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A Comprehensive Review of the Anesthetic Management of Patients with Pulmonary Hypertension Undergoing Cardiac Surgery

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ABSTRACT

Background: Pulmonary hypertension (PH) represents a formidable challenge in perioperative medicine, particularly in the context of cardiac surgery, where elevated pulmonary vascular resistance predisposes to right ventricular dysfunction, difficulty in weaning from cardiopulmonary bypass, and increased postoperative morbidity and mortality.

Main body of the abstract: Optimal management requires an integrative strategy encompassing vigilant monitoring, ventilatory adjustments, pharmacologic interventions, and preparedness for mechanical circulatory support. In recent years, attention has focused on the use of inhaled milrinone as a selective pulmonary vasodilator with potential advantages over systemic administration. This review synthesizes evidence from randomized controlled trials, meta-analyses, observational studies, and case reports (2010-2025) to evaluate the role of inhaled and intravenous milrinone, situating these within the broader framework of anesthetic and perioperative management of PH. Inhaled milrinone demonstrates theoretical and mechanistic benefits, including selective pulmonary vasodilation, preservation of systemic vascular resistance, and facilitation of separation from cardiopulmonary bypass, with some studies reporting reductions in extubation time and intensive care unit stay. However, comparative trials remain limited in size, heterogeneity of dosing regimens and timing persists, and definitive improvements in major outcomes such as survival have not been demonstrated.

Conclusion: Inhaled milrinone should not be considered a standalone therapy but rather one element of a multimodal strategy that integrates preoperative optimization, invasive and echocardiographic monitoring, careful anesthetic induction, tailored hemodynamic support, and postoperative vigilance. Future large-scale randomized studies are needed to clarify optimal dosing, comparative effectiveness against other pulmonary vasodilators, and long-term outcomes.

KEYWORDS: Pulmonary hypertension, right ventricular dysfunction, cardiac surgery, perioperative management, anesthetic strategies.

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BACKGROUND

Pulmonary hypertension (PH), characterized by elevated pulmonary arterial pressure and increased pulmonary vascular resistance, is a major risk factor for morbidity and mortality in patients undergoing cardiac surgery [1]. Its presence often portends right ventricular (RV) dysfunction, difficulty weaning from cardiopulmonary bypass (CPB), and adverse postoperative outcomes. The management of PH in the perioperative setting is therefore complex, requiring a nuanced understanding of pathophysiology, hemodynamics, pharmacotherapy, monitoring strategies, and risk mitigation [2]. In recent years, significant attention has been devoted to the use of inhaled pulmonary vasodilators (notably milrinone) as an adjunct to systemic therapy [3]. This review synthesizes and critiques the available evidence regarding anesthetic and perioperative strategies in PH, with a focus on the comparative role of inhaled versus intravenous milrinone, but also embedding that discussion in a broader management framework.

Classification and Etiology of Pulmonary Hypertension

PH is defined hemodynamically by a mean pulmonary arterial pressure ≥20 mmHg at rest, with a pulmonary vascular resistance exceeding 3 Wood units. The World Health Organization (WHO) has established a clinical classification system to categorize PH into five groups according to pathophysiological mechanisms, clinical presentation, and therapeutic implications [4]. These include pulmonary arterial hypertension (Group 1), PH due to left heart disease (Group 2), PH due to chronic lung disease or hypoxia (Group 3), chronic thromboembolic pulmonary hypertension (Group 4), and PH with multifactorial or unclear mechanisms (Group 5). A concise summary of these groups is presented in **Table 1**, which highlights their etiologies, hemodynamic features, and perioperative relevance.

