain unclear. We conducted an individual participant data (IPD) meta-analysis of baseline, procedural, and outcome data of pulmonary angioplasty in patients with SAPH.** ***Methods:*** **We performed searches and systematically reviewed references from PubMed, Embase, Cochrane, ClinicalTrials.gov, and grey literature. We included IPD of patients who underwent pulmonary angioplasty for SAPH. Those without definitive diagnosis of sarcoidosis or with other causes of pulmonary vascular stenosis or compression were excluded.** ***Results:*** **Of 1293 screened**

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references, 7 were included. IPD was obtained for 17 patients (mean age 58.6 (±9.1) years; 82.4% female); most of whom were Scadding stages III or IV and had NYHA FC III or IV. All patients with documented changes in 6-minute-walk distance (6MWD) had a significant improvement that ranged from 12.6 to 102.4% ($P < 0.01$). There were no deaths during a median follow-up of 6 (3-18) months. ***Conclusions:*** **Pulmonary angioplasty with or without stenting of focal stenosis or compressions of pulmonary vessels may lead to significant improvement in 6MWD in patients with SAPH. However, this study had a small sample and some methodological limitations, such as analysis mostly of case reports and series. Randomized controlled clinical trials and/or large multicenter registry studies are needed to provide higher evidence in this topic. (Curr Probl Cardiol 2021;46:100616.)**

INTRODUCTION

Sarcoidosis-associated pulmonary hypertension (SAPH) is considered a rare and terminal condition. Despite the advent of multiple vasodilators resulting in improvement in outcomes of World Health Organization (WHO) group 1 pulmonary hypertension (PH), this has not translated into a clear benefit for patients with SAPH. Studies on therapeutic interventions for SAPH are scarce and are typically small-sized, likely due to a combination of factors such as heterogeneity of the patient population with SAPH, incomplete pathophysiologic understanding of this entity, as well as underdiagnosis/delayed diagnosis and undertreatment of this condition.[1-8]

Given the pathophysiological complexity of SAPH, it is classified as WHO group 5.[9] This leads to an oversimplification and questionable recommendation of addressing only the underlying condition (sarcoidosis) and avoiding PH-directed therapies. As consequence, current standard alternatives are restricted to immunosuppressive regimens, typically ineffective for SAPH, palliative measures or, rarely, lung transplantation.[10] Nevertheless, over the last 12 years, some authors have described cases of SAPH associated with focal stenosis or external compression of the pulmonary vasculature amenable for balloon angioplasty (BA) and stenting.[11-13]

Although promising and thought-provoking, those experiences were mostly limited to case reports,[14-16] small case series,[11,12] and a small

cohort.[13] Such restricted data set, limited mainly to experiences about single or small groups of patients results, makes it difficult to generalize to the SAPH population, even more considering the existence of conflicting results. Therefore, we conducted a systematic review and individual participant data (IPD) meta-analysis of the baseline and procedural characteristics, and outcomes of patients with SAPH undergoing pulmonary BA with or without stenting for vascular stenosis or compression.

METHODS

This meta-analysis was designed and conducted in accordance to PRISMA IPD 2015 Guidelines.[17] The initial protocol for this study was registered in PROSPERO (ID CRD42020156522). The protocol underwent a subsequent edition after discussions with a senior interventional cardiologist, but PROSPERO did not allow to upload editions while the initial protocol was still undergoing revision for registration.

Search strategy

We conducted a systematic search in ClinicalTrials.gov, Embase, PubMed, and The Cochrane Library using combinations of "sarcoidosis" and "pulmonary hypertension" terms without restrictions of any sort. When allowed by the search engine, indexing terms were also used in the following fashion: ("sarcoidosis" OR [sarcoidosis indexing term]) AND ("pulmonary hypertension" OR [pulmonary hypertension indexing term]). In the case of PubMed, this led to the following search: (("Sarcoidosis"[Mesh] OR "sarcoidosis")) AND (("Hypertension, Pulmonary"[Mesh]) OR "pulmonary hypertension"). We performed the aforementioned searches on November 1, 2019.

