Atrial Septostomy

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Introduction

Lowering pulmonary input impedance is the obvious therapeutic target in right ventricular failure (RVF), if RVF has been caused by increased afterload. However, potential clinical gain can also be expected from attempts to unload the right heart by redistribution of blood to underfilled left-heart chambers or directly to the aorta. Atrial septostomy and pulmonary-aortic shunt (Potts anastomosis) represent clinically recognized methods serving this purpose at a cost of systemic desaturation. A more instrumentalized but physiologically appealing way of achieving similar hemodynamic goal, but with enriching the shunted blood with oxygen, is represented by venous-arterial extracorporeal membrane oxygenators. This chapter presents the physiological background and clinical value of atrial septostomy in the context of current management algorithms for patients with pulmonary hypertension.

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Rationale

Right ventricular systolic failure is the leading cause of death in patients with pulmonary arterial hypertension (PAH) and chronic thromboembolic pulmonary hypertension (CTEPH): two pulmonary vascular diseases characterized by progressive increase in RV afterload. There is convincing evidence that absolute RV elastance, reflecting its contractility, is increasing in PAH. However, the progression of pulmonary vascular disease (PVD) usually is too fast to be matched by appropriate functional remodeling of the RV. Moreover, although there is an initially beneficial stretch of the RV wall resulting in compensatory increase of RV performance—known as the Frank-Starling effect—this initiates a chain of unfavorable morphological and functional consequences starting a vicious circle, leading to uncoupling of the RV and pulmonary arterial bed. This, in turn, leads to progressive functional deterioration and ultimately to death. Indeed, the natural history of patients with PAH or CTEPH and chronic RV failure evidenced by a cardiac index (CI) below 2.0 L/min/m^2, and/or mean right atrial pressure (RAP) above 20 mmHg, is grim [1]. Moreover, any additional "second hit" leading to exacerbation of chronic RV dysfunction represents a life-threatening situation with in-hospital mortality of 25–60% despite advanced ICU management. Taken together, RV failure is responsible for about 3/4th of deaths

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within the 10% annual mortality among PAH and non-operable CTEPH patients.

All this clearly suggests an urgent need for effective and safe prevention of end-stage RV failure, if necessary, using interventional methods suitable for clinical application.

Theoretical Background

Atrial septostomy has been proposed as a treatment of RV failure secondary to pulmonary hypertension based on the reasoning derived from comparison of the outcome of two subgroups of PAH patients: with idiopathic PAH and those in whom PAH was associated with congenital shunts ultimately resulting in Eisenmenger syndrome.

Despite similar elevation of pulmonary artery pressure and resistance the patients with Eisenmenger syndrome were found to have much better life expectancy than those with idiopathic PAH [2, 3] (Fig. 20.1). Not only was overall mortality lower, but also in 30–55% it was due to sudden death and not end-stage RV failure [4–6].

Indeed, in most patients with Eisenmenger syndrome RV function and systemic perfusion are preserved, as evidenced by near-normal RA pressures and systemic cardiac output found at right-heart catheterization (Fig. 20.2). If the mechanisms of such adaptation of the cardiovascular system to extremely elevated RV afterload could be understood this might offer the chance of using them as new therapeutic approaches for patients with other forms of PAH.

Out of several adaptive mechanisms which have been suggested, including

- preservation of a "fetal" phenotype of RV myocytes
- appropriate RV hypertrophy
- preserved, more dense RV coronary network
- reversed shunt feeding the systemic circuit through a persisting defect

the latter could potentially be reproduced in non-Eisenmenger patients suffering from PAH. Opening a shunt between the atria has been practiced since the times of Rashkind, though for other indications.

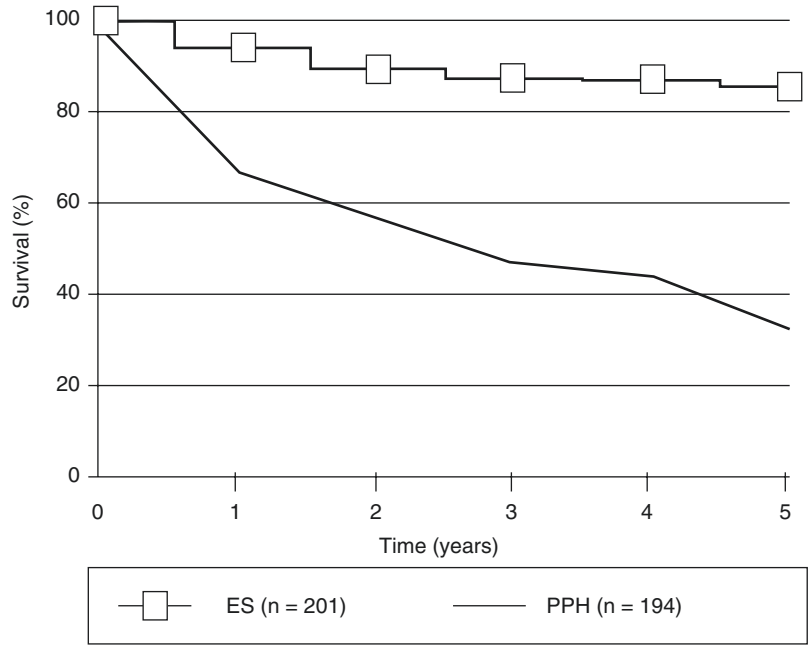

Fig. 20.1 Comparison of survival of patients with idiopathic pulmonary arterial hypertension and Eisenmenger syndrome. *ES* patients with Eisenmenger syndrome, *PPH* patients with idiopathic pulmonary arterial hypertension. (Based on data from Ref. [2])

