Interatrial Shunting with the Atrial Flow Regulator: Balancing Left- and Right-Sided Hemodynamics

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Abstract

Background: *Pulmonary hypertension (PH) and heart failure with preserved or reduced ejection fraction (HFpEF/HFrEF) are characterized by elevated filling pressures, limited therapeutic options, and high morbidity. The Occlutech Atrial Flow Regulator (AFR) is a percutaneously implanted, double-disc nitinol device that creates a controlled interatrial shunt. By facilitating left-to-right or right-to-left flow depending on the hemodynamic substrate, the AFR offers a mechanistically attractive approach to decompress atrial chambers and improve symptoms.*

Methods: *A systematic review was performed in accordance with PRISMA guidelines. Literature from PubMed, Scopus, and Google Scholar (2000–2024) were screened to identify clinical studies, registries, and case reports evaluating AFR implantation in patients with HF or PH. Data were synthesized regarding device design, procedural success, clinical efficacy, safety, and long-term outcomes, with emphasis on adverse events and hemodynamic thresholds.*

Results: *Across prospective studies in Group 2 PH/HF populations, AFR implantation demonstrated high procedural success, durable patency, and improvements in NYHA class, six-minute walk distance, pulmonary capillary wedge pressure, and quality of life. Safety outcomes were favorable, although right ventricular dilation and adverse remodeling were observed with larger shunt sizes or in patients with elevated pulmonary vascular resistance. In Group 1 PAH, compassionate-use series reported reductions in right atrial pressure, improvements in cardiac index and functional class, and resolution of syncope, though at the expense of systemic desaturation. Mortality in these cohorts was primarily determined by baseline disease severity rather than device complications. Evidence from comparator devices (IASD, V-Wave) and the REDUCE LAP-HF II trial underscores the critical importance of patient selection, with benefit concentrated in patients demonstrating preserved pulmonary vascular reserve.*

Conclusions: *The AFR represents a promising device-based therapy for patients with advanced HF or PAH by providing controlled interatrial shunting tailored to the underlying physiology. Current data establish its feasibility, safety, and symptomatic benefit in well-selected patients, but highlight risks of worsening PH and right-sided loading if applied outside defined hemodynamic thresholds. Ongoing pivotal trials, including FROST-HF and RESPONDER-HF, are essential to determine the role of AFR in routine clinical practice and to refine phenotypically guided patient selection.*

Keywords: Intra-atrial shunt, pulmonary hypertension, LV failure

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Introduction

Pulmonary hypertension (PH) and heart failure with preserved or reduced ejection fraction (HFpEF/HFrEF) are clinical syndromes defined by elevated cardiac filling pressures, limited therapeutic options, and high morbidity. Interatrial shunting has re-emerged as a mechanistically attractive intervention in this context. The Occlutech Atrial Flow Regulator (AFR) is a percutaneously delivered, double-disc nitinol device with a fixed fenestration that creates a controlled interatrial shunt.[1] Its principal on-label use is in patients with HFpEF or HFrEF with elevated left atrial pressures, where the AFR facilitates left-to-right flow, decompressing the left atrium, reducing pulmonary venous congestion, and improving symptoms.[2] Beyond this indication, the device has been applied off-label in pulmonary arterial hypertension (PAH, Group 1 PH), where right-to-left shunting can decompress the right atrium and augment systemic cardiac output in patients with advanced right ventricular (RV) failure or recurrent syncope.[1] While this strategy may stabilize patients or serve as a bridge to lung transplantation, it carries the inherent risk of systemic desaturation and may accelerate pulmonary vascular remodeling, potentially worsening long-term PH.[3] Thus, the AFR exists at the intersection of two distinct physiologic strategies—left-to-right unloading in HF and right-to-left unloading in PAH—highlighting both its versatility and complexity. This review provides a comprehensive synthesis of device design, clinical applications, efficacy, and safety, with particular emphasis on adverse outcomes such as right-sided remodeling and worsening PH, which remain critical considerations for clinical adoption.

Methodology

This systematic review follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure comprehensive and structured reporting. A literature search was conducted using multiple electronic databases, including PubMed, Google Scholar, and Scopus, to identify relevant studies involving the use of the AFR device. The search terms used included "Atrial Flow Regulator," "interatrial shunt device," "pulmonary hypertension," "heart failure," and "AFR complications." Studies published between 2000 and 2024 were considered, given the introduction and evolving use of the AFR device during this period.