Table 1

WHO Group	Etiology / Examples	Hemodynamic Characteristics	Clinical Relevance in Surgery
Group 1: Pulmonary Arterial Hypertension (PAH)	Idiopathic, heritable, drug/toxin-induced, connective tissue disease	mPAP ≥20 mmHg, PCWP ≤15 mmHg, PVR >3 WU	High perioperative risk: vasodilator therapy may be used pre/intraoperatively
Group 2: PH due to Left Heart Disease	LV systolic/diastolic dysfunction, valvular disease	Elevated PCWP, secondary PVR increase	Common in cardiac surgery; careful volume management critical
Group 3: PH due to Lung Disease / Hypoxia	COPD, interstitial lung disease, and sleep apnea	Hypoxia-induced PVR elevation	Ventilation optimization is crucial perioperatively
Group 4: Chronic Thromboembolic PH (CTEPH)	Pulmonary emboli → obstruction	mPAP ↑, PCWP normal	Thromboprophylaxis, surgical pulmonary endarterectomy may be indicated
Group 5: PH with Unclear / Multifactorial Mechanisms	Hematologic, metabolic, systemic disorders	Variable hemodynamics	Requires individualized management

Pathophysiological Challenges in Pulmonary Hypertension and Right Ventricular Failure

PH imposes a persistently elevated afterload on the right ventricle. Over time, chronic pressure overload leads to RV hypertrophy, decreased compliance, and eventual impairment of contractile reserve. In the context of surgical stress and CPB, acute rises in pulmonary pressures (due to hypoxia, acidosis, hypercarbia, inflammatory mediators, or microthrombosis) may precipitate catastrophic RV failure [5]. Because the RV is not well-suited to cope with sudden increases in afterload, small perturbations in hemodynamics may lead to a downward spiral of reduced forward flow, systemic hypotension, and worsening right-sided congestion [6].

A critical concept in perioperative PH management is the ventricular-arterial coupling of the right side. If RV contractility fails to adapt to sudden increases in pulmonary vascular resistance, the safety margin collapses. The anesthesiologist's goal is thus to maintain or optimize preload, minimize increases in pulmonary vascular tone, and support RV contractility while avoiding systemic hypotension (which can further compromise RV coronary perfusion) [7, 8]. McGlothlin, Ivascu, and Heerdt (2012) discuss this challenge in the context of anesthesia in PH, emphasizing that many of the triggers of elevated pulmonary pressures are modifiable (hypoxia, hypercapnia, acidosis, pain, high airway pressures) [9].

Furthermore, the intraoperative period presents multiple threats: (1) CPB may provoke inflammatory responses, endothelial injury, and pulmonary vasoconstriction; (2) ischemia-reperfusion injury to the pulmonary vascular bed; (3) hemodilution and hypothermia; (4) mechanical constraints from ventilation or surgical manipulation; (5) vasodilator-induced systemic hypotension. The confluence of these stresses places patients with preexisting PH at high risk for RV decompensation, difficulty separating from CPB, and poor postoperative outcomes [1]. In their review, Thunberg et al. argue that PH in cardiac surgery should not be viewed as a mere comorbidity but rather as a dynamic and modifiable risk factor demanding proactive management.

Given the high stakes, anesthetic care of patients with PH necessitates a multimodal approach: vigilant monitoring, careful fluid management, optimization of ventilation, and personalized pharmacologic support with pulmonary vasodilators and inotropes.

METHODS

Strategies for Intraoperative Monitoring and Hemodynamic Support Preinduction and Catheterization

One debated issue is whether to insert a pulmonary artery (PA) catheter before anesthetic induction in patients with severe PH or RV dysfunction. Hargrave (2017) argues against the routine preinduction placement of PA catheters, noting risks associated with catheter manipulation (arrhythmias, hemodynamic instability) and questioning whether the data justify those risks. He suggests that catheter placement be individualized and reserved for cases in which the data would change management. In contrast, supporters of early catheterization argue that real-time measurements of PA pressures, cardiac output, and wedge pressure allow more accurate titration of inotropes and vasodilators during induction when hemodynamics are most labile [10].

Moreover, Caddigan and Granlund (2021) provide a broad review of anesthesia for patients with PH or right heart failure, emphasizing that the anesthesiologist must anticipate rapid changes, maintain hemodynamic stability, and be prepared to act with vasodilators, inotropes, or mechanical support as needed. They advocate continuous hemodynamic monitoring (arterial line, central venous pressure, and often a PA catheter) but also caution that derived pulmonary artery pressures alone may mislead if pulmonary vascular resistance (PVR) calculations are not interpreted in context [11].