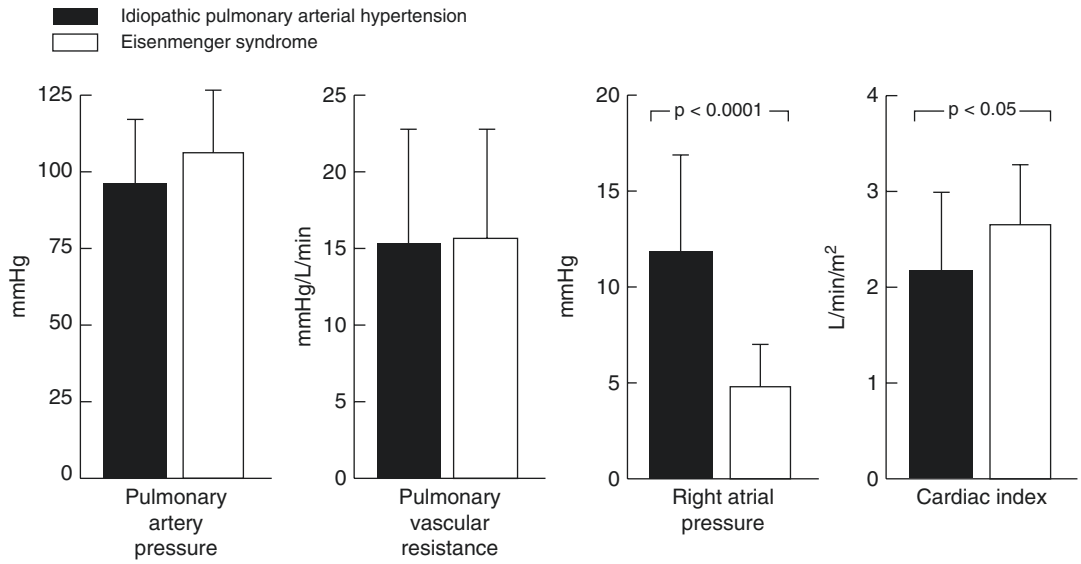

Fig. 20.2 Comparison of the hemodynamics of adults with severe idiopathic pulmonary arterial hypertension and Eisenmenger syndrome. (Based on data from Ref. [2])

Shunting blood from the right to left heart at the level of interatrial septum (Fig. 20.3) could potentially result in increase in systemic output by improving LV filling and in decompression of the RV alleviating its failure, with further improvements, e.g., better right ventricular coronary perfusion, less tendency for RV remodeling and functional tricuspid regurgitation, decreased kidney congestion, and their improved perfusion.

A price to pay would be systemic oxygen desaturation, particularly on exercise, with an unclear net result regarding tissue oxygen delivery and utilization.

Even more importantly, it is not clear whether and to what extent atrial septostomy alone would improve clinical outcome of patients with PAH if not accompanied by other adaptive mechanisms operating in patients born with congenital heart disease and steadily developing Eisenmenger syndrome. The evidence, that such an isolated shunt at the atrial level could be beneficial even if functionally opened only after development of PAH in the adult life, is based on a higher prevalence of patent foramen ovale in long-term survivors of PAH as reported by Rozkovec et al. [8] (Table 20.1).

Computational Models

Mathematical modeling of the effects of complex hemodynamic interventions, such as atrial septostomy in a setting of chronic PH, is tempting, particularly with increasing availability of advanced computational hardware and software. In a recent trial of Koeken et al., a Dutch group involving biomedical engineers assessed consequences of atrial septostomy with a multiscale computational model of cardiovascular system [7]. They suggested that atrial septostomy could improve symptoms of right-heart failure in patients with severe PH if net right-to-left shunt flow occurs during exercise. While their model confirmed that septostomy improves left ventricular filling and stroke volume (Fig. 20.4) and stabilizes systemic blood pressure, the expected beneficial effect on peripheral tissue oxygen delivery could not be found. The increase in systemic oxygen delivery after atrial septostomy has