The inclusion criteria for this review were: (1) studies that specifically evaluated clinical outcomes of AFR implantation, (2) studies involving both pediatric and adult populations with severe pulmonary hypertension or heart failure, and (3) case reports or series providing detailed postoperative data on complications and long-term follow-up. Exclusion criteria included non-English publications and studies without relevant data on outcomes.

Three reviewers independently assessed the studies for relevance and methodological quality. Data extraction was performed using a standardized form to collect information on study design, patient demographics, AFR indications, device size used, procedural success rates, short-term and long-term outcomes, and any reported complications. Discrepancies between reviewers were resolved through discussion, with a reviewer available for arbitration if necessary. Quantitative data were analyzed using descriptive statistics, while qualitative data were synthesized narratively.

Brief Pathophysiology of Pulmonary Hypertension and Rationale for Interatrial Shunting

Mean pulmonary artery pressure ≥25 mmHg (PH) is classified into five etiologic groups.[2] Among these, Group 2 PH arises from left heart disease, such as HFpEF or HFrEF, where an elevated left atrial pressure is transmitted backward into the pulmonary circulation.[2] In this setting, decompression of the left atrium through a controlled left-to-right shunt can reduce pulmonary venous congestion and improve symptoms.

In contrast, Group 1 PAH is characterized by pulmonary vascular remodeling, increased pulmonary vascular resistance (PVR), and progressive RV failure.[2] Here, a controlled right-to-left shunt may offload the RV and augment systemic output when right atrial pressure exceeds left atrial pressure. While this

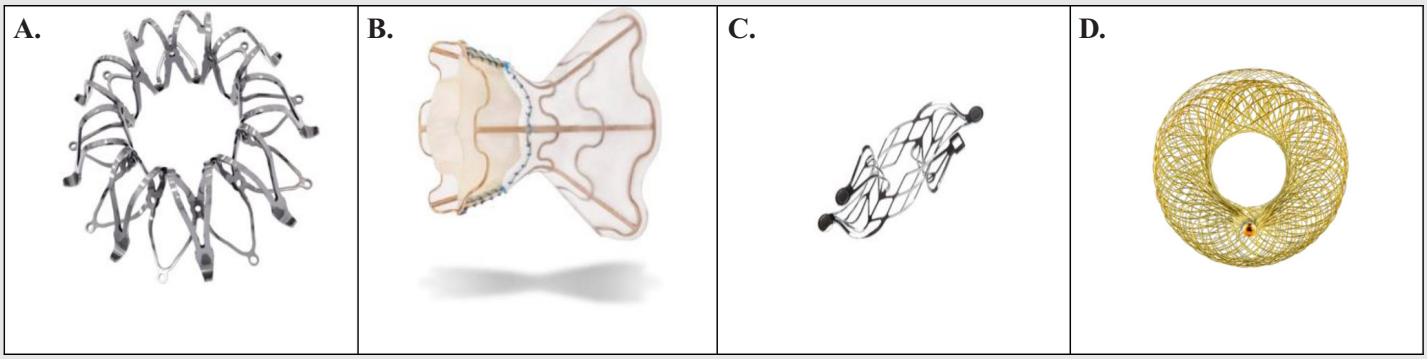

Figure 1. (**A**) IntraAtrial Shunt Device (IASD). (**B**) V-Wave Interatrial Shunt. (**C**) Atrial Flow Shunt (AFS). (**D**) Atrial Flow Regulator (AFR) Device.

strategy can reduce syncope and stabilize patients awaiting lung transplantation, it can result in right-sided HF and introduces systemic desaturation and/or hypoxic pulmonary vasoconstriction, which may contribute to worsening PH.[3]

Balloon atrial septostomy, first attempted in the 1980s as a palliative option, demonstrated proof-of-concept but was limited by unpredictable shunt size, hypoxemia, and high procedural mortality.[4] The Occlutech AFR device was developed as a predictable, durable, and size-calibrated alternative, offering controlled decompression for both physiologic scenarios—left-to-right shunting in Group 2 PH/HF and right-to-left shunting in Group 1 PAH—while aiming to reduce procedural risk.[1]