Beyond catheter-based monitoring, intraoperative transesophageal echocardiography (TEE) is often crucial. TEE allows dynamic assessment of RV size and function, leftward septal shift, tricuspid regurgitation, and volume status. Studies included TEE as a part of the perioperative pathway [12].

Hemodynamic Goals

The overarching hemodynamic goals in patients with PH are: (1) maintain mean arterial pressure (MAP) high enough to support

RV coronary perfusion (often at least 65 mmHg, but higher in compromised patients), (2) keep right atrial pressure / central venous pressure in a range sufficient for RV preload but not overloaded, (3) limit increases in PVR via control of ventilation and gas exchange, and (4) provide inotropic support if necessary to preserve RV output [13].

Intraoperative protocols often define "safe zones" for $PaCO_2$, PaO_2, pH, and ventilation parameters (e.g., limiting peak airway pressures, avoiding hyperinflation) to avoid exacerbating pulmonary vascular tone. Klick (in "Intraoperative Management of Pulmonary Hypertension") outlines that the anesthetic plan must avoid factors that acutely raise PVR (hypoxia, hypercapnia, acidosis, sympathetic stimulation) and should allow for prompt use of pulmonary vasodilator therapy when needed [14].

Pharmacologic Management: Inhaled vs Intravenous Milrinone Rationale for Milrinone in Pulmonary Hypertension

Milrinone is a phosphodiesterase-3 inhibitor that augments cyclic adenosine monophosphate (cAMP), producing positive inotropy and vasodilation in both the systemic and pulmonary circulations [15]. In the context of PH and RV dysfunction, milrinone's "inodilator" properties make it attractive: it can reduce pulmonary vascular resistance and support cardiac output. However, intravenous milrinone often induces systemic hypotension (via systemic vasodilation), which in turn may necessitate higher doses of vasopressors, thereby potentially worsening the vasoplegia burden [16].

To mitigate the risk of systemic hypotension, aerosolized or inhaled administration of milrinone (iMil) has gathered interest. The conceptual advantage is that inhaled milrinone selectively dilates pulmonary vasculature (where delivered) with limited systemic spillover, thereby reducing PVR without causing profound systemic hypotension. Bednarczyk et al. (2016) pose the notion of inhaled milrinone as a "silver bullet" but caution that it is rarely a standalone solution and must be integrated into a broader multimodal strategy. They emphasize the scarcity of large randomized controlled trials in this domain [17].

Bednarczyk, Strumpher, and Jacobsohn provide a critical appraisal of inhaled milrinone in high-risk cardiac surgical patients with PH. They observe that in patients with valvular lesions and elevated pulmonary pressures, PH prevalence may reach 15–40%, and that prolonged PH correlates with worsened postoperative outcomes (longer ventilation, ICU stay, mortality) [17]. A multicenter randomized controlled trial (Denault et al., cited within) investigated the prophylactic administration of inhaled milrinone before cardiopulmonary bypass (CPB) to facilitate separation from bypass. The study demonstrated that, although inhaled milrinone represents a promising strategy, it cannot be considered a "silver bullet" given the heterogeneity in dosing protocols, variability in timing of administration, and the current limitations of the evidence base [17, 18]. They advocate for its use as one element in a bundle of perioperative PH management.

Bednarczyk et al. further highlight some of the mechanistic benefits of iMil beyond vasodilation: reduced pulmonary endothelial injury, mitigated inflammation, and preserved endothelial function compared to intravenous administration in the context of CPB-associated injury [17]. However, they note that the magnitude of clinical benefits, especially in terms of major outcomes like mortality or need for prolonged support, remains uncertain. A more recent advance comes from the systematic review and meta-analysis by Kavanagh et al. (2025), comparing intravenous versus inhaled milrinone in adult patients with PH undergoing cardiac surgery. Their pooled analysis included approximately 400 patients over five prospective studies (four randomized controlled trials) [3].