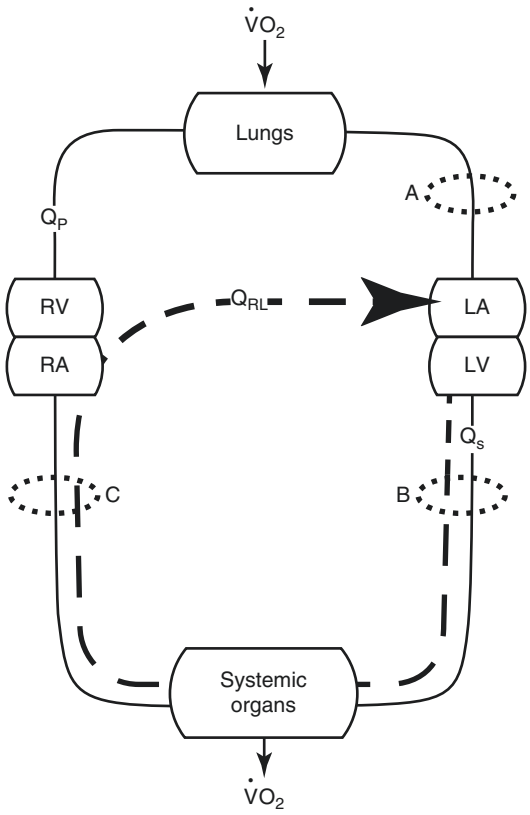

Fig. 20.3 Schematic representation of circulation with a right-to-left shunt through atrial septostomy. *LA* left atrium, *RA* right atrium, *RV* right ventricle, *Qs* systemic blood flow, *Qp* pulmonary blood flow, *QRL* right-to-left shunt through atrial septostomy, VO_2 total oxygen consumption by the body. In contrast to carbon dioxide removal and oxygen delivery that are determined by the effective Qp (*location A*) the delivery of nutrients (*location B*) and the removal of waste products (*location C*) are determined by systemic flow. Part of the venous return is redirected through atrial septostomy directly to the LA, thereby bypassing the pulmonary circulation. (Modified from Koeken et al. [7]. With permission from The American Physiological Society)

been examined by computer modeling, suggesting that the clinically observed beneficial effects of atrial septostomy may be more related to improved flow rather than oxygen delivery to perfused tissues [9].

Table 20.1 Factors predicting life expectancy in primary pulmonary hypertension, including the presence of patent foramen ovale (PFO)

	Survival		
	<5 years (n =)	>5 years (n =)	p
Family	1	1	NS
CTD	3	0	NS
Pregnancy	0	5	<0.02
PFO	0	4	<0.05
RHF any	18	10	<0.05

According to Rozkovec et al. [8]. (Reprinted from Rozkovec A, Montanes P, Oakley CM. Factors that influence the outcome of primary pulmonary hypertension. Br Heart J 1986;55:449–58. With permission from BMJ Publishing Ltd.)
CTD connective tissue disease, *Pregnancy* disease diagnosed during or after pregnancy, *RHF* right-heart failure

Experimental Models

Experimental evidence suggesting that atrial septostomy may be beneficial in chronic PH dates back to the work of Austen et al. [10] (Fig. 20.5). After inducing chronic RV pressure overload by pulmonary artery banding ten dogs were submitted to a second surgical intervention. Five had an ASD and the remaining five had a sham operation. Dogs with ASD were able to perform moderate and severe exercise on a treadmill, whereas dogs who had the sham operation could not tolerate it.

Other authors have also shown beneficial effects of similar interventions in canine models [11, 12].

The effect of an interatrial shunt on right atrial (RA) and right ventricular mechanics was reassessed by Zierer et al. [11]. After banding the pulmonary artery they used an 8 mm cannula to connect both atria. The model permitted controlled closing and opening of the shunt to assess potential hemodynamic effects of septostomy. Also, by changing the venous return two levels of shunting could be compared—15% and 30% of the total cardiac output, respectively. Comprehensive analysis based on the assessment of ventricular and atrial pressure/volume loops revealed that after "septostomy" RV and RA contractility did not change. Some changes were found in compliance of the right atrium, which

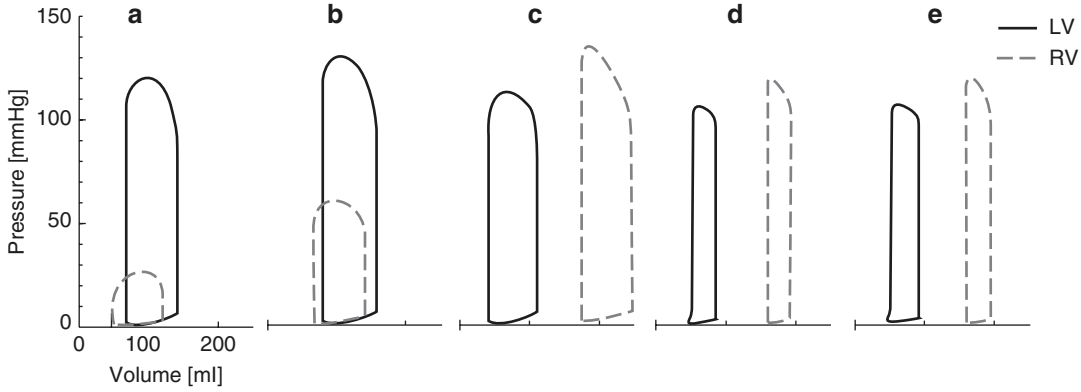

Fig. 20.4 Pressure-volume loops of the right (*dashed lines*) and left (*solid lines*) ventricles. *a* normal, *b* compensated pulmonary hypertension, *c* decompensated pulmonary hypertension, *d* severely decompensated pulmonary hypertension with decreased cardiac output, *e* same as *d* but after atrial septostomy of 14 mm in diameter. Note increased stroke volume of the left ventricle compared to *d*. (Modified from Koeken et al. [7]. With permission from The American Physiological Society)