We screened additional references cited in other articles found in this search, as well as relevant articles obtained for a previous review, and relevant citations identified on Google Scholar using multiple combinations of additional terms, such as "sarcoidosis," "pulmonary hypertension," "angioplasty," "stent," "pulmonary artery," "pulmonary veins," "pulmonary vessels," etc.

Study-level selection

We included all study designs (randomized-clinical trials, cohorts, case-controls, case series, case reports) and publication types (articles, abstracts, trial registries with results, and other scientific reports) with subjects that met patient-level selection criteria. For studies with both articles and abstracts available, the former was the one selected.

Patient-level selection

We included all patients with SAPH and pulmonary vascular stenosis and/or external compression that received BA and/or stenting of the pulmonary vasculature. Patients without definitive diagnosis of sarcoidosis or with other causes of pulmonary vascular stenosis or compression were excluded.

Data collection

All references retrieved were imported into EndNote X8 (Clarivate Analytics, Philadelphia, PA). Duplicates were eliminated using the automated identification processes of EndNote X8, and then Rayyan (Qatar Computing Research Institute, Doha, Qatar). Two investigators worked independently, in parallel to select and extract references and datapoints. Disagreements were solved by discussion and achievement of a consensus with help of a third investigator to achieve simple majority.

Missing information was requested to at least one author of each study. If no response was obtained, we attempted to reach another coauthor, if feasible. We provided a data-collection tool on a Microsoft Office Excel file (Microsoft Corporation, Redmond, WA) to authors who agreed to collaborate and provide unpublished data. Official communication and file-sharing was conducted using our institutional e-mails.

Variables

When available, the following variables were obtained:

At reference-level: first author, year of publication, country, institution where the procedures took place, and number of participants meeting inclusion criteria (Table 1).

At patient-level: a senior interventional cardiologist and a senior cardiologist specialized in advanced heart failure and PH participated in the selection and definition of variables. They also helped to mediate disagreements in the data collected by other investigators of the team. Most important IPD variables are listed in Tables 2-4.

Data synthesis and analysis

Continuous variables with normal distribution were summarized with mean (standard deviation). Those with non-normal distribution were described with median (p 25-75). Categorical variables were summarized using percentages. Changes in 6-minute-walk distance (6MWD), New

TABLE 1. Reference-level characteristics of included studies

Author	Year of publication	Study type	Institution	Country	Number of patients with SAPH*
Hamilton-Craig[12]	2009	Case series	The Prince Charles Hospital (Brisbane, QLD)	Australia	2
Ferguson[20]	2010	Case series	Mayo Clinic (Rochester, MN)	USA	1
Sekiguchi[16]	2013	Case report	Mayo Clinic (Rochester, MN)	USA	1
Condado[11]	2016	Case series	Emory University School of Medicine (Atlanta, GA)	USA	3
Liu[13]	2016	Prospective cohort	Xijing Hospital (Shaanxi, Xi'an)	China	8
Bazmpani[14]	2017	Case report	AHEPA University Hospital (Thessaloniki)	Greece	1
Tramper[15]	2018	Case report	VU University Medical Centre (Amsterdam)	The Netherlands	1

*Number of patients that underwent balloon angioplasty with or without stenting. SAPH, sarcoidosis-associated pulmonary hypertension.

TABLE 2. Individual participant data of the baseline and postprocedural functional outcomes

