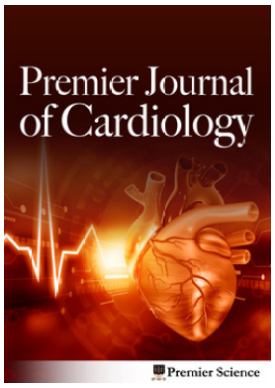

Unlocking the Potential of Prophylactic Milrinone in Off-Pump Coronary Artery Bypass Grafting: A Narrative Review

Manoranjan Padhi, Dharmajivan Samantaray, Manmaya Padhy and Sweta Mohanty

ABSTRACT

Off-pump coronary artery bypass grafting (OPCAB) is a prevalent cardiac surgical technique designed to avoid the complications of cardiopulmonary bypass (CPB). Despite its benefits, OPCAB poses significant hemodynamic challenges, such as reduced cardiac output, increased atrial pressures, and mitral regurgitation due to mechanical shifts during surgery. Milrinone, a selective phosphodiesterase III inhibitor, has been proposed as a valuable adjunct to address these challenges. The present study provides a broad overview of the efficacy of prophylactic Milrinone administration in patients undergoing OPCAB procedures.

Keywords: Prophylactic milrinone, Off-pump coronary artery bypass grafting, Hemodynamic challenges, Cardiac surgery, Inotropic agent

Department of Cardiothoracic and Vascular Anaesthesia, Care Hospital, Bhubaneswar, Odisha, India

Correspondence to: Sweta Mohanty, sweta620@gmail.com, Dharmajivan Samantaray, drdharmajivan@gmail.com

Additional material is published online only. To view please visit the journal online.

Cite this as: Padhi M, Samantaray D, Padhy M and Mohanty S. Unlocking the Potential of Prophylactic Milrinone in Off-Pump Coronary Artery Bypass Grafting: A Narrative Review. Premier Journal of Cardiology 2025;2:100002

DOI: https://doi.org/10.70389/PJC.100002

Received: 4 December 2024
Revised: 20 January 2025
Accepted: 20 January 2025
Published: 7 February 2025

Ethical approval: N/a
Consent: N/a
Funding: No industry funding
Conflicts of interest: N/a
Author contribution: Manoranjan Padhi, Dharmajivan Samantaray, Manmaya Padhy and Sweta Mohanty – Conceptualization, Writing – original draft, review and editing
Guarantor: Manoranjan Padhi
Provenance and peer-review: Commissioned and externally peer-reviewed
Data availability statement: N/a

Introduction

Coronary artery bypass grafting is the most commonly performed cardiac surgical procedure globally, primarily aimed at improving outcomes for patients with coronary artery disease.[1] One approach developed to minimize the effects associated with cardiopulmonary bypass (CPB) is the Off-pump Coronary artery bypass technique (OPCAB), which can be performed without cardiopulmonary bypass and has been identified for the following merits. The postoperative inflammation is relatively minimal; early graft patency and postoperative assessment are considerably favorable.[2] However, in OPCAB, there are significant changes in decrements of the CO, alterations in the geometry of the atrium, and pressure overloading, which may exacerbate mitral regurgitation due to mechanical shifts of the heart during surgery.[3] These issues are more pronounced in patients with poor left ventricular function or those undergoing posterior coronary circulation procedures that require substantial cardiac motion.[4]

Milrinone is a potent inotropic agent that has been extensively studied in the context of cardiac surgery. It has been shown to improve hemodynamic parameters, reduce the incidence of low cardiac output syndrome, and potentially improve clinical outcomes in patients undergoing cardiac surgeries.[5] This narrative review aims to synthesize the current evidence regarding the efficacy and safety of Milrinone in patients undergoing off-pump coronary artery bypass grafting, emphasizing its pharmacology, pharmacodynamics, properties, and clinical outcomes.