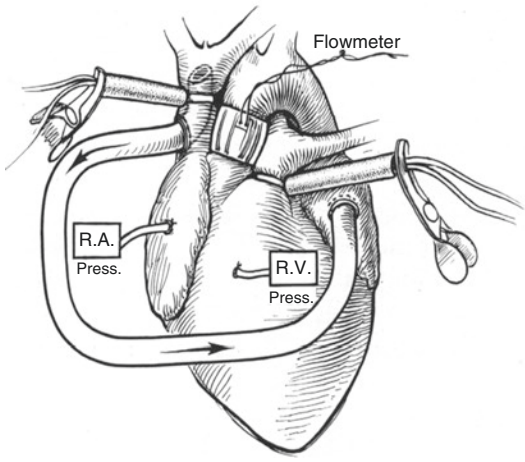

Fig. 20.5 Animal model used for assessing the acute effects of right-to-left atrial shunting, as described by Austen et al. in 1964. *RA* right atrium, *LV* left ventricle. *Arrow* indicates pulmonary artery banding used to chronically increase right ventricular afterload

increased especially at lower shunt flows. There was also a significant shift from the reservoir to the conduit function ratio in this chamber. While the experiment confirmed that cardiac output and systemic oxygen delivery increased after septostomy, this effect was present only with right-to-left shunting corresponding to 15% of cardiac output. At higher shunt flow beneficial effects on systemic oxygen delivery were lost.

Similar message was conveyed by Weimar et al. [12], who found a right-to-left shunt flow of 11% of baseline cardiac output at the atrial level to be an optimal therapeutic target in severe RV pressure overload. The authors suggested that atrial septostomy was not of significant hemodynamic benefit in moderate RV pressure overload. However, in contrast to previously discussed models, in the latter trial banding was done acutely, and thus the results and conclusions may not be fully representative for chronic pulmonary hypertension.

Clinical Evidence

The evidence regarding hemodynamic effects of atrial septostomy in patients with right ventricular dysfunction caused by increased RV afterload is limited, when compared to data regarding pharmacological treatment of pulmonary arterial hypertension. This limitation is a consequence of relatively low number of patients submitted so far to AS as well as to the insufficient quality of data due to the design of trials. At best the information comes from short case series. At present published series provide data on about 350 procedures performed in over 300 patients [13–32]. No randomized trials have ever been performed to

assess the long-term effects of AS. In some reports the outcome was compared to that of matched historical controls followed earlier by the same clinical team. The dynamic changes in medical care and availability of pharmacological therapy of PAH over time make such comparisons questionable.

Nevertheless, the published evidence, as well as our personal observations, permits analysis of hemodynamic effects, clinical benefits, and safety of AS. To allow generally applicable conclusions we decided to exclude single case reports from such analyses, which are more likely to be affected by favorable publication bias.

Characteristics of Patients Submitted to Atrial Septostomy

Out of 304 patients in whom AS was performed at least once, 76 were pediatric patients, 201 (71.6%) were female, and 277 (91%) suffered from PAH. All the patients were either in third or in fourth WHO functional class with almost 50% reporting syncope [13–32].

In a vast majority of cases balloon atrial septostomy was performed (see below for explanation). Out of 79 procedures in which blade balloon septostomy was used as either the main or the contributing method, 32 were performed before the year 2000 and others performed afterwards—were almost entirely (41/42) in young children.

Safety, Clinical and Hemodynamic Effects of Atrial Septostomy

There were 24 deaths within the first 24 h after the procedure, resulting in 6.8% periprocedural mortality. Cumulative mortality at 1 month was 10.8%. Interestingly, 11.5% (35/304) of patients could be transplanted.

Hemodynamic effects of AS could be analyzed for 104 procedures for which complete hemodynamic data sets were available. In order to provide some practical guidance regarding indication for AS in various stages of RV dysfunction we report the results according to the level of mean right atrial pressure before the procedure (Table 20.2).

Based on this analysis AS appears to result in immediate improvement of left-heart filling, and systemic flow regardless of the baseline level of RA pressure. In patients with RAP elevated at baseline its significant decrease immediately after the procedure was noted. Those beneficial effects occurred at a cost of fall of systemic oxygen saturation, most marked in patients with RAP >20 mmHg at baseline (Table 20.3). Despite clinically relevant increase in systemic CI (from 1.6 to 2.2 L/min/m^2, i.e., 37%) the periprocedural mortality in this subgroup was very high, with 11 deaths after 26 procedures (42%) contrasting with 2 periprocedural deaths in patients with RAP below 20 mmHg (2.5%) (Table 20.3).

