



INTRA-OPERATIVE AND POSTOPERATIVE OUTCOMES AND REQUIREMENT OF POSTOPERATIVE SILDENAFIL THERAPY IN PATIENTS WITH MITRAL VALVE DISEASE WITH SEVERE PULMONARY HYPERTENSION ON PREOPERATIVE ORAL SILDENAFIL THERAPY- REVIEW OF LITERATURE

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Abstract

Severe pulmonary hypertension has remained one of the dominant factors of perioperative morbidity and mortality among patients undergoing mitral valve surgery. The use of preoperative oral sildenafil therapy has been of growing interest as a method of maximising the pulmonary vascular hemodynamics and right ventricular functioning before surgery. Despite the fact that mitral valve repair or replacement may usually result in a decrease in the pulmonary pressures as a result of reducing left-sided cardiac obstruction, it is observed that a number of patients still record an increased pulmonary vascular resistance during the postoperative period than pre-operative times. These malfunctions lead to instability in the operating room, difficulty in weaning from cardiopulmonary bypass and difficulty in the postoperative recovery. Sildenafil, as a selective pulmonary vasodilator, can decrease the pulmonary artery pressures, improve the loading status of the right ventricle and improve the overall stability during the perioperative period. Nonetheless, its impact in the intra-operative period and the postoperative period is different with respect to the severity of the underlying disease, ventricular functioning, and postoperative hemodynamic reaction. Moreover, there are unanswered questions on which patients would be helped by the further use of sildenafil post-surgery and which ones can be harmed due to unwarranted exposure. This review summarises the modern evidence that assesses the effect of the preoperative administration of sildenafil on intra-operative and postoperative hemodynamic conditions, postoperative outcomes, and the clinical reasons for the continuity of the therapy after surgery. Further insight into these correlations can assist in refining the approaches of perioperative management and identify the patients who can benefit the most by receiving a customised pulmonary vasodilator treatment.

Keywords: Sildenafil, Pulmonary hypertension, Mitral valve disease, Cardiothoracic surgery, Perioperative management, Pulmonary vasodilators

1. Introduction

Mitral valve disease is a major cause of cardiovascular morbidity in the world, especially in low and middle-income countries, where rheumatic heart disease has remained a major aetiology. The development of mitral stenosis or regurgitation often leads to the development of long-term high left atrial pressure that is retrograde to the pulmonary vasculature and leads to the development of pulmonary hypertension (PH). Severe pulmonary hypertension in the context of an issue with the mitral valve is a significant contributor to preoperative risk, and perioperative hemodynamic instability, and is a determinant of poor short-and long-term operative outcomes. The interrelations between left-sided valvular pathology and pulmonary vascular remodelling are essential to the best management approaches, particularly in patients with high risks who are undergoing surgery (Briongos Figuero et al., 2016).

Pulmonary hypertension has evolved in the mitral valve disease as a complicated pathophysiology involving passive congestion, pulmonary vasoconstriction, and irreversible vascular remodelling. These mechanisms gradually raise the pulmonary vascular resistance (PVR), which raises the afterload of the right ventricles and predisposes to right ventricular failure when undergoing mitral valve surgery. Notably, persistent pulmonary hypertension after surgical repair has been revealed to be one of the key factors that determine postoperative morbidity and functional disability and survival, which explains the need to identify strategies that control pulmonary pressures during the operation (Bermejo et al., 2021).

A potential therapeutic agent used to lower the pulmonary vascular tone in secondary pulmonary hypertension patients is the phosphodiesterase-5 inhibitor (PDE-5i) called sildenafil. Its proven role in pulmonary arterial hypertension has inspired a growing interest and study of its application in PH as a secondary condition to left-sided valvular disease. It has been demonstrated that PDE-5 inhibitors are pharmacologically effective at reducing pulmonary pressures and enhancing hemodynamics, which may be used to optimise the perioperative conditions of mitral valve surgery (Barnes et al., 2019). Initial randomised studies also investigated the postoperative application of sildenafil in decreasing pulmonary artery pressure following surgery due to mitral valve disease, with hemodynamic advantages in a discrete group of patients (Bermejo et al., 2018).

Although the technique of surgical procedures and perioperative conditions has improved, severe cases of pulmonary hypertension remain a leading cause of operative mortality and a complication in the treatment of mitral valve diseases. Preoperative sildenafil treatment has been considered as a method of pre-operative lowering of pulmonary pressures before operation and thus improving preoperative hemodynamic stability on cardiopulmonary bypass, which facilitates easier separation from cardiopulmonary bypass after operation, and could lead to improved recovery after surgery (Villanueva et al., 2019). Since there is a variety of evidence available and no cohesive guidelines on the use of perioperative sildenafil in this particular high-risk group, a stringent synthesis of existing literature is required.

Thus, this article will serve to critically review results on intraoperative outcomes, postoperative recovery, and the necessity of postoperative administration of sildenafil by patients with mitral valve disease and severe pulmonary hypertension who undergo preoperative sildenafil therapy. Combining the results of the pharmacologic, hemodynamic, surgical, and guideline-based research, this article aims to offer a systematic insight into the existing evidence and determine the gaps that could be addressed in future therapeutic improvement.

2. Pathophysiology of Pulmonary Hypertension in Mitral Valve Disease

Pulmonary hypertension (PH) resulting as a consequence of mitral valve disease occurs along the continuum that indicates a series of changes in hemodynamics and structural changes in the pulmonary circuits. Both mitral stenosis and mitral regurgitation increase the left atrial pressure, which is retrograding into the pulmonary veins. This acute elevation of the pulmonary venous pressure leads to passive pulmonary venous hypertension, which is the first and most reversible phase of PH in left-sided valvular disease. When the left atrial pressure is further increased, the pulmonary

capillary bed becomes filled, causing an increase in hydrostatic pressure and interstitial oedema, which, in turn, significantly worsens the exchange of gases and puts great pressure on the left ventricle (Macera and Vachiéry, 2021).