Author	Patient #	Sex	Age (years)	Race	Scadding stage	Pre-procedural steroids	Baseline NYHA FC	Baseline 6MWD (m)	Baseline mPAP (mm Hg)	Post-procedural NYHA FC	Post-procedural 6MWD (m)	Post-procedural mPAP (mm Hg)
Hamilton-Craig[12]	1	M	71	-	1	No	3	210	42	2	425	36
	2	F	48	-	-	-	-	-	-	-	-	-
Ferguson[20]	3	F	58	-	-	-	-	-	-	-	-	-
Sekiguchi[16]	4	F	60	W	2	No	-	-	26	-	-	-
Condado[11]	5	F	63	AA	-	Yes	-	244	50	-	390	45
	6	F	42	AA	-	Yes	-	-	90	-	-	42
	7	F	60	AA	-	Yes	-	-	48	-	-	29
Liu[13]	8	F	55	A	3	Yes	3	236 (± 36.7)	42.5 (± 4.6)	Improved*,†	456.4 (± 48.2)*	20.5 (± 3.2)*
	9	F	46	A	3	Yes	4					
	10	M	65	A	3	Yes	3					
	11	F	68	A	3	Yes	3					
	12	F	58	A	3	Yes	3					
	13	F	69	A	4	Yes	4					
	14	F	67	A	4	Yes	4					
	15	M	62	A	4	Yes	4					
Bazmpani[14]	16	F	62	W	1	No	-	-	-	-	-	-
Tramper[15]	17	F	43	AA	-	Yes	3	422	48	2	475	22

*All patients in this cohort had a postprocedural improvement in 6MWD, mPAP, and NYHA FC.

†No numerical data was available for individual participant but it was documented that all patients in this cohort had improvement in this outcome. Hyphen (-), no information available; 6MWD, six-minute walk distance, A, Asian; AA, African American; C, Caucasian; F, female; M, male; m, meter; mm Hg, millimeters of mercury; mPAP, mean pulmonary arterial pressure; NYHA FC, New York Heart Association Functional Class; W, white.

TABLE 3. Individual participant data of the anatomical location of the pulmonary vascular stenosis or obstructions

Author	Patient #	Location of the stenosis or compression						
		Main PA trunk	LPA trunk	RPA trunk	LPA branches	RPA branches	Multiple arterial stenosis	Pulmonary veins
Hamilton-Craig[12]	1	0	1	1	1	1	1	0
	2	-	-	-	-	-	-	0
Ferguson[20]	3	0	0	1	0	0	0	0
Sekiguchi[16]	4	0	0	1	1	0	1	0
Condado[11]	5	0	0	1	1	1	1	1
	6	0	0	0	1	1	1	0
	7	0	1	0	1	1	1	1
Liu[13]	8	-	-	-	-	-	-	0
	9	-	-	-	-	-	-	0
	10	-	-	-	-	-	-	0
	11	-	-	-	-	-	-	0
	12	-	-	-	-	-	-	0
	13	-	-	-	-	-	-	0
	14	-	-	-	-	-	-	0
	15	-	-	-	-	-	-	0
Bazmpani[14]	16	0	0	0	0	1	1	0
Tramper[15]	17	0	0	0	0	1	1	0

Note: Hyphen (-), no information available; Zero (0), absence of lesion; One (1), presence of a lesion; LPA, left pulmonary artery; PA, pulmonary artery; RPA, right pulmonary artery.

TABLE 4. Individual participant data of the procedural characteristics and outcomes

Author	Encounter #*	Patient #	Stenting†						BA						Procedural outcomes					
			LPA trunk	RPA trunk	LPA branches	RPA branches	Bilateral	Pulmonary veins	LPA trunk	RPA trunk	LPA branches	RPA branches	Bilateral	Pulmonary veins	Mortality	Restenosis	Underwent subsequent procedure	Emergent procedure	Arterial dissection	Any adverse event
Hamilton-Craig[12]	1	1	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0
	2	2	-	-	-	-	-	-	-	-	-	-	-	-	0	1	1	0	0	1
	3	2	-	-	-	-	-	-	-	-	-	-	-	-	0	0	0	0	0	0
Ferguson[20]	4	3	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Sekiguchi[16]	5	4	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
Condado[11]	6	5	0	0	1	1	1	0	0	0	0	0	0	0	0	0	1	0	0	0
	7	5	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
	8	6	0	0	1	1	1	0	0	0	0	0	0	0	0	0	1	1	0	1
	9	6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10	7	0	0	0	0	0	1	0	0	0	0	0	0	0	1	1	0	0	1
	11	7	1	0	0	0	0	0	0	0	0	0	0	1	0	1	1	0	0	1
	12	7	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
Liu‡,[13]	13	8	-	-	-	-	-	0	-	-	-	-	-	0	0	0	0	1	0	1
	14	9	-	-	-	-	-	0	-	-	-	-	-	0	0	0	0	1	1	1
	15	10	-	-	-	-	-	0	-	-	-	-	-	0	0	0	0	0	0	0
	16	11	-	-	-	-	-	0	-	-	-	-	-	0	0	0	0	0	0	0
	17	12	-	-	-	-	-	0	-	-	-	-	-	0	0	0	0	0	0	0