In a recently published systematic review and meta-analysis by Khan et al. [33], the acute hemodynamic effects of atrial septostomy were confirmed. The review included 16 studies comprising 204 patients (mean age, 35.8 years; 73.1% women). Meta-analysis revealed significant and beneficial changes in two of the hemodynamic variables associated with survival in PAH, namely a decrease in right atrial pressure (−2.77 mmHg [95% CI, −3.50, −2.04]; $p < 0.001$) and an increase in cardiac index (0.62 L/min/m^2 [95% CI, 0.48, 0.75]; $p < 0.001$) following BAS, along with a significant reduction in arterial oxygen saturation (−8.45% [95% CI, −9.93, −6.97]; $p < 0.001$). In this analysis, the pooled incidence of procedure-related (48 h), short-term (<30 days), and long-term (>30 days) mortality was 4.8% (1.7–9.0%), 14.6% (8.6–21.5%), and 37.7% (27.9–47.9%), respectively. Spontaneous closure of the orifice due to elastic recoil occurred in 23.8% of cases. The authors concluded that this analysis suggests that BAS is relatively safe in advanced PAH, with beneficial hemodynamic effects. They considered relatively high postprocedural and short-term survival contrasting with less impressive long-term outcomes as a suggestion of suitability of BAS as a bridge to lung transplantation.

There is hardly any information on hemodynamic effects of septostomy during exercise.

Table 20.2 Hemodynamic effects of atrial septostomy according to the level of right atrial pressure prior to the procedure [13–32]

Variable	Baseline RAP < 10 mmHg ($N = 27$)		$p <$	Baseline RAP 10–20 mmHg ($N = 51$)		$p <$	Baseline RAP > 20 mmHg ($N = 26$)		$p <$
	Before	After		Before	After		Before	After	
RAP, mmHg	5.8 ± 1.96	5.48 ± 3.1	NS	14.1 ± 3.2	11.4 ± 3.8	0.001	25.8 ± 4.9	19.2 ± 4.4	0.001
LAP, mmHg	4.9 ± 2.47	6.5 ± 2.5	0.05	5.3 ± 3.6	7.9 ± 4.2	0.001	7.9 ± 3	10.4 ± 3.7	0.02
R-L atrial pressure, mmHg	1.17 ± 3.2	−1.32 ± 3.2	0.02	8.4 ± 4.1	3.3 ± 5.5	0.001	17.3 ± 5	7.7 ± 5.3	0.001
Mean PAP, mmHg	62.8 ± 17	64 ± 19.6	NS	64.9 ± 16.7	65.6 ± 16.7	NS	64.8 ± 23	69.9 ± 24.7	NS
Cardiac index, L/min/m^2	2.37 ± 0.61	2.80 ± 0.7	0.001	2.10 ± 0.70	2.7 ± 0.9	0.001	1.6 ± 0.5	2.2 ± 0.6	0.001
SaO_2%	93.5 ± 4.1	87.2 ± 7.4	0.001	92.9 ± 4.1	82.8 ± 7.4	0.001	92.2 ± 4.5	78.3 ± 9.7	0.001

RAP mean right atrial pressure, *LAP* mean left atrial pressure, *R-L* right to left, SaO_2 systemic oxygen saturation

Table 20.3 Clinical characteristics and procedure-related mortality according to right atrial pressure before the operation

	Baseline RAP < 10 mmHg	Baseline RAP 10–20 mmHg	Baseline RAP > 20 mmHg
	(*N* = 27)	(*N* = 51)	(*N* = 26)
Age, years	23 ± 14	28 ± 14	27.5 ± 12
Syncope (%)	73.9	66.7	36
RVF (%)	34.7	73.8	88
Procedure-related mortality 1 month	0/27 (0%)	2/51 (4%)	11/26 (42.3%)

RAP mean right atrial pressure, *RVF* right ventricular failure

Fig. 20.6 Residual, hemodynamically noneffective orifice (arrow) seen postmortem at the interatrial septum 6 months after initially successful atrial septostomy

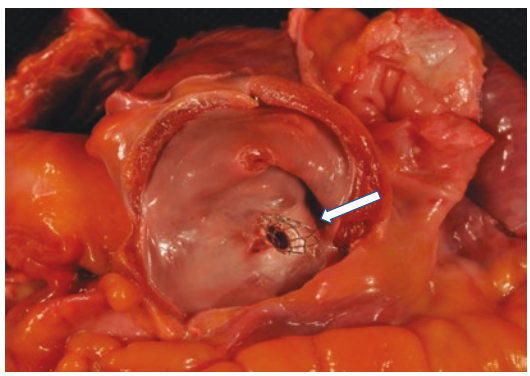

Fig. 20.7 Stent-protected septostomy orifice found fully patent at autopsy performed 5 years after intervention. (From Ref. [34] with permission)

While many series reported increased exercise tolerance [19, 24, 31], particularly increased distance covered during 6-min walk test, it is difficult to judge the contribution of psychological factor in patients who were submitted to septostomy. The assessment of long-term effects of septostomy on exercise capacity is complicated by common tendency of the created orifice to shrink or close (Fig. 20.6).

Recently a largest-ever series of 68 BAS protected with stents from elastic recoil has been reported suggesting excellent chronic patency of creating orifices [34] (Fig. 20.7). Together with 39 earlier reported cases a total of 107 stented BAS seem to suggest this strategy as being safer and more hemodynamically and clinically effective in long term than oversized septostomy orifices or repeated procedures performed after reocclusion occurs. Studies aiming to further improve long-term BAS patency, such as cryoplasty to freeze the margins of the newly created atrial defect, are ongoing (PROPHET trial: *https://clinicaltrials.gov/ct2/show/NCT03022851*).