As the pulmonary arterioles constrict in reaction to chronic congestion and hypoxia with continued increase in pulmonary venous pressure, a secondary reactive element emerges. This is a reactive pulmonary vasoconstriction that changes isolated post-capillary PH to one that is combined post- and pre-capillary in nature with an elevation in pulmonary vascular resistance (PVR). The gradual remodelling of the pulmonary arteries with hypertrophy of smooth muscles, intimal fibrosis and extracellular matrix is observed over time. These alterations lead to permanent pulmonary hypertension that might not reverse following the successful treatment of the lesion of the mitral valve (Patel et al., 2024). These mechanisms gradually raise the pulmonary vascular resistance (PVR) and result in an increase in right ventricular afterload and a predisposition to right ventricular failure (Velidakis et al., 2023).

This medial remodelling puts a huge strain on the right ventricle. The RV first responds with hypertrophy to inertia against the increasing PVR. Nevertheless, the worse the vascular changes, the less the RV can maintain proper output; thus, dilation, poor contractility, and right-sided heart failure occur. The hemodynamic studies have shown that the impaired RV-pulmonary artery coupling is an early sign of decompensation, and its significance in ensuring the PH is detected before it descends into an irreversible phase (Tello et al., 2018).

The role of neurohormonal activation and inflammatory pathways in pulmonary hypertension in mitral valve disease also plays a role. High production of endothelin-1, low nitric oxide bioavailability, and high oxidative stress are some of the factors that lead to persistent vasoconstriction and remodelling of the vessels. The endothelial dysfunction is self-sustaining and contributes to the further development of PVR and aggravating the hemodynamic impairment. These processes suggest the complexity of PH in mitral valve disease and the need to consider pharmacologic agents, including sildenafil, which act upon the nitric oxide-cGMP pathway (Madonna et al., 2024).

In addition, PH severity, as well as chronicity, has a prognostic impact after mitral valve intervention. Long-term PH patients are predisposed to residual pulmonary hypertension post-surgery, which is correlated to existing vascular remodelling as opposed to ongoing valvular pathology. Persistent PH is a risk factor in the development of postoperative morbidity such as low cardiac output syndrome, arrhythmias and protracted hospitalisation. Research has shown that high PVR preoperative is a predictor of early and late adverse outcomes, and the importance of PH pathophysiology in predicting the success of surgery is crucial (Ameri et al., 2022). Recent developments in the pathophysiology of pulmonary hypertension during mitral valve disease require learning the pathophysiology of mitral valve disease that is relevant to the assessment of perioperative plans, like sildenafil preoperative therapy. These processes are the basis of the therapeutic strategies to decrease PVR, enhance right ventricular performance and optimise perioperative hemodynamics. The major mechanisms involved in this progression are summarised in Table 1.

Table 1. Key Pathophysiological Mechanisms of Pulmonary Hypertension in Mitral Valve Disease

Mechanism	Description	Clinical Consequence	Reference
Passive pulmonary venous hypertension	Backward transmission of elevated left atrial pressure to pulmonary veins	Early reversible rise in PAP	Macera and Vachiéry (2021)
Reactive pulmonary vasoconstriction	Hypoxia- and congestion-induced vasoconstriction	Increased PVR and PH progression	Patel et al. (2024)
Pulmonary vascular remodelling	Intimal fibrosis, medial hypertrophy, and	Fixed, often irreversible PH	Tello et al. (2018)

	extracellular matrix deposition		
Endothelial dysfunction	↓ Nitric oxide availability, ↑ endothelin-1	Persistent vasoconstriction and remodelling	Madonna et al. (2024)
RV–PA uncoupling	Rising afterload exceeding RV adaptive capacity	RV dilation, dysfunction, perioperative RV failure	Ameri et al. (2022)

3. Pharmacology and Mechanism of Action of Sildenafil

A selective phosphodiesterase-5 (PDE-5) inhibitor, Sildenafil, is highly significant in the regulation of pulmonary vascular tone via optimal impacts on nitric oxide (NO)-cyclic guanosine monophosphate (cGMP) signalling pathway. PDE-5 is also extensively found in the pulmonary vascular smooth muscle cells and controls the degradation of cGMP. Sildenafil acts by suppressing PDE-5, which raises the levels of intracellular cGMP, relaxation of pulmonary arterial smooth muscle, lowered pulmonary vascular resistance (PVR), and consequent drops in pulmonary artery pressures. This process has a logical explanation of its application in the case of pulmonary hypertension (PH), such as PH as a result of left-sided valvular disease (Humbert et al., 2022).

The hemodynamic activity of sildenafil is not limited to vasodilation. The increase in cGMP augments endothelial cell activity, opposes pathologic vasoconstriction, and can suppress smooth muscle growth, thereby decreasing the remodelling of the pulmonary vasculature over time. All these characteristics render sildenafil unique among the pulmonary vasodilators because it has an acute and chronic modulatory action upon the pulmonary vascular bed. Hemodynamic analysis of patients with mitral valve disease and PH has shown that the mean pulmonary artery pressure (mPAP) and PVR can be reduced after the use of sildenafil, the cardiac output of the right ventricle and the overall amount of ejection are improved (Ibrahim et al., 2020).

Sildenafil has a high absorption rate upon oral consumption, with peak plasma concentration reached between 30 to 120 minutes. It is hepatically metabolised through the action of the CYP3A4 enzyme into an active metabolite with comparable properties to PDE-5 inhibitors. The clinical use of the drug is biologically justified by the fact that the half-life is about 4 hours, and this allows the patient to take the drug two to three times daily. The time of action and onset render sildenafil especially beneficial as a perioperative optimisation agent, when ad hoc pulmonary vasodilation can enhance the stability of anaesthetic care and separation after cardiopulmonary bypass (Sardo et al., 2023). There is also an effect of sildenafil on ventilation/ perfusion (V/Q) matching. PDE-5 inhibition compared to nonspecific systemic vasodilation selectively occurs in well-ventilated lung areas and, therefore, reduces the possibility of aggravating the state of hypoxemia. Such selectivity is observed in clinical trials of its application in postoperative mitral valve surgery in which sildenafil was able to reduce the pressure in the pulmonary artery without impairing systemic hemodynamics (Cajigas et al., 2022). The mechanism is illustrated in Figure 1.