(*continued on next page*)

TABLE 4. (*continued*)

Author	Encounter #*	Patient #	Stenting†						BA						Procedural outcomes					
			LPA trunk	RPA trunk	LPA branches	RPA branches	Bilateral	Pulmonary veins	LPA trunk	RPA trunk	LPA branches	RPA branches	Bilateral	Pulmonary veins	Mortality	Restenosis	Underwent subsequent procedure	Emergent procedure	Arterial dissection	Any adverse event
	18	13	-	-	-	-	-	0	-	-	-	-	-	0	0	0	0	0	0	0
	19	14	-	-	-	-	-	0	-	-	-	-	-	0	0	0	0	0	0	0
	20	15	-	-	-	-	-	0	-	-	-	-	-	0	0	0	0	0	0	0
Bazmpani [14]	21	16	0	0	0	0	0	0	0	0	0	1	0	0	0	1	1	0	0	1
	22	16	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Tramper [15]	23	17	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	0	1	1

*Each patient may have had one or more encounter/admission to the catheterization laboratory for elective or emergent procedures to treat pulmonary vascular stenoses/compressions and/or adverse events.

†Vascular segments that received BA and stented were accounted for only under the stented category.

‡In Liu's cohort, five patients underwent stenting, but it was not specified which ones. Hyphen (-), no information available; Zero (0), no/negative; One (1), yes/positive; Encounter #, number of the encounter in the cardiovascular catheterization laboratory; BA, balloon angioplasty; LPA, left pulmonary artery; RPA, right pulmonary artery.

York Heart Association Functional Class (NYHA FC), and mean pulmonary arterial pressure (mPAP) were analyzed using sign tests.

Variables with missing data; that were not provided by authors of the selected references, were analyzed only with available information without strategies for value imputation. The number of subjects per variable is provided (Tables 2-4). All statistical analyses were performed using StataSE 14 (College Station, TX).

Data quality (risk of bias) assessment

Two investigators independently analyzed the risk of bias of every major outcome of each study. Cases of disagreement were solved with the help of a third investigator. An adaptation of the WHO-Uppsala Monitoring Centre (WHO-UMC) System for Standardised Case Causality Assessment tool[18] was used to assess for data quality (risk of bias) of each outcome of interest obtained from included patients from case reports and case series. We used the Newcastle-Ottawa Assessment of Quality Scale for Cohort Studies[19] to assess the risk of bias of such study for each outcome. To decrease the risk of bias, we did not consider lack of documentation of an adverse outcome as absence of such complication. Hence, such cases were considered as missing data and were not attributed any causality points.