Late Effects of Septostomy on Right Ventricular Function

Improved left ventricular filling and reduced preload of the right ventricle in patients in whom it had been severely increased before septostomy should lead to improved right ventricular function and—hopefully—its reversed remodeling. Indeed, better LV filling may improve RV systolic performance by direct support through interventricular septum. Also, reduced RV wall stress could mitigate increased RV myocardial oxygen demand and potential ischemia, particularly during exercise. Decrease in BNP plasma

levels reported after septostomy support reduced diastolic wall stretch and reduced RV afterload [29]. Moreover, in some reports improvement in hemodynamics after septostomy, as evidenced by RAP and CI, was even more marked at long-term follow-up than immediately after the procedure [15, 28]. Also echocardiographic follow-up demonstrated reduction of RA and RV dimensions up to 6 months after septostomy suggesting persistent beneficial effects of this intervention on right-heart remodeling [35].

Such effects may also be induced by restoration of more physiological autonomic system balance. It has been demonstrated that sympathetic overdrive may be one of the mechanisms involved in the pathophysiology of RV failure in patients with PAH. Ciarka and coworkers showed a significant decrease in initially elevated muscle sympathetic nerve activity after the procedure [27]. Less sympathetic drive can reduce myocardial oxygen demand, ischemia, and tendency to arrhythmia. Of note, heart rate did not increase despite a significant systemic oxygen desaturation following septostomy.

Effects on Blood Gases and Oxygen Transport

The effects of septostomy on systemic oxygen transport (SOT) and its tissue delivery are unclear. An increase in SOT resulting from the increase in CI despite the drop in SaO_2% has been suggested in some clinical studies [36] but seems unlikely and has not been confirmed when tested in recently developed computational models addressing this issue [7, 9]. Whether better perfusion of peripheral tissues improve local utilization of oxygen even if delivered in similar quantities remains unclear.

A potential adverse effect induced by acute systemic desaturation on pulmonary hemodynamic has been suggested by Kurzyna et al. Within an hour after successful septostomy and despite initially stable and well-controlled degree of SaO_2 they noticed unexpected "secondary" significant drop in oxygen saturation [26]. It occurred in patients who were not receiving chronic targeted therapy and could be effectively reversed by inhalation of a prostanoid (iloprost). The authors linked this observation with an increase in PVR seen in some of their patients soon after completion of atrial septostomy [26]. This increase correlated in turn with the degree of desaturation of mixed venous blood entering pulmonary arterial bed, which was a direct consequence of acutely reduced systemic SaO_2. Hypoxemic constriction of pulmonary arterioles as a reaction to profound sudden reduction in SvO_2 despite alveolar normoxia has been suggested, but could not be proved. We generally think that it is alveolar hypoxia rather than hypoxemia that causes pulmonary vasoconstriction so this is a surprising conclusion. Interestingly, the hemodynamic data collected from 104 patients indeed show a trend towards increase of PAP after septostomy (Table 20.2). An alternative explanation of such a trend might however come from improved RV output supported through interventricular septum by a better filled LV. In view of protection of patients from potential pulmonary hypoxic/hypoxemic vasoconstriction by powerful vasodilating drugs the clinical relevance of this potential side effect of septostomy was abrogated [32].

Risks and Limitation of Atrial Septostomy

Atrial septostomy is not an easy procedure. There is an important difference between puncturing interatrial septum to perform mitral annuloplasty or ablation in the left heart and atrial septostomy in severe pulmonary hypertension. The remodeling of the heart, and particularly reduced distance between interatrial septum and left atrial free wall as well as disturbed topography of the ascending aorta, increases the risk of perforation with potentially immediate fatal consequences. Fluoroscopy alone is used to guide the procedure in some experienced centers. However, with less experience more comprehensive imaging is needed to monitor the procedure. Parallel use of fluoroscopy and transesophageal imaging of the interatrial septum are probably the best choice.

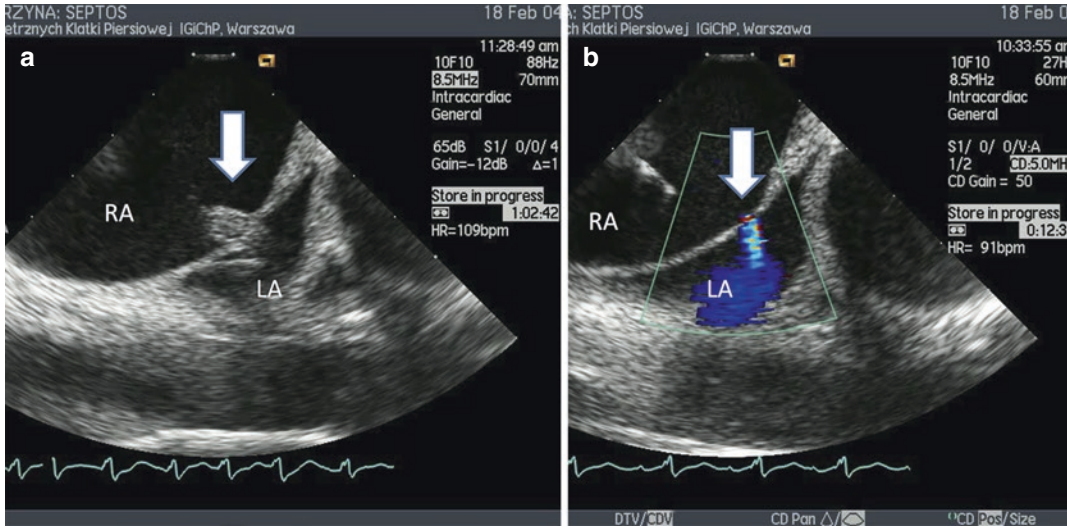

Fig. 20.8 Intracardiac echocardiographic monitoring of (**a**) balloon inflation (*arrow*) and (**b**) right-to-left shunt after puncturing interatrial septum. *RA* right atrium, *LA* left atrium. The intracardiac echocardiographic transducer is introduced via jugular vein and placed in high right atrium