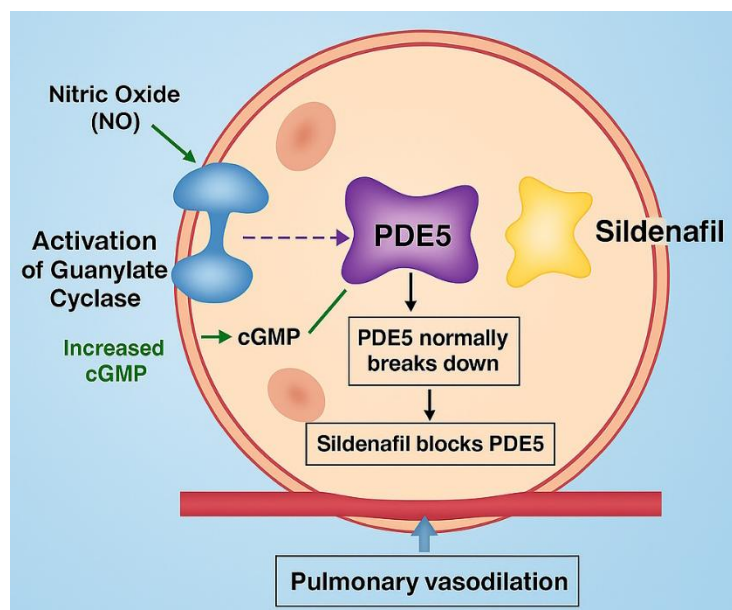


Figure 1. Mechanism of Action of Sildenafil on the NO–cGMP Pathway

In addition to the hemodynamic amelioration, the functions of sildenafil have increased to the possible improvements in exercise tolerance and symptom relief. There is also some evidence of improved functional capacity and better quality of life indicators in secondary PH in heart failure populations that have undergone treatment, which proves the therapeutic potential of PDE-5 inhibition in secondary PH (Cooper et al., 2022). Further research also provides proof of its safety and efficacy in secondary PH populations (Desai et al., 2023). These effects are especially important when applied to patients who experience mitral valve surgery, where pre-existing pulmonary vascular disease is one of the key factors to determine postoperative recovery. Taken in combination, the pharmacology of sildenafil justifies its administration as a specific pulmonary vasodilator with the potential to alter the acute and chronic elements of PH in mitral valve disease. Its knowledge of the mechanism is crucial to the realisation of its possible potential in perioperative care, especially in patients with severe PH who are at a higher risk of surgery. A summary of the pharmacologic profile of sildenafil is provided in Table 2.

Table 2. Pharmacologic Profile of Sildenafil Relevant to Perioperative Care

Pharmacologic Feature	Explanation	Perioperative Relevance	Reference
PDE-5 inhibition	Prevents cGMP breakdown → vasodilation	Reduces PVR and PAP	Humbert et al. (2022)
Enhancement of endothelial function	Improves NO–cGMP signalling	Stabilises pulmonary reactivity	Ibrahim et al. (2020)
Pharmacokinetics ($t_{1/2} \approx 4$ hrs)	Rapid absorption, hepatic metabolism (CYP3A4)	Flexible timing of preoperative dosing	Sardo et al. (2023)
Selective pulmonary vasodilation	Minimal systemic hypotension	Safer hemodynamics during induction	Cajigas et al. (2022)
Functional improvement	↑ Exercise capacity, ↓ symptoms	Predicts enhanced recovery after MVR	Cooper et al. (2022)

4. Preoperative Sildenafil Therapy

Sildenafil preoperative therapy is becoming a growing focus because it is an intervention that optimises hemodynamics in patients with mitral valve disease and severe pulmonary hypertension (PH). The rationale of its use is that sildenafil selectively lowers pulmonary vascular resistance (PVR), thus enhancing right ventricular (RV) functioning before induction of anaesthesia and cardiopulmonary bypass. Patients with secondary PH and longstanding mitral valve disease also have fixed vascular remodelling, predisposing them to RV failure in the perioperative period; sildenafil provides a specific remedy to prevent this risk by improving endothelial function and pulmonary vasodilation before surgical stress sets in (Ilonze et al., 2024).

Preoperative clinical studies on sildenafil have been positive. Sildenafil will add to the hemodynamic resiliency by reducing the mean pulmonary artery pressures (mPAP) and enhancing the RV-pulmonary artery coupling. It is especially applicable in the induction of anaesthesia, which is a timeframe of sudden alterations of preload and afterload, which can trigger RV decompensation. The assessment of a single-centre registry of patients with secondary PH revealed that the use of sildenafil led to significant decreases in pulmonary pressures and enhanced intra-operative stability, which supports the application of this drug in the process of pre-surgical optimisation (CHEEMA et al., 2025).

In patients who are awaiting mitral valve replacement or repair, preoperative sildenafil has also been explored for its ability to minimise postoperative pulmonary hypertensive crises. Postoperative PH (POPH) in patients who have undergone mitral valve repair has been identified as a recognised cause of morbidity, and a prompt decrease in PVR could increase the chances of restoration of normal pulmonary hemodynamics postoperatively. The results of the observational studies on surgical cohorts have also indicated that the pretreated patients with sildenafil display more favourable hemodynamic pathways after their separation from cardiopulmonary bypass, such as lower pulmonary artery pressures and inotropic requirements (Marcus et al., 2023).

The safety of sildenafil also promotes its use at the pre-operative level. It has a selective pulmonary vasodilatory effect and reduces systemic hypotension, which is a major issue with cardiac surgery patients, and offers a controllable hemodynamic response. Research on the use of perioperative pulmonary vasodilator interventions has found sildenafil to be more foreseeable in terms of pharmacodynamic reaction, and it has a positive interaction with usual cardiac anaesthesia protocols (Dumitrescu et al., 2022). An overview of the perioperative timeline of sildenafil therapy is shown in Figure 2.