Pharmacology of Milrinone (Figure 1)

Milrinone is a selective phosphodiesterase III inhibitor that exerts its effects through a dual mechanism of action, combining positive inotropic effects with vasodilation.[5] This unique pharmacological profile is particularly useful in managing hemodynamic disturbances during off-pump coronary artery bypass procedures. By inhibiting PDE-3, Milrinone prevents the breakdown of cyclic adenosine monophosphate, a crucial intracellular signaling molecule in cardiac and vascular smooth muscle cells.[6] Increased cAMP levels enhance calcium handling in cardiac myocytes and facilitate smooth muscle relaxation, improving cardiac contractility and reducing vascular resistance.[5]

The elevated cAMP activates protein kinase A within cardiac myocytes, which phosphorylates critical proteins involved in calcium regulation. This encompasses the L-type calcium channel, which enhances activity and increases calcium influx during the action potential.[7] Furthermore, phosphokinase A (PKA) phosphorylates phospholamban, a regulatory protein that inhibits the sarcoplasmic reticulum calcium ATPase, reducing its inhibitory effect and accelerating calcium reuptake into the sarcoplasmic reticulum during diastole.[8] This increases calcium storage for subsequent cardiac contractions, resulting in stronger and more efficient myocardial contractions, even in patients with compromised myocardial function.[9]

Milrinone improves diastolic relaxation by influencing calcium reuptake, a process known as positive lusitropy. By facilitating the rapid sequestration of calcium into the sarcoplasmic reticulum, Milrinone reduces cytosolic calcium concentrations during diastole, allowing the myocardium to relax more effectively.[6]

This effect is crucial for patients with diastolic dysfunction or conditions such as left ventricular hypertrophy, where impaired relaxation can compromise ventricular filling.

Milrinone's effects extend beyond the myocardium to the vascular system. In vascular smooth muscle, elevated levels of cAMP enhance uptake by the sarcoplasmic reticulum, thereby reducing intracellular calcium concentrations.[10] This leads to vasodilation of both the systemic and pulmonary vascular beds.[6,11] These effects decrease afterload, which is advantageous to both the right and left ventricles by decreasing the efforts required for myocardial contraction.

The pharmacokinetic properties of Milrinone further support its clinical utility in perioperative settings. It has a short half-life of 48–56 minutes, facilitating rapid titration of its effects.[9] Milrinone is typically administered as a loading dose of 50 μg/kg over 10 minutes, followed by a continuous infusion of 0.375–0.75 μg/kg/min.[5] The principal metabolic pathways for Milrinone involve oxidation and conjugation, with glucuronidation being the primary biotransformation pathway. The major route of elimination is excretion into urine.[12] This dosing regimen allows clinicians to tailor

administration based on the patient's hemodynamic requirements, ensuring a balance between therapeutic benefits and potential adverse impacts (Figure 2).

Potential Risks

While Milrinone has shown beneficial impacts, it is not devoid of potential risks. The most typical adverse effects are hypotension, abnormal heart rhythms, and low platelet count.

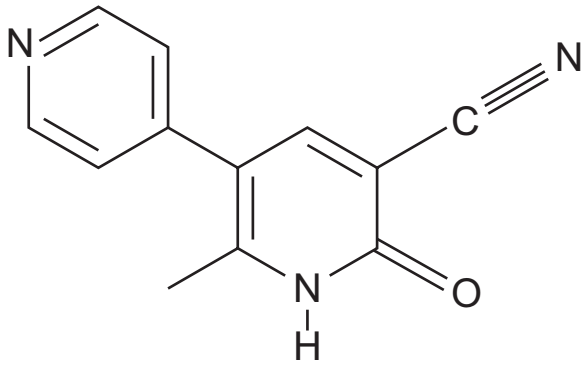

Fig 1 | Structure of Milrinone. It is a member of the class of bipyridines 2-pyridone, which is substituted at positions 3, 5, and 6 by cyano, pyrid-4-yl, and methyl groups, respectively

Hypotension

Milrinone, an agent known to relax the smooth muscles of blood vessels, may induce a significant decrease in systemic blood pressure, particularly when administered intravenously in loading dose or in patients sensitive to changes in their vascular resistance. To reduce this risk, the rate of infusion should be regulated conservatively and closely observed.[13]

Arrythmias

The drug can also lead to various cardiac arrhythmias like ventricular tachycardia, atrial fibrillation, and supraventricular tachycardia because it overloads cardiac myocytes with intracellular calcium.[14,15] Clinicians should closely monitor cardiac rhythm and be ready to intervene promptly.