Prolonged insertion of TEE probe however requires general anesthesia, which is not without risks in severe pulmonary hypertension. Good collaboration of anesthesiologist, interventionist, and PAH expert is crucial to avoid problems. Transthoracic echocardiography offers some support during the procedure but is far less informative than TEE. Intracardiac ultrasound is an acceptable alternative (Fig. 20.8). While not as versatile as TEE, it can be performed without discomfort to the patient without anesthesia.

Once the septum is punctured the next important step is to select the optimal orifice size. This is difficult with the blade balloon technique, which has been gradually abandoned because of the risk of creating tears in the septum which may result in oversized shunts with uncontrollable and life-threatening hypoxemia. Stepwise balloon technique is now used by most active centers. It allows precise control over the size of created orifice.

As an example, the procedure used in the Institute of Cardiology in Mexico is the following: baseline right and left-heart pressures are recorded simultaneously with a pigtail catheter in the ascending aorta just over the aortic valve to serve as an additional marker lowering the risk of aortic puncture. Cardiac output is calculated by the Fick method. Following transseptal puncture using standard technique, the septostomy orifice is balloon-dilated in a carefully graded step-by-step approach, beginning at a diameter of 4 mm, and followed by 6, 8, 12, and 16 mm dilatations, as appropriate. Between each step and after 3 min allowed for stabilization of hemodynamics, left ventricular end-diastolic pressure (LVEDP) recordings and arterial oxygen saturation (SaO_2) are obtained. The final size of the defect is individualized in each patient and limited by the time at which any of the following first occurred: (1) an LVEDP increase of ≥18 mmHg; (2) a SaO_2 reduction to 80%; or (3) a 10% SaO_2 decrease from baseline. Follow-up of the patients is done in the intensive care area for the first 48 h, where continuous supplementary oxygen is administrated and appropriate anticoagulation is started. All patients are followed at outpatient clinic with particular care to maintain correct oral anticoagulation and appropriate hemoglobin levels [32].

The stepwise approach is safer but tedious, time consuming, and expensive, as many balloons have to be used. Moreover, balloon dilatation does not protect from elastic recoil and closure (Fig. 20.6). Therefore, some teams aim at a predefined single-size orifice but protected from closure with a butterfly stent [37, 38] or

fenestrated occluding device [25]. However, follow-up revealed occlusion of this device in four out of nine patients despite chronic anticoagulation or antiplatelet therapy [30] making such approach questionable. Butterfly stents seem to be more effective, but they have to be prepared and positioned on a septostomy balloon on-site by the operator during the procedure. This again significantly increases procedural time, and requires dedicated personnel and a long time slot of the hemodynamic laboratory. Recently a new concept of cryoablation to septostomy borders has also been applied with a good long-term result after the second septostomy, which was performed because the first one closed (J. Sandoval, personal communication, 2014). In our experience and not unexpectedly the small orifices closed most often suggesting that septostomies should be made earlier—in patients with no more than mildly elevated RAP—but larger.

Closing of septostomy can be suspected if at pulse oximetry checkups SaO_2 gradually returns towards baseline values. In such a case an attempt to push the leader across a still patent orifice avoiding risky puncture and limiting the procedure to balloon dilatation is tempting. However finding the residual hole may be very difficult and usually a new puncture is needed.

Atrial Septostomy and Therapeutic Strategy in Pulmonary Hypertension

Based on the available evidence as well as our personal experience regarding the efficacy and safety of atrial septostomy it seems that this procedure has both a place and—even more importantly—a potential to play a more prominent role in the management of patients with PAH and right ventricular dysfunction. This is justified by

- Sound pathophysiological background
- Experimental and computational evidence consistent with clinical findings
- Convincing data on increased systemic output due to improved left ventricular preload and resulting in clinical improvement
- Lack of clinically significant consequences of systemic desaturation
- Better understanding of periprocedural risk and optimal patient selection

These characteristics permit considering atrial septostomy particularly in patients who are suboptimally controlled by modern medical therapy. Syncope and fluid retention may be relieved by septostomy and time can be gained increasing the chance to survive on the lung transplantation list. If septostomy is considered in a patient it is of paramount importance not to miss the optimal moment characterized by still preserved acceptable oxygen saturation without prohibitive levels of RAP.

Septostomy may be particularly useful in countries/centers who have suboptimal access to lung transplantation programs or to expensive double- and triple-targeted therapy.