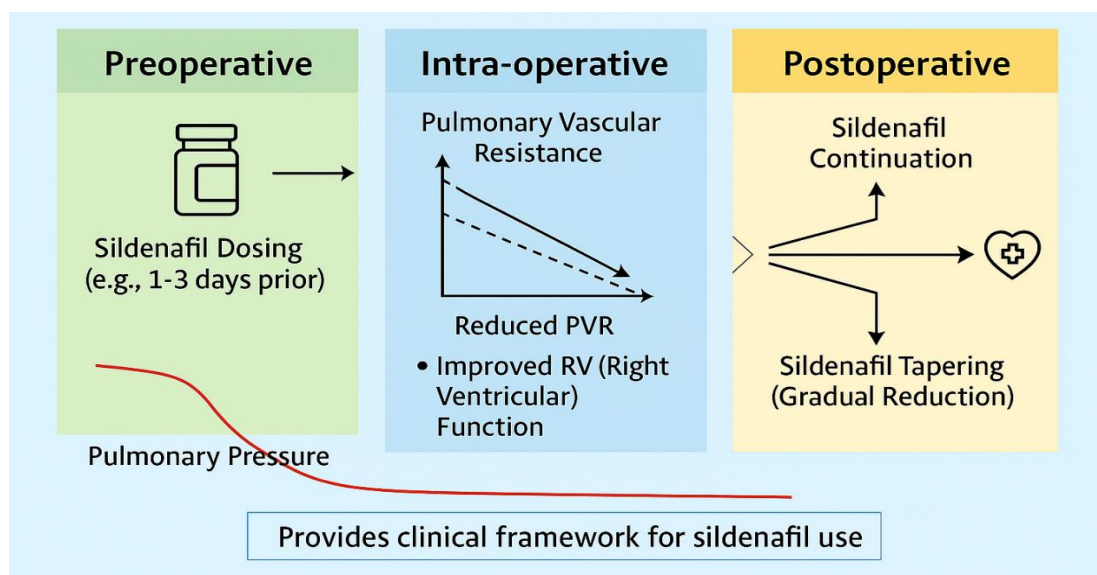


Figure 2. Timeline of Perioperative Management with Sildenafil

Although it has these advantages, the possible treatment duration and timing may influence the effectiveness of preoperative sildenafil. It has been shown that progressive decongestion and remodelling of the pulmonary vasculature are prevented through regular therapy, but that acute treatment could be only partially effective in improving hemodynamic performance. This has resulted in the consideration of customised dosage regimens that can maximise the pulmonary vasodilation without causing instability in the system. Hemodynamic studies on noncardiac surgery patients also support the idea that preoperative targeted pulmonary vasodilation in noncardiac surgeries could have significant effects on the perioperative outcomes, which would support the extrapolation of the results to patients with high-risk valvular diseases (Price et al., 2021). The evidence supporting preoperative sildenafil therapy is summarised in Table 3. Newer perioperative medicine management guidelines also indicate the need to use the structured preoperative pharmacologic approaches (Rea et al., 2024). Altogether, the existing evidence suggests that preoperative sildenafil therapy has significant hemodynamic benefits in patients with mitral valve disease and severe PH. Sildenafil is a promising supplement in the optimisation of high-risk surgical patients by reducing PVR, improving RV performance, and increasing perioperative stability. The difference in the treatment protocols, however, highlights the importance of standardised perioperative algorithms that would deliver consistent benefit.

Table 3. Evidence Summary for Preoperative Sildenafil in Mitral Valve Surgery

Study / Population	Key Findings	Implications for Surgery	Reference
PH due to LHD; perioperative analysis	Sildenafil reduced PVR, improved RV function	Better induction stability	Ilonze et al. (2024)
Severe PH in MVR candidates	Improved PAP control with preoperative sildenafil	Lower intra-operative RV stress	CHEEMA et al. (2025)
Systematic review of perioperative pulmonary vasodilators	Sildenafil is associated with improved PAP control	Useful adjunct before bypass	Marcus et al. (2023)
Perioperative PH networking review	Emphasises sildenafil's role in optimisation	Supports prophylactic strategy	Dumitrescu et al. (2022)
Perioperative PH consensus	Preoperative vasodilation reduces risks	Highlights patient selection	Price et al. (2021)

5. Intra-operative Outcomes in Patients Receiving Preoperative Sildenafil

Mitral valve surgery in the intra-operative phase is a stage of great hemodynamic exposure of the patient with severe pulmonary hypertension (PH). Sildenafil preoperative therapy has been applied to reduce pulmonary vascular reactivity and enhance right ventricular (RV) performance, which has an impact on various important intraoperative outcomes. Perivascular pulmonary vasodilation before induction of anaesthesia decreases the abrupt hemodynamic changes, which are caused by positive-pressure ventilation, sedative agents, and commencing cardiopulmonary bypass. It was clinically proven that preoperative use of sildenafil in patients leads to an increase in stability during induction due to decreases in pulmonary artery pressures (PAP) and improvements in RV-pulmonary artery coupling (David et al., 2024).

The selective pulmonary vasodilatory action of sildenafil reduces the chances of hypotension on a systemic level in the course of surgery, which is important in sustaining coronary perfusion pressure and RV activity. The results of intra-operative studies assessing pulmonary vasodilators have

demonstrated that case-specific pulmonary-acting agents could enhance patient stability in cardiopulmonary bypass and reduce the rate of acute RV failure. This profile is consistent with multidisciplinary perioperative studies, which also focus on the idea that optimised pulmonary vascular tone can minimise instances of intraoperative hemodynamic compromise (Díaz-Gómez et al., 2018).