Device Overview

The AFR consists of two self-expanding nitinol discs connected by a central waist, with a fenestration diameter ranging from 4–10 mm (Figure 1).[5] The waist height (5–10 mm) is chosen to match the septal thickness.[5] Implantation involves transseptal puncture, balloon septostomy, and delivery through a 12–14 French sheath under fluoroscopic and transesophageal echocardiographic guidance.[5] In the PRELIEVE trial, device sizing was guided by hemodynamics: an 8-mm fenestration was used if the resting pulmonary capillary wedge pressure (PCWP) was ≥15 mmHg, and 10 mm if the PCWP was <15 mmHg at rest but ≥25 mmHg during exercise.[6] Shunt hemodynamics typically yield a Qp:Qs ratio of ~1.2, considered safe for relieving left atrial pressure without overloading the right heart.[6]

In addition to the Occlutech's AFR, other atrial septal shunt devices have been developed to reduce left heart pressures. These devices include the InterAtrial Shunt Device (IASD) and V-Wave interatrial Shunt by Corvia Medical, which are under investigation in the REDUCE LAP-HF II and RELIEVE-HF trials, respectively.[5] Edwards Lifesciences' Atrial Flow Shunt (AFS) is also being evaluated for its potential to alleviate pressure in heart failure patients.[7] The goal of these devices is to reduce strain on the failing heart, but they differ in design, target patient populations, and clinical outcomes. The IASD and V-Wave devices are more focused on specifically managing left-sided HF, while the Occlutech AFR remains the only device with consistent application across both HF and PAH.[7]

Indications

The AFR currently holds a European regulatory approval for use in patients with symptomatic HFpEF or HFrEF and elevated left atrial pressure despite optimal medical therapy.[8] In this population, the device creates a controlled left-to-right shunt, lowering left atrial pressure, reducing pulmonary venous congestion, thus leading to symptomatic improvement.

Beyond this approved indication, the AFR has been applied in off-label settings, most notably in

advanced PAH with refractory right heart failure, recurrent syncope, or as a bridge to lung transplantation. In these cases, the device permits right-to-left shunting, decompressing the right atrium and augmenting systemic output, though at the cost of systemic desaturation and with uncertain long-term effects on pulmonary vascular remodeling.[8–10]

In the United States, Occlutech AFR does not yet have FDA approval for routine clinical use. Its use is currently limited to clinical trials under investigational device exemptions. Several prospective studies and registries—including PROPHET (PAH), PROLONGER (predictors of response), the AFteR registry, and the pivotal sham-controlled FROST-HF trial—are ongoing to clarify the AFR's role, refine patient selection, and define long-term outcomes across these populations.[3,9]

Clinical Efficacy

Heart failure (Group 2 PH)

The PRELIEVE trial provided the first prospective evaluation of the Occlutech AFR in patients with symptomatic HFrEF and HFpEF with elevated filling pressures. Early results (2021, n = 53) demonstrated high procedural success, durable shunt patency, and early benefits in NYHA class, quality of life, six-minute walk distance (6MWD), and a ~5 mmHg reduction in PCWP at three months, with Qp:Qs maintained near 1.2.[6] Adverse events were rare, limited to one embolization and one major periprocedural complication.[6] Final 1-year outcomes (2023, n = 109) confirmed safety and efficacy, with all-cause mortality of 21% in HFrEF and 7% in HFpEF, reduced HF hospitalizations, and maintenance device patency without occlusion or embolization.[6] Functional benefit persisted, and echocardiography showed mild RV dilation with 10 mm fenestrations but preserved RV function with 8 mm devices, reinforcing the importance of shunt sizing.[6]

In contrast, the REDUCE LAP-HF II trial was the first large, multicenter, sham-controlled study of an interatrial shunt (Corvia IASD) in HFpEF/HFmrEF (n = 626).[11] At 12 months, the device did not reduce the composite endpoint of cardiovascular death, nonfatal stroke, HF events, or health status compared with sham (win ratio 1.0; p = 0.85).[11] Heart failure events and Kansas City Cardiomyopathy Questionnaire (KCCQ) improvements were similar between groups, though NYHA class improved modestly more in device patients (p = 0.006).[11] Safety concerns arose with higher major adverse cardiac events (4% vs. 1%).[11] Subgroup analysis identified potential harm in patients with high exercise pulmonary artery systolic pressures (>70 mmHg), enlarged RA volume index (≥29.7 mL/m^2), or male sex, whereas those with preserved PVR (exercise PVR <1.74 WU) derived clinical benefit.[11]