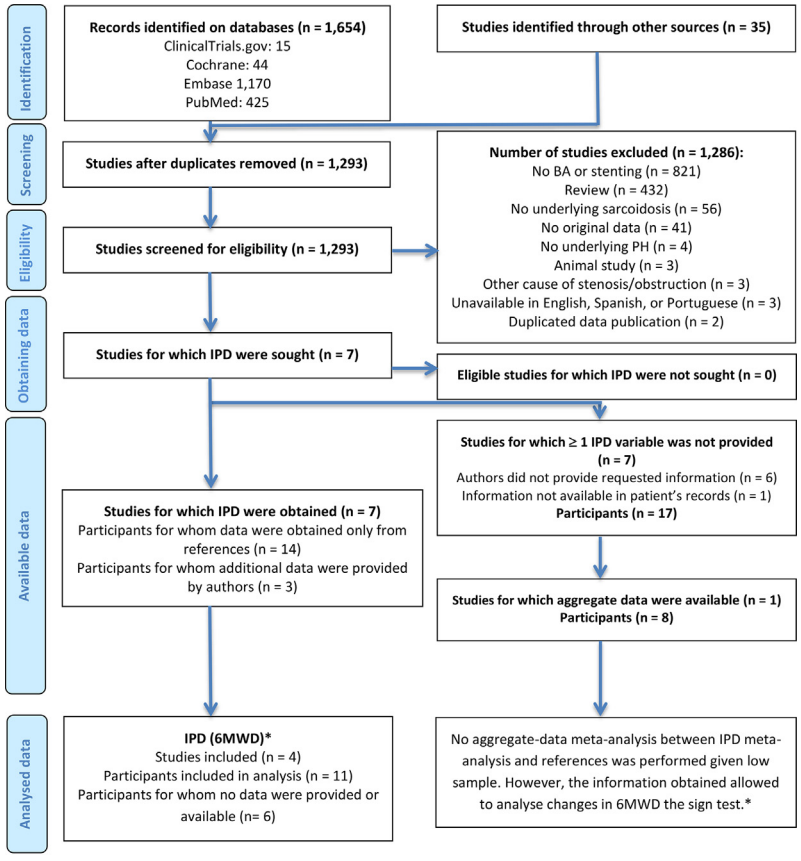
RESULTS

Reference-level results

A total of 1,654 references were retrieved from all sources (ClinicalTrials.gov: 15; Cochrane: 44; Embase: 1,170; PubMed: 425; other sources: 35). After removal of duplicates, 1293 were identified and screened. Seven met selection criteria for our meta-analysis (Fig 1). Among included studies, one was a prospective cohort,[13] 3 were case series,[11,12,20] and 3 were case reports[14-16] (Table 1). All selected references were full articles. One of the case series included patients with fibrosing mediastinitis of several etiologies but only the case with sarcoidosis was included in this meta-analysis.[20] Three references were from the USA, 2 from Europe, 1 from China and 1 from Australia. No study had control arm.

Patient-level results

General baseline data. Seventeen patients were identified, of whom 82.4% were female. The mean age was 58.6 (±9.1) years. The most



*This section corresponds only to the outcome "six-minute walk distance". Studies and participants included as well as data not provided or available was different among variables. 6MWD, six-minute walk distance; BA, balloon angioplasty; IPD, individual participant data; PH, pulmonary hypertension.

Fig. 1. PRISMA IPD Flow Diagram (selection of references and patients).

common reported ethnic group was Chinese (57.1%), followed by African American (28.6%). Staging of the pulmonary sarcoidosis was documented in 13 patients, of which 84.6% were Scadding stages III or IV. At least 58.8% were NYHA FC III or IV. Baseline mPAP was available for 6 patients from case reports/series with a mean of 50.6 (±21.2) mm Hg. Additionally, aggregate data from a cohort study of 8 patients showed a baseline mPAP 42.5 (±4.6) mm Hg that significantly decreased to 20.5 (± 3.2) mm Hg; postprocedurally (p 0.035).

Twelve of 15 identified patients received a medical regimen with steroids prior to the index procedure. Evaluation prior to index procedure included

computed tomography in at least 15 patients, and a ventilation/perfusion (V/Q) scan in at least 5. General baseline data is summarized in Table 2. Authors were contacted to request additional data about their patients, although initial agreement was obtained in 2 cases, only authors of one study provided additional information.[11]

Functional outcomes. Changes in 6MWD were documented in 11 patients, all of whom had a longer postprocedural 6MWD ($P < 0.01$). Among those patients in whom IPD was available, the magnitude of increase of the 6MWD ranged from 12.6% to 102.4%.