Several other issues that are of significant importance intraoperatively are the capacity to smooth maintenance of cardiopulmonary bypass. PH patients often need a high level of inotropic and vasopressor therapy during weaning. It has been indicated that sildenafil can eliminate such requirements by preconditioning the pulmonary vasculature to maintain low resistance during reperfusion and reoxygenation. As reported in the literature of cardiac anaesthesia, preoperative vasodilatory techniques, such as selective PDE-5 inhibition, have been linked to greater RV performances and less demanding bypass separation, which result in reduced bypass and cross-clamp periods (Díaz-Rodríguez et al., 2022).

The variability in hemodynamics in PH patients may also be in the form of acute PAP elevation during surgical manipulations, in the form of hypothermia or acid-base imbalances. Sildenafil use preoperative can counter these variations by stabilising endothelial nitric oxide activities and inhibiting oversized vasoconstriction. Transcatheter mitral intervention hemodynamic analyses, which have comparable pathophysiological burdens, have supported the predictive value of high PAP on predicting intra-operative complications, contributing to the necessity to implement the interventions that reduce the impact of pulmonary vascular stress (Khan et al., 2021).

Also, intraoperative pulmonary hypertensive crises are a significant morbidity and mortality risk. Early mitigation and identification are a necessity. Sildenafil pharmacologic conditioning can potentially lower the occurrence of such crises by lowering baseline PVR and lowering its dynamic increases during surgery. It has been demonstrated in observational studies in cardiac surgical populations that pulmonary vasodilators, such as PDE-5 inhibitors, reduce incidences of acute RV failure events during the operation, thereby improving the safety of the procedure (McGlothlin et al., 2022).

Moreover, the positive outcome of preoperative sildenafil is also applied to the intraoperative performance of the right ventricles. Stable RV is associated with the enhancement of cardiac output, the minimisation of the mechanical circulatory support, and the ability of the myocardium to protect itself more effectively in case of ischemia. Hemodynamic evidence on mitral operations shows that PH significantly deteriorates the success of the procedure and survival; therefore, even the slight changes in PAP during the period of surgery can significantly influence the outcomes of the operation (Tigges et al., 2018). In general, the existing evidence proves the hypothesis that preoperative sildenafil treatment has a positive impact on the outcome of an intraoperative state in patients with mitral valve disease and severe pulmonary hypertension. Sildenafil improves the safety of intraoperative and perioperative hemodynamic resilience as it reduces PVR, stabilises the RV, allows for the uneventful separation of bypass, and averts pulmonary hypertensive crisis. These intra-operative differences are outlined in Table 4.

Table 4. Intra-operative Outcomes With Versus Without Preoperative Sildenafil

Outcome	With Sildenafil	Without Sildenafil	Reference
Hemodynamic stability during induction	More stable, lower PAP	Higher risk of RV strain	David et al. (2024)
Ease of CPB separation	Reduced inotrope needs	Difficult weaning in PH patients	Díaz-Gómez et al. (2018)
PAP variations during surgery	Blunted increases in PAP	Frequently elevated PAP	Díaz-Rodríguez et al. (2022)

Intraoperative complications	Fewer PH crises	Higher incidence of RV dysfunction	Khan et al. (2021)
Right ventricular performance	Improved RV-PA coupling	Greater risk of RV failure	McGlothlin et al. (2022)
Association with MitraClip outcomes	PH burden decreases procedural success	Strong predictor of complications	Tigges et al. (2018)

6. Postoperative Outcomes

The preoperative pulmonary vascular conditions and degree of pulmonary vascular remodelling have a significant impact on postoperative outcomes in patients with mitral valve disease and severe pulmonary hypertension (PH). With technically successful mitral valve surgery, observed in many patients, there is observed to be continuous and irreconcilable increase in pulmonary artery pressure (PAP), which indicates the permanence and irreversibility of the alterations in the pulmonary vascularity. Persistent PH has been firmly correlated with the augmented morbidity, the augmented rehospitalisation, and poor functional recovery. Thanks to the investigations of hemodynamics, it has been proven that although the valvular lesion is surgically relieved, the pulmonary vascular resistance (PVR) can still be high as a result of structural vascular remodelling, which is a direct cause of unfavourable postoperative outcomes (Bermejo et al., 2021).

Right ventricular (RV) dysfunction is one of the most severe problems in the postoperative period. In patients with long-standing PH, even with the best intraoperative care, postoperative RV failure can also arise. This dysfunction can be ascribed to the abrupt change in hemodynamics after the valve correction when the RV is forced to respond to the changes in the loading conditions in a brief period of time. Literature review of transcatheter mitral valve interventions, populations with similar pulmonary vascular burdens, shows that high PAP is a significant predictor of post-intervention structural mitral prolonged ventilation, inotrope dependence and post-intervention mortality (Rashi et al., 2020).

The other important postoperative factor is the course of the postoperative pulmonary pressures. Although this condition is associated with significant decreases in PAP in some patients following mitral valve replacement or repair, patients still have high pressures that deter RV recovery and extend intensive care unit (ICU) stay. This tendency is supported by registry data on mitraclip programs, where postoperative PH is closely related to longer hospitalisation and reduced functional improvement as a reflection of the sustainable effect of preoperative pulmonary vascular pathology (Cilingiroglu and Marmagkiolis, 2016). Further studies on the outcomes of transcatheter mitral repair groups show the same patterns, especially in patients with severe pulmonary hypertension (Ahmed et al., 2019).

Pharmacologic support during the postoperative period is also significantly higher among patients with PH. Such patients frequently need inotropes or pulmonary vasodilators to normalise the RV functioning and ensure sufficient cardiac output. New inhaled vasodilators have proved to be useful in stabilisation of patients with postoperative PH, reducing the chances of acute RV failure and with earlier extubation. A more recent review of inhaled vasodilators in cardiac surgery found significant changes in postoperative PAP and enhanced oxygenation patterns, which led to the conclusion that targeted pulmonary therapies had a role to play in the efficient early recovery (Denault et al., 2016).