Kavanagh et al. found no statistically significant difference in mean pulmonary artery pressure (MPAP) between inhaled and intravenous milrinone (mean difference –4.80 mmHg, 95% CI –10.57 to 0.98). Interestingly, inhaled milrinone was associated with a greater systemic vascular resistance index (SVRI; MD: 259.21) and a greater reduction in pulmonary capillary wedge pressure (–4.64 mmHg). There were no significant differences in mean arterial pressure (MAP), cardiac index, central venous pressure, or pulmonary vascular resistance. The authors concluded that while iMil has theoretical and observed physiological benefits (especially in preserving SVR and improving oxygenation), evidence for a major hemodynamic or clinical benefit is not yet robust, and that larger randomized trials are needed [3]. Kavanagh et al. also underscore the limitations of the current evidence: heterogeneity in dosing regimens (dose, timing, duration), variable endpoints, and moderate risk of bias in the included trials [19]. Thus, while iMil may offer some hemodynamic advantages, its superiority over ivMil remains unproven in many clinically meaningful outcomes.

In addition, studies offer support or contrasting results. For instance, the double-blind trial by Jorairahmadi et al. (2022) compared nebulized milrinone to intravenous milrinone in cardiac surgery patients with PH. They reported that the nebulized group had significantly better MAP and MAP/MPAP ratios, as well as shorter extubation time, ICU stay, and hospital stay. They conclude that nebulized milrinone may accelerate weaning from CPB while preserving systemic hemodynamics [20] (**Table 2**).

Other observational and perioperative analyses suggest that perioperative milrinone use (either systemic or inhaled) is associated with reductions in pulmonary pressures and a lower incidence of low cardiac output syndrome [21]. Meanwhile, Stamov et al. (2024) discuss the potential of inhaled milrinone in non-cardiac surgical settings with severe PH, noting its ability to reduce pulmonary arterial pressures with limited systemic effects. They caution that clinical evidence remains sparse and further trials are warranted [22]. Other comparative data (e.g. studies of inhaled iloprost, inhaled nitric oxide) highlight that the concept of selective pulmonary vasodilation is not novel; milrinone is part of a broader arsenal of aerosolized vasodilator strategies [23]. The success of pharmacologic therapy must always be tempered by vigilance for side effects (e.g., hypotension, ventilation–perfusion mismatch, rebound pulmonary hypertension) and careful titration of therapy. However, while inhaled agents minimize systemic spillover, their effect is localized to ventilated lung regions and may not reach poorly ventilated or poorly perfused lung

zones, which limits their uniformity of effect in diseased lungs [24].

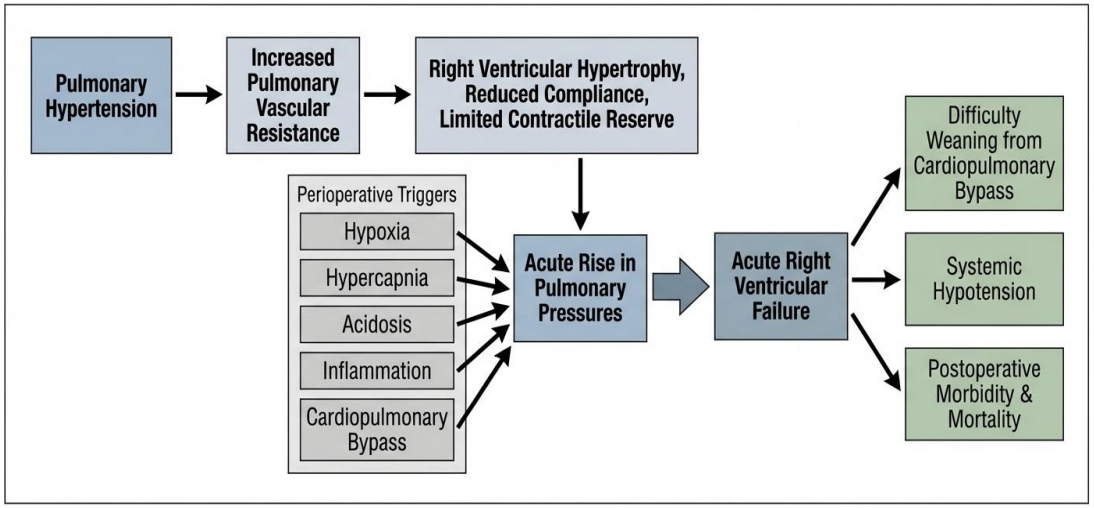

Figure 1. Pathophysiological cascade linking pulmonary hypertension to right ventricular failure and perioperative complications during cardiac surgery