Changes in NYHA FC were documented for 10 patients; 6 of whom were NYHA FC III, and the other 4 were NYHA FC IV. All 10 patients had a postprocedural improvement to NYHA FC II ($P < 0.01$).

Follow-up. The median follow-up was 6 (3-18) months.

Angiographic outcomes. The most frequently affected pulmonary arterial system was the right pulmonary artery and its branches (Table 3). No patient had compression or stenosis of the main pulmonary arterial trunk. Only 2 patients were reported to have significant venous compression or stenosis.

Procedural outcomes. Seventeen patients had total of 24 admissions to the catheterization laboratory (CL). Eleven (64.7%) patients had only 1 encounter for BA and/or stenting but each of the other 6 (35.6%) required a total of 2-3 CL admissions; either for dilatation of new vessels or to treat adverse outcomes related to previous procedures.

There were 9 adverse outcomes from 24 CL admissions. Three patients had in-stent restenosis during follow-up, which were treated in a total of 4 subsequent encounters in the CL. Two patients had arterial dissections; 1 case was self-limited and other required balloon-compression of 2 arteries.

Three patients received additional emergent or urgent procedures to treat their complications; including catheter-directed thrombolysis in 2 cases; 1 with concomitant thrombectomy. A third patient had balloon compression for arterial dissection.

There were no periprocedural deaths or during follow-up.

Arterial procedures. Two of the 12 arterial systems that initially had received only BA (without stenting) had to undergo additional CL encounters for BA to treat restenosis. However, 1 patient in whom initial BA was suboptimal refused to undergo a second elective procedure for further BA and stenting.[16]

Only 1 patient developed arterial in-stent restenosis and was treated with BA to expand the stent.

Venous procedures. Two patients received venous stents. One of them received several venous stents that had to be re-expanded (second CL encounter) and then re-stented (third CL encounter).

Assessment of quality of evidence (risk of bias)

Twelve patients from 3 studies represented all the experience of each center or team; at least for the corresponding time frame delineated. All patients were found to be representative of the general population of interest. Documented postprocedural outcomes were found to be "certainly" caused by the procedure in all cases. However, some outcomes were not appropriately documented in some patients. In such cases, they were considered "unassessable" datapoints; hence, not included for analysis.

DISCUSSION

Summary of major findings

The present systematic review and IPD meta-analysis summarizes all the evidence available for the use of pulmonary BA with or without stenting in patients with SAPH. To our knowledge, this is the first meta-analysis to gather, synthesize, and analyze such available information. The most important findings of this study are: (1) female patients represented 82.4% of the sample and the mean age was 58.6 (±9.1) years; (2) the most common ethnicity was Chinese as one prospective cohort from China provided 8 of the 17 patients analyzed; (3) most patients were NYHA FC III or IV; (4) 84.6% of the patients were Scadding stages III or IV; (5) all patients with documented changes in 6MWD had a longer walk distance after dilatation of the stenosed or compressed pulmonary vessels; (6) the most frequently affected pulmonary arterial system was the right pulmonary artery and its branches; (7) almost a third of the patients had 2-3 CL encounters for dilatation or to treat adverse outcomes; (8) there were no deaths during the 6 (3-18) month follow-up.

Although the median age and female gender preponderance corresponded to what has been described in the general SAPH population,[21] the most common race in our study was Chinese, rather than African descendant. This was due to their overrepresentation (8 patients) from a prospective cohort from China. In that study, patients were followed in a large referral center and

treated with oral steroids for 2 months, and those without appropriate response in mPAP underwent pulmonary BA with stenting in some cases.[13]

The high functional impairment (NYHA FC III or IV) and advanced stages of pulmonary sarcoidosis (Scadding stage III or IV) in this sample correlates with the expected severity of disease of the type of patients in whom such off-label procedure would be performed and likely beneficial in clinical practice.