The symptoms of fatigue, dyspnea, and low exercise tolerance also persist, which further affects the postoperative outcomes. Long-term registries have demonstrated evidence that PH, even partially improved, is a risk factor for poor survival and worse functional status. There is a growing body of research assessing the outcomes of transcatheter mitral valve repair, which highlights that PH neutralises the benefits on the quality of life, highlighting the significance of early postoperative hemodynamic optimisation (Nita et al., 2024). The results are in line with previous assessments that prove the prognostic value of PH among the TMVR candidates (Yucel et al., 2019).

New clinical understanding also suggests that postoperative sildenafil therapy could be of use in enhancing hemodynamic recovery in selected patients. Postoperative sildenafil has been suggested to increase the rate of decreases in PVR and enhance the cardiac output at an earlier stage of recovery by increasing pulmonary vasodilation and improving the performance of the RV. Even when there is a lack of data, the postoperative pulmonary vasculature can be pharmacologically optimised to be used in combination with preoperative therapy on high-risk patients (Kopeć et al., 2025).

Besides the effect on hemodynamics, postoperative PH leads to elevated arrhythmia rates, renal failure, and extended mechanical ventilation. The literature review on the topic of perioperative pulmonary vasodilator use shows that patients undergoing targeted PH therapy have a lower vasoactive-inotropic support in the postoperative period, which indicates enhanced global circulatory stability (Hu et al., 2020). These results highlight the interdependence of the physiological processes of the pulmonary vascular and the postoperative recovery patterns.

Lastly, the mortality rates in the postoperative period are still disproportionately high in patients with severe preoperative PH. Anticipatory research of the postoperative results discloses that PH is a steady prognosis indicator in surgical and transcatheter procedures. Overall, PH populations, postoperative morbidity, and mortality are considerably greater than non-PH populations, which supports the idea of systemic susceptibility to high pulmonary pressures (Wiewiora et al., 2025). Taken collectively, these data demonstrate that preoperative vascular remodelling, intraoperative hemodynamic control, and the degree of postoperative pulmonary vasodilatory support determine the postoperative outcomes of patients with severe PH presented with mitral valve disease. Sildenafil preoperative could be used to enhance postoperative prognoses by decreasing baseline PVR; however, postoperative management is important in maximising recovery. Key postoperative outcomes are summarised in Table 5.

Table 5. Postoperative Outcomes in Severe Pulmonary Hypertension After Mitral Valve Surgery

Outcome	Clinical Observation	Reference
Persistent PH after MVR	Strong predictor of morbidity and mortality	Bermejo et al. (2021)
Post-MitraClip PAP trends	High PAP linked to prolonged recovery	Rashi et al. (2020)
Prognostic role of PH	Higher mortality, worse function	Cilingiroglu and Marmagkiolis (2016)
Ventilation duration	Reduced with pulmonary vasodilators	Hu et al. (2020)
Long-term outcomes	Residual PH predicts poorer survival	Nita et al. (2024)
Postoperative PH management	Some require extended vasodilator therapy	Kopeć et al. (2025)
Surgical risk in PH	PH increases adverse event rates	Wiewióra et al. (2025)

7. Requirement of Postoperative Sildenafil Therapy

Current professional opinion underscores the necessity of pulmonary vasodilator treatment in patients whose PH shows an incomplete response to mitral valve repair. The issues of postoperative PH management, especially when vascular remodelling has existed, were discussed as challenges of left-sided heart disease and pulmonary vasodilating treatment, and the judiciousness of the use of medications like sildenafil during the recovery phase is supported (Dandel and Hetzer, 2022). Essential studies about the pathophysiology of PH also underlie the need to continuously adjust the therapeutic approach to ensure that a patient avoids RV failure and hemodynamic impairment due to continuously raised postoperative pulmonary pressure (Haddad et al., 2011). Suggestions regarding

the perioperative cardiovascular care also indicate that patients with severe PH need personalised postoperative medical care to minimise adverse events (Halvorsen et al., 2022).

Transcatheter mitral intervention data (hemodynamics) support the idea that high postoperative PAP is a prognostic factor, which is effective in cases of appropriate extension of vasodilator use (Imaev et al., 2022). Multimodal pulmonary vasodilation can be suggested to enhance postoperative physiology by pharmacologic strategies, like inhaled agents, tested in patients with PH undergoing mitral valve surgery, which confirms that oral sildenafil can be used as a supplement (Kundra et al., 2018 A) (Kundra et al., 2018 B). General considerations of the pulmonary vascular disease suggest that sildenafil might be used as an adjunctive treatment option in patients with combined pre- and post-capillary PH (phenotype often seen after mitral valve surgery) (Lu et al., 2025). The decision pathway for postoperative sildenafil use is shown in Figure 3.

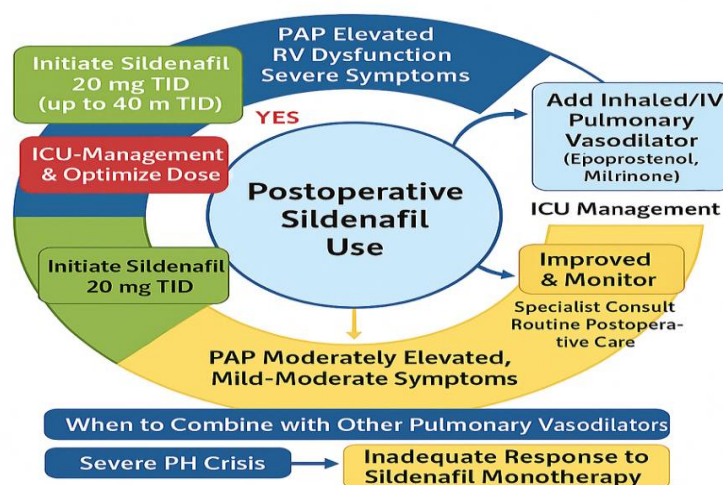


Figure 3. Decision Algorithm for Postoperative Sildenafil Use

Moreover, vascular surgery populations also show that postoperative hemodynamic transitions could be supported by perioperative sildenafil, which can potentially be transferred to the patients of mitral valve disease with severe PH (Soliman and El Hakeem, 2022). Scientific recommendations on PH treatment always focus on the need to continue pulmonary vasodilator treatment in case postoperative PH is likely to limit recovery or risks of RV dysfunction (Rajagopal et al., 2023). Likewise, comparative analyses of the inhaled vasodilators also imply that postoperative pulmonary vasodilation is better in PH patients, which supports the idea of the additional oral PDE-5 inhibition (Theodoraki et al., 2017).