Chronic elevation in pulmonary vascular resistance increases right ventricular afterload, leading to hypertrophy, reduced compliance, and limited contractile reserve. Perioperative triggers including hypoxia, hypercapnia, acidosis, inflammation, and cardiopulmonary bypass can precipitate acute rises in pulmonary pressures, culminating in right ventricular failure, difficulty separating from cardiopulmonary bypass, systemic hypotension, and adverse postoperative outcomes.

Table 2

Author / Year	Study Design	Patient Population	Intervention	Primary Outcomes	Key Findings
[17]	Review / Editorial	High-risk cardiac surgery patients with PH	Inhaled milrinone (iMil) vs standard therapy	Hemodynamic optimization	iMil can selectively reduce PVR, facilitate separation from CPB, but not a standalone therapy
[3]	Systematic review & meta-analysis	400+ adults with PH undergoing cardiac surgery	iMil vs intravenous milrinone (ivMil)	MPAP, PVR, MAP, ICU stay	iMil preserved SVR, reduced wedge pressure; no significant difference in MPAP; more data needed
[25]	Prospective RCT	Adult cardiac surgery with PH	Two ivMil regimens	Hemodynamics (MPAP, CI, SVR)	High-dose regimen improved pulmonary pressures but risked hypotension
[20]	Double-blind RCT	Cardiac surgery patients with PH	Nebulized iMil vs ivMil	MAP, extubation time, ICU stay	iMil group had better MAP, shorter ICU stay and extubation time

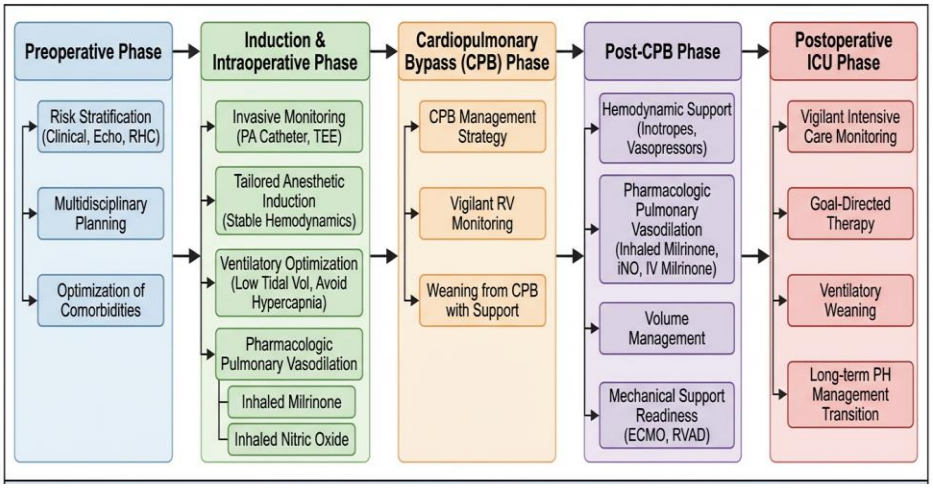

Figure 2. Integrated perioperative anesthetic management framework for patients with pulmonary hypertension undergoing cardiac surgery.

Effective management requires a multimodal strategy incorporating preoperative risk stratification, invasive and echocardiographic monitoring, tailored anesthetic induction, ventilatory optimization, pharmacologic pulmonary vasodilation (including inhaled and intravenous milrinone), hemodynamic support, and vigilant postoperative intensive care. Inhaled milrinone functions as an adjunct within this broader framework rather than as a standalone therapy.