There was a unanimous improvement in the 6MWD of patients after BA with or without stenting. Although data was missing for some patients, thus preventing further statistical meta-analytical tests, the magnitude of improvement in 6MWD was found to be statistically significant in the prospective cohort included in the analysis.[13] This observation is particularly important for 2 reasons; first, improvement in 6MWD has been the most commonly utilized objective therapeutic goal of PH-directed therapies and the basis for approval of pivotal clinical trials of PH-directed therapies, furthermore, improvement in 6MWD also correlates with an improvement in quality of life in patients with PH.[22,23] Second, the use of pulmonary vasodilators in patients with lung disease leading to pathophysiologic shunting and V/Q mismatch is a major concern for the development of worsening hypoxia, dyspnea, and exercise intolerance, and considerations for pulmonary vasodilators in SAPH have been recommended only on a case by case basis.[24] Nevertheless, aggregate data from a cohort study included in this meta-analysis demonstrated a significant increase in PaO_2 from 51.2 ($\pm$4.8) to 71.5 ($\pm$4.3) in all 8 SAPH patients after pulmonary BA (with or without stenting).[13]

Most of the areas of stenosis or compressions were observed in the right pulmonary vasculature as these vessels have a longer trajectory from and into the heart, which may expose them to more compression from mediastinal fibrosis and lymphadenopathy.

Although there were reported adverse outcomes and some patients required multiple procedures, there were no deaths during all follow-up. We therefore suspect that as operators in major referral centers become more experienced and patient selection improves, pulmonary BA with or without stenting could be performed in a safer, staged fashion.

Of notice, all patients included in the meta-analyses had SAPH with at least a component of extrinsic and focal compression of pulmonary vessels, mainly by hilar nodes. This has important implications, as theoretically only patient with focal and critical vessel stenosis may benefit from this intervention, whereas those with diffuse diminished caliber of pulmonary vessels or those with PH with focal but not critical stenoses might not be amenable candidates.

Strengths and limitations

Although our IPD meta-analysis provides a valuable input on this topic by summarizing all the available evidence in the literature, we were unable to include additional patients from unpublished cases for logistical reasons.

There is a possibility that some patients may have had additional unpublished vascular lesions, stenosis or compressions, or even procedures after the time of publication of their respective cases. We attempted to obtain all possible information regarding these concerns, but most authors did not respond, and the ones that did, confirmed the information we had extracted from their publication, and contributed with additional datapoints.[11]

Although it was challenging to calculate rates of certain baseline or procedural characteristics, and outcomes, we reported the absolute numbers or percentages of the information available in the most transparent fashion to allow the reader to have the most objective synthesized information.

Given the low sample size, it was not feasible to perform inference statistical analysis; such as predictive models, or to compare statistical differences between groups, or aggregate meta-analytical tests with the results of the cohort study that did disclose data of interest for each individual patient. Nevertheless, this IPD meta-analysis represents the most complete and highest level of evidence regarding the baseline and procedural characteristics; as well as, postprocedural outcomes after pulmonary BA with or without stenting. This study can serve as foundation for future randomized clinical trials and multicenter registries, and to aid clinical and procedural management of patients with SAPH and focal stenosis or compressions of their pulmonary vasculature.

Conclusions

BA with or without stenting of focal stenosis or compressions of pulmonary vessels may lead to significant improvement in 6MWD in patients with SAPH.

Despite promising results observed in this meta-analysis, more evidence is still needed to estimate more accurately the magnitudes and rates of functional improvement and adverse outcomes, as well as obtaining more procedural experience to better define appropriate indications for stenting. However, in major PH referral centers with highly qualified and experienced interventional cardiologists, selected patients with SAPH and vascular stenosis or compression can benefit from pulmonary BA with or without stenting. Randomized controlled clinical trials and/or large multicenter registries with standard and specific baseline

characteristics and outcomes on both BA and stenting are needed to fill the knowledge gap in this field.

Declaration of Competing Interest

None.

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None.

Disclosures

SAM is a paid speaker for United Therapeutics Corporation and Bayer.
VB is a consultant for Edwards Life sciences and Abbott Vascular.
All other authors declare no conflicts of interest.

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