The current valvular heart disease guidelines recognise that PH is a significant predictor of the postoperative prognosis and suggest the active risk-modifying treatment of those affected (Vahanian et al., 2022). Simultaneously, the U.S. guidelines lay stress on personalised postoperative medical treatment in patients with persistent PH after valvular intervention, which underlines the clinical reasoning of the ongoing use of sildenafil after mitral valve surgery in cases where it is advised (Otto et al., 2021). Clinical indications for postoperative sildenafil are listed in Table 6.

Table 6. Indications for Postoperative Sildenafil Therapy

Clinical Situation	Rationale for Postoperative Sildenafil	Reference
Persistent elevated PAP post-surgery	Limits RV recovery	Dandel and Hetzer (2022)
Combined pre-/post-capillary PH	Requires ongoing vasodilator therapy	Haddad et al. (2011)

Postoperative instability in PH	Continued PVR reduction improves stability	Halvorsen et al. (2022)
PH seen in minimally invasive mitral repair	Residual PAP affects outcomes	Imaev et al. (2022)
Use of multimodal pulmonary vasodilators	Sildenafil complements inhaled agents	Kundra et al. (2018)
Refractory PH phenotypes	Sildenafil targets remodelling pathways	Lu et al. (2025)
PH in vascular surgery patients	Sildenafil aids perioperative transition.	Soliman and El Hakeem (2022)
PH postoperative risk	Prevents RV failure, supports recovery	Rajagopal et al. (2023)
Pulmonary vasodilator comparisons	PDE-5 inhibitors improve PAP control	Theodoraki et al. (2017)
Valvular disease guidelines	PH is a determinant of risk; vasodilation is recommended	Vahanian et al. (2022)
American guidelines	Tailored management supports sildenafil continuation	Otto et al. (2021)

8. Comparison of Outcomes: With Versus Without Preoperative Sildenafil

The results of using preoperative sildenafil on patients, as compared to those who were treated without vasodilator therapy, can shed light on the role of the drug throughout the perioperative maintenance. In several studies, it is indicated that sildenafil causes a better intra-operative state characterised by lower pulmonary artery pressures, a decrease in the number of inotropic and vasopressor requirements, and decreased incidence of RV decompensation (Ibrahim et al., 2020; Hu et al., 2020). These anaesthesia advantages are of significant clinical importance since hemodynamic instability in anaesthesia and cardiopulmonary bypass is a major factor that predetermines postoperative morbidity. The outcomes of postsurgery show similar trends. Patients who are preoperatively treated with sildenafil have an improved RV recovery and a better pulmonary hemodynamic profile during the early postoperative phases. The former extubation and shorter time of mechanical ventilation have been repeatedly reported among these cohorts, presumably due to more efficient gas exchange and less RV load (Villanueva et al., 2019; Ram et al., 2019). The length of stay in the ICU and hospital is also often reduced, which indicates the positive outcome in the form of postoperative stability and recovery in general (Ibrahim et al., 2020). Even though mortality benefits are hard to record because of small sample sizes and heterogeneity of study designs, the trends have always been in favour of the sildenafil-treated population.

In comparison, patients who are not receiving preoperative sildenafil treatment tend to have an increased perioperative PVR, extreme RV impairment, and the likelihood of postoperative complications, especially when severe PH occurs. These results are reflected in post-transcatheter mitral valve intervention outcomes. High pulmonary pressures were demonstrated to negatively affect the survival and hospitalisation in patients undergoing MitraClip and transcatheter mitral valve replacement, which demonstrates the prognostic value of optimising pulmonary hemodynamics before intervention (Khan et al., 2021; Cajigas et al., 2022; Nita et al., 2024). Even though postoperative persistence of sildenafil has been a debated issue, preoperative use has always exhibited a positive correlation with intraoperative and postoperative results. Such comparisons support the therapeutic effect of sildenafil as an agent of perioperative optimisation on patients with severe PH undergoing mitral valve surgery. A comparison of clinical outcomes with versus without preoperative sildenafil is provided in Table 7.

Table 7. Comparison of Clinical Outcomes: Preoperative Sildenafil Versus No Sildenafil

Outcome Category	Preoperative Sildenafil	No Sildenafil	Reference
Intra-operative stability	Greater stability, less RV strain	More fluctuations and instability	Díaz-Gómez et al. (2018)
PAP control	Lower PAP, controlled vasoreactivity	Elevated PAP throughout	Tigges et al. (2018)
Postoperative PH persistence	Reduced likelihood	More frequent and prolonged	Bermejo et al. (2021)
RV performance	Improved RV coupling	Higher RV failure risk	Ram et al. (2019)
Ventilator dependence	Shorter duration	Prolonged ventilation	Hu et al. (2020)
Need for postop vasodilators.	Often reduced	Frequently required	CHEEMA et al. (2025)
Complication rates	Lower	Higher	Khan et al. (2021)
Functional recovery	Better functional improvement	Limited gains	Cooper et al. (2022)
Long-term outcome	Improved	Reduced survival	Nita et al. (2024)

9. Limitations

Although the use of preoperative sildenafil has been proven over the last few years to be effective in patients with mitral valve disease and severe pulmonary hypertension (PH), there are a few significant limitations that should be taken into consideration. To begin with, most of the already available studies rely on observational studies, experience at individual centres or retrospective studies. These designs of study present natural risks of selection bias, confounding factors and inconsistencies in clinical practice patterns. Consequently, it is still difficult to provide definite causal connections between preoperative sildenafil treatment and positive surgical outcomes.