Perioperative Anesthetic Management in Special Cases and Case Reports

While high-level randomized trials in PH remain limited, numerous reports and observational studies illustrate practical challenges and solutions in perioperative management for patients with PH in diverse surgical contexts (**Table 3**). In the field of congenital heart surgery, Quinonez et al. (2018) describe anesthetic management in tetralogy of Fallot with pulmonary atresia and major aortopulmonary collateral arteries. Here, balancing pulmonary and systemic flows is critical; pulmonary vasodilator therapy must be carefully managed to avoid pulmonary steal or systemic hypotension. The discussion shows that in children with complex physiology, the anesthesia team often must adjust the balance of pulmonary vasodilation to maintain optimal circulatory dynamics without destabilizing systemic pressures [26].

Stein et al. (2022) examine pediatric patients with pulmonary hypertension and report on "serious adverse events" associated with cardiac catheterization. They emphasize that PH patients (especially children) are at heightened risk of hemodynamic lability during anesthesia, and that centers specializing in PH should be involved in planning [27]. Madaan & Gupta (2022) discuss anesthetic management in a patient with a large atrial septal defect and severe pulmonary hypertension undergoing surgery. They emphasize tailored induction, maintenance of right heart preload, avoidance of high PVR triggers, and readiness for pulmonary vasodilators or extracorporeal support if needed [28]. Mimica et al. (2025) contribute a case report of regional anesthesia in a surgical patient with severe PH, demonstrating that under certain conditions, regional (rather than general) anesthesia may be feasible, though with careful hemodynamic support and backup plans. This underscores that an anesthetic strategy must be individualized [29].

Additionally, Noorrahman et al. (2024) present perioperative anesthetic management in a patient undergoing diaphragmatic hernia repair with coexisting atrial septal defect and pulmonary hypertension. Their report echoes the recurring principle: maintain systemic pressure, limit pulmonary vasoconstrictive stimuli, rationally use vasodilator/inotrope therapy, and optimize ventilation/oxygenation [30]. Other sources, such as Pratiwi & Miarta (2025), address congenital heart disease cases, in which pulmonary hypertension often coexists, and reinforce the same perioperative vigilance and strategy [31].

These case-based narratives complement more formal studies by illustrating real-world adaptation of pharmacologic and monitoring strategies to individual patient physiology and surgical context.

Table 3

Phase	Key Considerations	Strategies / Interventions
Preoperative	Assess the severity of PH, RV function, and comorbidities	Echocardiography, right heart catheterization (selective), optimization of medications, and patient education
Induction	Avoid hypotension, RV ischemia, and PVR spikes	Slow induction, opioid-sparing techniques, maintain oxygenation, avoid hypercapnia/acidosis
Intraoperative	Maintain RV preload, avoid high PVR, facilitate CPB separation	Ventilation: low tidal volumes, minimal PEEP; pulmonary vasodilators (iMil, nitric oxide); inotropes as needed
Post-CPB / Emergence	Support RV function, avoid rebound PH	Continue inhaled or IV vasodilators; vasopressors for systemic hypotension; careful fluid management
Postoperative ICU	Prevent RV decompensation, monitor complications	Continuous hemodynamic monitoring, early detection of arrhythmia or low output syndrome, and analgesia to minimize sympathetic stimulation

DISCUSSION

Integrative Considerations, Challenges, and Future Directions: Strengths, Limitations, and Gaps in Literature

The body of evidence surrounding inhaled versus intravenous milrinone in PH is promising but not definitive. The strengths include:

- The physiological rationale is sound: inhaled delivery offers localized pulmonary vasodilation while reducing systemic hypotension.
- The meta-analysis by Kavanagh et al. synthesizes multiple RCTs, lending greater power to detect differences in hemodynamics [3].
- Smaller trials report clinically meaningful advantages in extubation time and ICU stay [20].
- Mechanistic studies *suggest inhaled delivery might confer additional protection to pulmonary endothelium in the CPB context (less inflammation, less endothelial dysfunction) [17]*.