Following actions are urgently needed:

- Identification and implementation of the best method to prevent reocclusion of atrial septostomy
- Designation of referral septostomy teams with appropriate experience and perspectives to create a high-volume/high-quality environment with appropriate quality monitoring
- Preparation of a properly designed interactive registry offering standardized management suggestions and at the same time collecting evidence with a goal of using the results for future optimization of patient selection and methodology of procedure. Such registry—if extended to centers not performing septostomy—would also allow comparison of long-term outcome between matched groups of patients to whom septostomy was or was not offered.

To optimize the risk/benefit ratio of atrial septostomy as well as introduce this procedure as a preventive measure which delays failure of the right ventricle despite progressive pulmonary vascular disease new data are needed. This includes a prospective trial to verify whether atrial septostomy may be effective in the setting of moderate right ventricular hypertension.

Such an early intervention has been recently suggested by a clinical retrospective study but seems not to be supported by experimental data [12, 32].

In view of great achievements regarding assessment of efficacy and safety of modern pharmacotherapy of PAH and continuing problems with availability of donors for lung transplantation programs the community caring for patients with PH and the patients themselves have to mobilize resources and enthusiasm to arrange a landmark trial identifying optimal positioning of atrial septostomy in the future management strategy. New technical developments, including remote-controlled devices with modifiable shunt fractions and preventing from reocclusion of the septostomy orifice, should encourage the industry to support our efforts, hopefully in the near future. This may be facilitated by a recently emerging interest in using atrial septostomy in another much more prevalent indication, indirectly confirming the clinical benefits of creating and regulating interatrial shunt.

Atrial Septostomy Plus Dedicated Devices for the Management of HF with Preserved Ejection Fraction

In the last few years there has been a conceptual transfer of the use of atrial septostomy plus dedicated devices to treat heart failure with preserved ejection fraction as that seen in group 2 of pulmonary hypertension, which appears an appealing concept given the lack of an effective treatment in this group. Elevated left atrial (LA) filling pressure leading to pulmonary congestion is the common final pathway in decompensated HF. This provides the basis for creating a left-to-right shunt for reducing LA pressures, and relieving volume excess from the left atrium, thus improving symptoms (particularly during exercise) and functional class and reducing rehospitalizations [39–43]. The rationale for this proposal is based on several clinical observations: (1) It has been recognized that patients with the rare combination of an atrial septal defect and mitral stenosis (Lutembacher's syndrome) do better and are less symptomatic than patients with isolated mitral stenosis, presumably because the shunt allows for LA decompression [39–42]. (2) Increase in left atrial pressure and acute pulmonary edema has been described after closure of congenital atrial septal defects, particularly in patients with preexisting or unrecognized left ventricular dysfunction [44]. (3) Balloon atrial septostomy or placement of a transseptal cannula has been associated with ventricular recovery in patients who could not be weaned from extracorporeal membrane oxygenation for intractable pulmonary edema [45]. (4) It has been reported that a residual communication after percutaneous mitral valve repair (using a MitraClip device through a 22F guiding catheter) resulted in a volume and pressure relief of the left atrium [46].

Atrial septostomy with shunt device placement in the setting of HF with preserved ejection fraction may be superior to exclusive static balloon dilatation of the interatrial septum [41]. Devices used for this purpose include InterAtrial Shunt Device (IASD®, Corvia Medical Inc., Tewksbury, MA, USA), V-Wave device (V-Wave, Caesarea, Israel), Second-generation (valveless) V-Wave device (V-Wave, Caesarea, Israel), and ROOT device (Edwards Lifesciences) [43]. Besides its use, in PAH patients [47] the future application of the atrial flow regulator (Occlutech) device may also be extended to other heart failure populations. Implantation of this device may permit left-heart decompression via fenestration. Further clinical trials are still required.

Current evidence for interatrial shunting alone or with dedicated devices is based on observational studies and small randomized trials showing the feasibility, safety, and preliminary efficacy in patients with PH and left HF [43]. These data seem to be insufficient to modify current clinical practice but support the use of interatrial shunting as a palliative therapy in selected patients with PH or left HF that remain symptomatic despite optimal treatment based on current guidelines. Several ongoing randomized trials will provide definite evidence about the exact role of this therapy for the treatment of HF patients [43]. If the results are positively associated with improved

clinical outcomes, device-mediated left-to-right atrial shunting might become an important new approach to the treatment of this population.

It must be emphasized that the creation of an atrial communication is a palliative not a curative approach. The restrictive character of a generated shunt makes this mechanical therapeutic measure a helpful, low-risk treatment. However, an oversized atrial communication with shunt-dependent pressure equalizing between both atria should be avoided [41]. Overall, shunt device size in HF patients has ranged from 5 to 8 mm. In a validated cardiovascular simulation model, it has been shown that with a shunt of 8–9 mm there is no increase in right atrial and pulmonary artery pressures [48]. However, further studies are needed to determine the optimal shunt size for patients with left HF. Also, because of the introduction of a left-to-right shunt, patients with evident right ventricular dysfunction or significant pulmonary arterial hypertension (PA systolic >60 mmHg) should be excluded [39, 49]. However, milder cases of postcapillary pulmonary hypertension due to left ventricular failure with its preserved systolic function may potentially benefit from a bidirectional interatrial shunt dynamically regulating filling of both ventricles.

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