A responder versus non-responder paradigm was clarified in a *post hoc* analysis by Borlaug et al. Responders—patients with preserved PVR and no rhythm devices—had improved win ratio (1.31; p = 0.038), fewer HF events, and greater KCCQ gains (+5.5 points).[12] Non-responders, particularly those with latent pulmonary vascular disease (exercise PVR ≥1.74 WU), pacemakers, or RV maladaptation, fared worse (win ratio 0.60; −6.2 KCCQ points).[12] Resting PVR did not predict outcomes, underscoring the importance of invasive exercise hemodynamics for patient selection. Echocardiographic analysis by Patel et al. provided mechanistic insight, showing reverse remodeling of LV and LA volumes and function without deterioration of RV systolic function, again concentrated in responder phenotypes.[13] At two years, results remained neutral overall (win ratio 1.01) but confirmed high device patency and safety concerns, with major adverse cardiac events more common in device patients.[13] Importantly, responders had a 51% reduction in HF events (IRR 0.49), while non-responders experienced worse outcomes.[14]

Multiple reviews place these findings into context. Guimaraes et al. highlighted the broad therapeutic rationale for interatrial shunting in both acute and chronic HF.[14] In acute settings such as VA-ECMO support, balloon septostomy provides LA decompression and facilitates LV recovery, though mortality remains high due to disease severity.[14] In chronic HF, device-based shunts, including the IASD, V-Wave, and AFR, have consistently reduced LA/PCWP (particularly during exercise) with improvements in NYHA class, 6MWD, and quality of life, though long-term outcome data were lacking at that time. Riccardi

et al. expanded on this, underscoring that elevated LA pressure is the key driver of pulmonary congestion in HFpEF and that interatrial shunting provides a mechanistically sound approach to symptom relief.[7] Early device trials consistently showed feasibility, safety, and symptomatic benefit, though REDUCE LAP-HF II demonstrated that efficacy is not universal and patient selection is critical. Similarly, Jørgensen et al. summarized pilot experiences across devices, reporting exercise PCWP reductions of 3–11 mmHg, improved NYHA class, and modest 6MWD gains.[15] Safety was generally favorable, though device embolization, arrhythmias, and bleeding events occurred in small numbers.[15] Exploratory analyses suggested that baseline hemodynamics (e.g., PCWP to right atrial pressure gradients) may identify responders, anticipating the later responder or non-responder insights of REDUCE LAP-HF II.[15]

Building on feasibility and safety signals from PRELIEVE, the FROST-HF trial (NCT05136820) has been launched as the pivotal, randomized, sham-controlled study of AFR. Target enrollment is roughly 700 patients with varying cardiovascular ejection fractions, randomized by resting PCWP to varying fenestration sizes.[3] The primary endpoint is a hierarchical composite of cardiovascular death, transplant or left ventricular assist device, recurrent HF events, and KCCQ score change at six months.[3] Unlike REDUCE LAP-HF II, FROST-HF does not mandate invasive exercise hemodynamics and does not exclude patients with high PVR or rhythm devices, broadening generalizability but raising concerns about right-sided overload and dilution of responder-specific benefit.[3]

Taken together, available evidence establishes AFR as a safe, feasible, and durable approach to left atrial decompression, with consistent symptomatic and functional improvements in both HFrEF and HFpEF. However, lessons from the IASD experience highlight that indiscriminate use is not appropriate: efficacy depends critically on pulmonary vascular physiology and RV adaptation. Responders with preserved PVR derive both symptomatic and structural benefit, while non-responders may be harmed. Future trials such as RESPONDER-HF and FROST-HF will be pivotal in validating phenotypically guided selection and determining whether interatrial shunting can achieve consistent clinical benefit in Group 2 PH.

Pulmonary arterial hypertension (Group 1 PH)

Evidence for AFR in Group 1 PAH remains limited to compassionate-use series and observational studies but demonstrates meaningful functional improvements. In a retrospective, multicenter series of 35 patients across seven international centers, AFR implantation resulted in marked clinical improvement: baseline NYHA III/IV symptoms fell from 77% to 9% at long-term follow-up, and syncopal episodes were eliminated.[1] Functional capacity improved significantly, with 6MWD increasing from 370 to 434 m ($p = 0.0001$), while mean right atrial pressure decreased from 10.6 to 8.5 mmHg ($p = 0.0009$).[1] Interestingly, mean pulmonary arterial pressure remained unchanged (74.8 to 76 mmHg, $p = 0.58$), highlighting that symptomatic gains were achieved through atrial decompression rather than direct reduction of pulmonary vascular load.[1] Four deaths occurred during follow-up, which were attributed to progressive ventricular dysfunction, severe desaturation, and comorbidities; importantly, no excess risk was seen in patients with RA pressures >20 mmHg, a level historically considered a contraindication to septostomy.[1] Only one device-related issue was observed (fenestration occlusion), successfully bridged to heart-lung transplantation.[1]