However, important limitations and challenges persist:

- Heterogeneity of protocols: There is wide variation in dosage (e.g. µg/kg/min equivalence), timing (pre-CPB, post-CPB, continuous), and duration of inhaled therapy.

- Endpoint variability: Some studies focus on surrogate hemodynamic outcomes (MPAP, PVR, SVR), whereas few assess hard endpoints such as mortality, length of stay, need for prolonged mechanical support, or long-term survival.
- Bias and trial quality: Many trials are small, single-center, unblinded, or at moderate risk of bias. The meta-analysis itself notes "some concern" in bias risk [3].
- Generalizability: Many patients in existing trials have valvular disease or elective surgery; it is unclear if benefits translate to emergency surgery or noncardiac cases.
- Ventilation heterogeneity: The inhaled agent's effectiveness depends on ventilation–perfusion matching; in diseased lungs, nonuniform delivery may limit efficacy.
- Cost, logistics, and equipment: Aerosolization systems, nebulizers, and consistency of delivery intraoperatively add complexity.
- Comparative benchmarks: Some trials compare inhaled milrinone to intravenous milrinone, but fewer compare it head-to-head with other pulmonary vasodilators (nitric oxide, prostanoids, etc.). Thus, the incremental benefit over other inhaled agents is less clearly defined.

Given these gaps, as Bednarczyk et al. caution, inhaled milrinone should not be viewed as a "silver bullet" but as one component of a comprehensive perioperative PH management strategy [17].

Practical Recommendations and a Perioperative Pathway Steppan et al. (2018) and others give a plausible perioperative pathway that might include the following considerations [12] [2, 32].

- Patients identified preoperatively with moderate to severe PH should undergo careful optimization (pulmonary vasodilators, diuresis, control of comorbid lung disease). Before induction, the anesthetic team should plan for continuous invasive monitoring (arterial line, central venous pressure, possible PA catheter or TEE) and ensure vasoactive/inotropic agents (e.g., milrinone, dobutamine, norepinephrine) are primed and available.
- Induction should proceed gradually, avoiding precipitous decreases in systemic vascular resistance (which would compromise RV coronary perfusion) or sudden increases in PVR. A balanced anesthetic technique (e.g., low-dose opioids, inhaled anesthetics, careful neuromuscular blockade) may be preferable. After induction and before CPB, administration of inhaled milrinone (if used) may help to "preemptively" reduce PVR and smooth the transition to bypass.
- During CPB, avoidance of hypoxia, hypercarbia, acidosis, hypothermia, and excessive fluid shifts is crucial. After cross-clamp release and re-establishment of native pulmonary circulation, the timing of inhaled milrinone (or systemic boluses) may be critical to assist weaning and protect the right heart. The team may also consider adjunctive inhaled vasodilators (e.g., nitric oxide, prostacyclins) as needed.
- When weaning from CPB, continuous hemodynamic monitoring allows titration of inotropes, vasopressors, and pulmonary vasodilators in response to changes in PA pressures, cardiac output, and filling pressures. If the patient develops RV failure (rising CVP, low output, hypotension), escalation to mechanical support (right-sided assist devices or extracorporeal membrane oxygenation) must remain a fallback.
- Postoperatively, continued use of inhaled or systemic pulmonary vasodilators may help during the early recovery phase when the pulmonary vasculature remains reactive. Monitoring should continue into ICU care, with attention to volume balance, avoidance of hypoxia/acidosis, analgesia to blunt sympathetic surges, and weaning of vasopressors/inotropes as tolerated. The comparison of common Pulmonary Vasodilators is discussed in Table 4 below.