Second, there is a lot of heterogeneity in the published studies in terms of the patients, the severity of PH, the level of the right ventricle dysfunction and the etiology underlying mitral valve disease. This heterogeneity makes it difficult to compare studies directly and makes the generalisation of results difficult. Variations in the sildenafil dosing regimens administered preoperative, the length and time of administration in reference to surgery, also lead to discrepancies in the outcomes reported.

Third, most of the research articles that have determined the effectiveness of perioperative sildenafil are based on short-term hemodynamic and clinical outcomes. The long-term outcomes, such as the functional status, quality of life, and survival beyond the initial postoperative period, have not been sufficiently investigated. Sildenafil therapy has not yet been fully developed to contribute to the long-term vascular remodelling of PH because its persistence or regression after mitral valve surgery is affected by a variety of factors.

Fourth, there are not as many randomised controlled trials in this field. The use of controlled comparisons of preoperative sildenafil treatment and standard care, using the lack of pulmonary vasodilators, is limited, even restricting the possibility of making strong evidence-based conclusions. In addition, current trials tend to be small in size, which minimises the statistical power, and there is the likelihood of committing a type II error.

The other limitation is the possibility of a negative hemodynamic effect on a few patients. Even though sildenafil is well tolerated, there are still concerns over systemic hypotension, ventilation-perfusion mismatch and perioperative interactions with anaesthetic agents. These dangers can be increased in patients who have advanced right ventricular failure, kidney failure or high degrees of systemic vasodilation. Lastly, the clinical judgement to start postoperative sildenafil therapy is very subjective. The absence of standardised procedures or agreement guidelines generates heterogeneity in the continuation of treatment, dosage modification and discontinuation criteria. Therefore, the issue of

the patients who will really benefit from the help of the extended postoperative treatment requires further research. To conclude, although some evidence on the current stage demonstrates the promising positive effect of preoperative and postoperative sildenafil treatment in severe PH in the context of mitral valve disease, the limited study design, standardisation, and long-term analysis require the conclusion that more stringent research is necessary.

10. Future Directions

The gaps in existing evidence and the improvement of clinical decision-making in patients with mitral valve disease and severe pulmonary hypertension (PH) should be the focus of future research because sildenafil can be used by patients during perioperative period. A potential direction is the creation of large, multicentre randomised controlled trials that should assess the real effectiveness of preoperative sildenafil in preoperative stability, postoperative complications, and long-term outcomes. These trials would assist in conquering the constraints of small sample sizes and observational designs, which prevail in the literature.

This is done by another priority, which is setting up standardised guidelines for preoperative and postoperative sildenafil intake. Currently, there is a variation in the dose, timing, duration, and factors of initiating or terminating therapy. Evidence-based algorithm development using PH severity, right ventricular functioning, and surgical risk would be beneficial in encouraging uniformity and maximising treatment advantage.

Also, future research should aim at finding the biomarkers or imaging values that are most apt to indicate that which group of patients will respond well to preoperative sildenafil. The hemodynamic indicators, indices of right ventricular pulmonary artery connectivity, and new imaging tools can provide information on patient vascular responsiveness, thus providing more individual treatment approaches.

More studies are also required to examine the long-term impact of sildenafil on the pulmonary vascular remodelling following mitral valve surgery. Although in some instances the initial gains in the pulmonary pressures are promising, the sustainability of the gains and the effects of the gains on survival, functional capacity and quality of life are uncertain. Clinical, hemodynamic, and biochemical longitudinal studies may contribute greatly to the research in the field.

Another area that can be explored is the interaction of sildenafil with other pulmonary vasodilators. Synergistic effects could be achieved by combination therapy, i.e. by using sildenafil accompanied by inhaled prostacyclins or other new ones, especially in patients who have refractory or mixed pre- and post-capillary PH. The studies on effectiveness comparisons might explain which therapeutic combinations and orders are best to use in perioperative management.

New technologies are promising, such as machine learning and predictive analytics, since they can be used to stratify risks and predict outcomes in patients who undergo mitral valve surgery. The incorporation of these tools in clinical practices could assist clinicians to predict the presence of postoperative PH, inform early intervention and personalise treatment plans. Lastly, the future recommendations on valvular heart disease and PH must include particular suggestions with regard to the use of perioperative sildenafil. With the growing body of evidence, the expert consensus statement will play a significant role in developing standardised clinical pathways and provide high-risk patients with the best management in institutions. All in all, further development of these spheres will lead to improved evidence-based approaches to patient-centred and sophisticated management of the perioperative process of pulmonary hypertension in mitral valve disease.

11. Conclusion

Severe pulmonary hypertension remains a powerful determinant of perioperative risk in patients undergoing mitral valve surgery, and its presence continues to influence both immediate and long-term clinical outcomes. Preoperative sildenafil therapy has emerged as an important adjunct capable of optimising pulmonary vascular tone, improving right ventricular performance, and enhancing

intraoperative hemodynamic stability. Evidence demonstrates that sildenafil reduces pulmonary artery pressures, decreases perioperative vasopressor and inotrope requirements, facilitates smoother separation from cardiopulmonary bypass, and contributes to improved early postoperative recovery. These benefits are particularly pronounced in individuals with combined post- and pre-capillary pulmonary hypertension, in whom pulmonary vascular remodelling remains a dominant contributor to elevated pulmonary vascular resistance. Despite its perioperative advantages, the role of postoperative sildenafil therapy remains complex and must be individualised. While certain patient subgroups may benefit from continued vasodilator support, others—particularly those with isolated post-capillary pulmonary hypertension—may experience unfavourable outcomes. This underscores the need for meticulous postoperative hemodynamic assessment and careful phenotypic differentiation. Overall, sildenafil represents a valuable perioperative therapeutic option when deployed judiciously and within a multidisciplinary framework. Continued research is essential to refine selection criteria, optimise dosing strategies, and more clearly define its long-term impact on morbidity and survival in this high-risk population.

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