Sivakumar et al. studied 39 patients, including nine children, with advanced PAH presenting with syncope or right HF.[10] Atrial flow regulator implantation was technically successful in all, with no procedural complications. Hemodynamically, right atrial pressure decreased (9.4 to 6.9 mmHg, $p = 0.02$), cardiac index improved (2.4 to 3.0 L/min/m^2, $p < 0.001$), and systemic oxygen transport increased significantly.[10] Functionally, 6 MWD rose from 310 to 376 m ($p < 0.001$), NYHA class improved, and syncope resolved entirely.[10] A reduction in pericardial effusion and inferior vena cava congestion accompanied improvements in tricuspid annular plane systolic excursion and RV strain. Desaturation was observed, with resting SpO_2 falling from 96% to 92% and exercise saturation to roughly 80%.[10] Mortality was confined to high-risk patients with REVEAL scores >12

or inotrope dependence. Device patency was universal, with a median duration of 33 months.[10]

Furthermore, Kopeć et al. reported a multicenter Polish experience in nine severely ill adults with advanced PAH on maximal triple therapy, all listed for transplantation.[9] Atrial flow regulator implantation significantly improved cardiac index (2.46 to 2.92 L/min/m², $p = 0.04$), reduced PVR (13.2 to 7.2 WU, $p = 0.01$), lowered mean pulmonary artery pressure (64 to 52 mmHg, $p = 0.04$), and halved NT-proBNP levels.[9] WHO functional class improved, 6MWD increased, and diuretic burden decreased. However, four patients died of progressive HF during follow-up, two underwent successful transplantation, and recurrent ascites occurred in those with 6 mm fenestrations.[9] No procedural deaths or device failures were reported.

Together, these findings suggest that AFR offers durable hemodynamic and symptomatic benefits in PAH, although survival is primarily determined by disease severity rather than device efficacy.

Hemodynamic Selection as a Determinant of Shunt Safety

Concerns regarding worsening PH and right-sided loading emerge consistently across interatrial shunt studies, particularly when devices are implanted outside carefully defined hemodynamic thresholds. In the PRELIEVE first-in-man and final one-year results, device patency and left atrial unloading were favorable, yet patients receiving the larger 10 mm AFR demonstrated a tendency toward right ventricular dilation without functional improvement, suggesting that shunt size and baseline right-sided reserve are critical determinants of safety.[6] The broader review by Jørgensen et al. similarly emphasized that while interatrial shunting reduces left atrial pressure, it may exacerbate PH and precipitate right-sided decompensation if applied in patients with elevated PVR or pre-existing RV dysfunction.[15] This concern was reinforced by the REDUCE LAP-HF II trial, during which right atrial and ventricular volumes increased significantly more in the shunt group, and adverse clinical outcomes—including higher rates of cardiovascular death and stroke—were concentrated among non-responders, defined by elevated PVR or the presence of rhythm devices.[14] In contrast, responders with favorable hemodynamics demonstrated symptomatic benefit and less adverse remodeling, underscoring that the safety of atrial shunting depends heavily on strict patient selection criteria.[14] Collectively, these data highlight that while atrial shunt devices are feasible and structurally tolerated in well-selected patients, use outside of established hemodynamic boundaries carries a risk of worsening PH, maladaptive right heart remodeling, and poorer clinical outcomes.

Conclusion

The Occlutech AFR occupies a unique position among interatrial shunt devices, offering a predictable and durable method of atrial decompression in both left- and right-sided HF syndromes. Evidence from early-phase and observational studies confirms procedural safety, long-term patency, and clinically meaningful improvements in functional status and hemodynamics. However, the lessons of REDUCE LAP-HF II make clear that efficacy is not universal—benefit is confined to patients with favorable hemodynamic reserve, while indiscriminate use risks maladaptive right heart remodeling and worsening PH. The challenge ahead lies in refining hemodynamic thresholds and phenotypic criteria that distinguish responders from non-responders. Large, sham-controlled trials such as FROST-HF and RESPONDER-HF will be decisive in validating AFR as a therapeutic option and establishing evidence-based guidelines for its use. Until then, the AFR should be regarded as a powerful but selective tool—capable of transforming outcomes when applied judiciously within the boundaries of hemodynamic precision.