Table 4

Drug	Route	Mechanism	Pros	Cons / Cautions
Milrinone	IV / Inhaled	PDE-3 inhibitor → ↑cAMP → pulmonary vasodilation, positive inotropy	iMil: selective pulmonary effect, preserves SVR; facilitates CPB separation	IV: systemic hypotension; iMil: requires nebulizer setup, limited in poorly ventilated lung areas
Nitric Oxide	Inhaled	Activates guanylyl cyclase → cGMP → vasodilation	Selective pulmonary vasodilation, rapid onset/offset	Expensive, rebound PH if withdrawn abruptly
Prostacyclins (Epoprostenol, Iloprost)	IV / Inhaled	cAMP-mediated vasodilation, platelet inhibition	Potent vasodilators	Systemic hypotension, complex administration, infection risk (IV)

Future Directions

Given the promising but limited evidence base, future research should aim to:

1. Conduct larger, multicenter, double-blind randomized trials comparing inhaled and intravenous milrinone (with standardized dosing, timing, and delivery methods), with hard clinical endpoints such as mortality, use of mechanical circulatory support, length of ICU and hospital stay, and long-term RV function.
2. Compare inhaled milrinone directly against other inhaled vasodilators (e.g., nitric oxide, prostanoids) or in combination therapies to define optimal regimens.
3. Explore pharmacokinetic and pharmacodynamic modeling of inhaled milrinone delivery, titration strategies, and ventilation matching in diseased lungs.

4. Investigate the role of inhaled milrinone in noncardiac surgeries or in emergency settings (where much of the current data is lacking).
5. Incorporate imaging and biomarkers (e.g., echocardiographic indices of RV function, biomarkers of endothelial dysfunction) to tailor therapy and predict responders.
6. Develop perioperative management pathways (or checklists) incorporating inhaled milrinone, monitoring strategies, and decision algorithms, and validate them in prospective cohorts.

Conclusions

Pulmonary hypertension in the perioperative and cardiac surgical setting represents a formidable clinical challenge due to its propensity to precipitate right ventricular failure and complicate hemodynamic management. Among the pharmacologic strategies available, inhaled milrinone holds promise for selectively lowering pulmonary vascular resistance while mitigating systemic hypotension, an advantage over intravenous administration. The literature suggests that inhaled milrinone may offer hemodynamic benefits, though the evidence is not yet definitive for superiority in major clinical outcomes. In practice, inhaled milrinone is best integrated into a broader perioperative PH management strategy that emphasizes optimized monitoring, ventilatory strategies to limit increases in pulmonary vascular tone, judicious fluid management, and readiness for mechanical support. Robust randomized trials and mechanistic studies are required to establish optimal dosing regimens, identify responder phenotypes, and define inhaled milrinone's role relative to other pulmonary vasodilators. Until then, clinicians must rely on physiological reasoning, close hemodynamic monitoring, and individualized adaptation of available evidence to safely manage surgical patients with pulmonary hypertension.

List of abbreviations

Table 5

Abbreviation	Meaning	Abbreviation	Meaning
PH	Pulmonary hypertension	**CI**	Confidence interval
RV	Right ventricle or right ventricular	**ICU**	Intensive care unit
CPB	Cardiopulmonary bypass	**RCT**	Randomized controlled trial
WHO	World Health Organization	**PDE-3**	Phosphodiesterase-3
mPAP	Mean pulmonary arterial pressure	**cAMP**	Cyclic adenosine monophosphate
PCWP	Pulmonary capillary wedge pressure	**cGMP**	Cyclic guanosine monophosphate
PVR	Pulmonary vascular resistance	**LV**	Left ventricle
COPD	Chronic obstructive pulmonary disease	**PA**	Pulmonary artery
CTEPH	Chronic thromboembolic pulmonary hypertension	**TEE**	Transesophageal echocardiography
iMil	Inhaled milrinone	**SVRI**	Systemic vascular resistance index
ivMil	Intravenous milrinone	**MAP**	Mean arterial pressure
MPAP	Mean pulmonary arterial pressure		

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Table Legends

Table 1: Classification and Etiology of Pulmonary Hypertension (WHO Groups).
Table 2: Summary of Key Studies on Inhaled vs. Intravenous Milrinone in Cardiac Surgery with PH.
Table 3: Perioperative Anesthetic Considerations and Strategies in Pulmonary Hypertension
Table 4: Mechanisms and Comparison of Pulmonary Vasodilators.
Table 5: Abbreviations used in this manuscript.