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References

1. Vettukattil J, Rajeshkumar R, Dahdah N, et al. Clinical impact of creating a predetermined atrial communication in severe pulmonary hypertension using the atrial flow regulator device. J Am Coll Cardiol. 2018;71(11):A1948. https://doi.org/10.1016/S0735-1097(18)32489-6
2. Sysol JR, Machado RF. Classification and pathophysiology of pulmonary hypertension. Cont Cardiol Educ. 2018; 4(1):2–12. https://doi.org/10.1002/cce2.71
3. Jagadeesan V, Gray WA, Shah SJ. Atrial Shunt Therapy for Heart Failure: An Update. J Soc for Cardiol Angiogr Interv. 2023;2:6. https://doi.org/10.1016/j.jscai.2023.101203.
4. Chiu JS, Zuckerman WA, Turner ME, et al. Balloon atrial septostomy in pulmonary arterial hypertension: effect on survival. J Heart Lung Transplant. 2015;34(3):376–80. https://doi.org/10.1016/j.healun.2015.01.004
5. Guimaraes L, del Val D, Bergeron S, et al. Interatrial shunting for treating acute and chronic left heart failure. Eur Cardiol Rev. 2020;15:18. https://www.ecrjournal.com/articles/interatrial-shunting-treating-acute-and-chronic-left-heart-failure
6. Paitazoglou C, Bergmann M, Kilicaslan B, et al. The PRELIEVE trial: Final 1-year outcomes of the prospective atrial flow regulator study AFR. Eur Heart J. 2023;44:2. https://doi.org/10.1093/eurheartj/ehad655.1060
7. Riccardi M, Tomasoni D, Vizzardi E, et al. Device-based percutaneous treatments to decompress the left atrium in heart failure with preserved ejection fraction. Heart Fail Rev. 2022;28:315–330. https://doi.org/10.1007/s10741-022-10280-4
8. Butera G, Piccinelli E, Kolesnik A, et al. Implantation of Atrial Flow Regulator devices in patients with congenital heart disease and children with severe pulmonary hypertension or cardiomyopathy—an international multicenter case series. Frontiers in Cardio Med. 2024;10. https://doi.org/10.3389/fcvm.2023.1332395.
9. Kopeć G, Araszkiewicz A, Magoń W, et al. Results of atrial flow regulator implantation in pulmonary arterial hypertension with severe heart failure despite maximal medical therapy. Pol Heart J. 2024;82(1):75–8. https://doi.org/10.33963/KP.a2023.0167
10. Sivakumar K, Rohitraj GR, Rajendran M, et al. Study of the effect of Occlutech Atrial Flow Regulator on symptoms, hemodynamics, and echocardiographic parameters in advanced pulmonary arterial hypertension. Pulmonary Circulation. 2021; 11(1):1–10. https://doi.org/10.1177/2045894021989966
11. Shah SJ, Borlaug BA, Chung ES, et al. Atrial shunt device for heart failure with preserved and mildly reduced ejection fraction (REDUCE LAP-HF II): a randomized, multicenter, blinded, sham-controlled trial. Lancet. 2022;399:1130–40. https://doi.org/10.1016/S0140-6736(22)00016-2
12. Borlaug BA, Blair J, Bergmann MW, et al. Latent pulmonary vascular disease may alter the response to therapeutic atrial shunt device in heart failure. Circulation. 2022;145: 1592–1604. https://pubmed.ncbi.nlm.nih.gov/35354306/
13. Patel RB, Silvestry FE, Komtebedde J, et al. Atrial shunt device effects on cardiac structure and function in heart failure with preserved ejection fraction. JAMA Cardiol. 2024;9(6): 507–22. https://pmc.ncbi.nlm.nih.gov/articles/PMC11024798/
14. Gustafsson F, Petrie MC, Komtebedde J, et al. 2-year outcomes of an atrial shunt device in HFpEF/HFmrEF: Results from REDUCE LAP-HF II. JACC Heart Fail. 2024;12(8): 1425–38. https://pubmed.ncbi.nlm.nih.gov/38934964/
15. Jørgensen TH, Søndergaard L. Transcatheter implantation of interatrial sunt devices to lower left atrial pressure in heart failure. Int J Heart Fail. 2022;4:12–23. https://pmc.ncbi.nlm.nih.gov/articles/PMC9383341/