Thrombocytopenia

Prolonged exposure to Milrinone causes plasma concentrations that interfere with platelet aggregation and might, therefore, be associated with an increased risk of

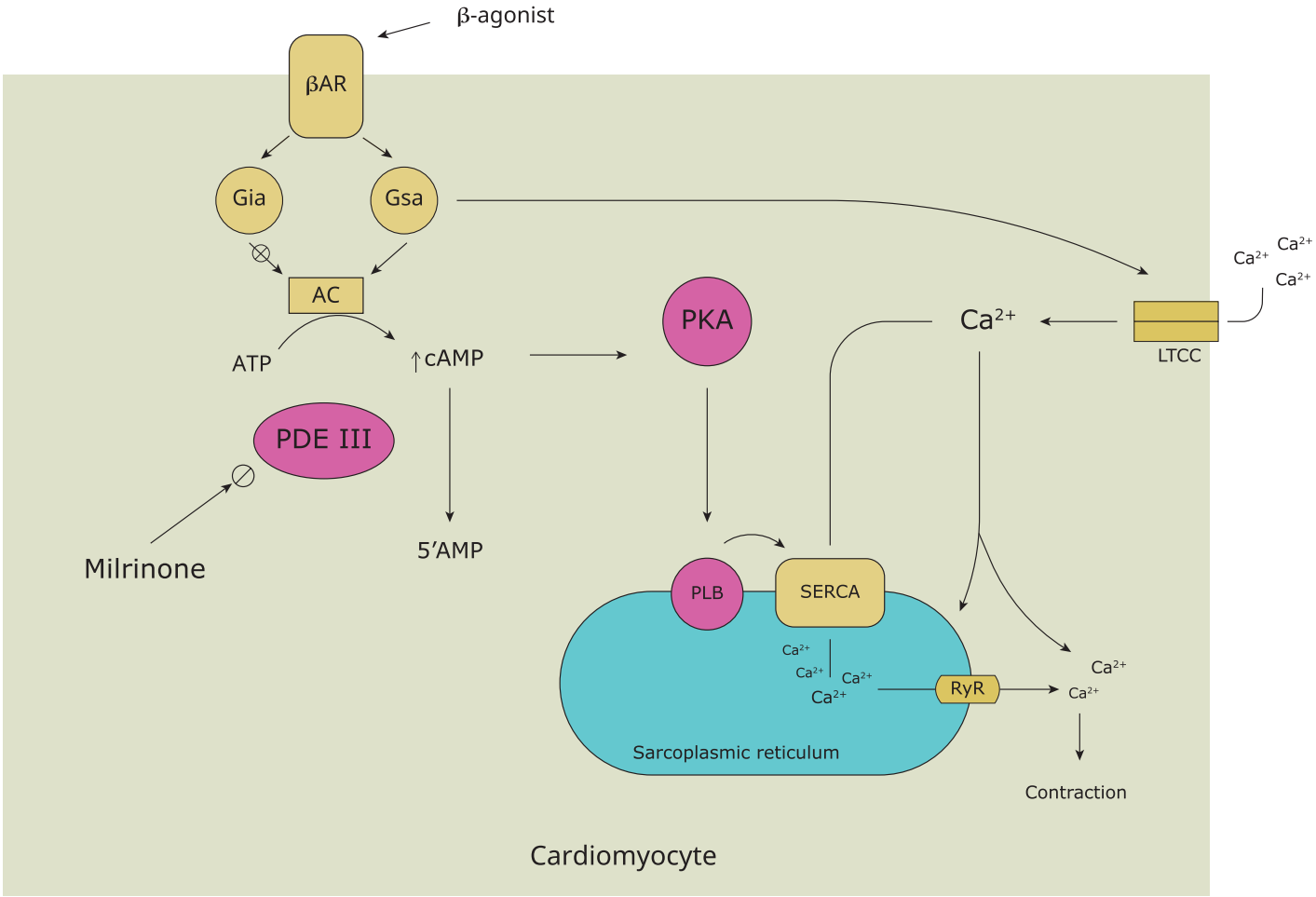

Fig 2 | Milrinone inhibits phosphodiesterase III enzyme (PDE-III). This increases cyclic adenosine monophosphate (cAMP), activating phosphokinase A (PKA). PKA promotes the influx of calcium ions through L-type calcium channels (LTCC) and ryanodine receptors (RyR) into the cytosol. ATP: adenosine triphosphate; PLB: phospholamban; PDE: phosphodiesterase; Gαi: G inhibitory alpha protein; Gαs: G stimulatory alpha protein; SERCA: sarcoplasmic reticulum calcium ATPase

DOI: https://doi.org/10.70389/PJC.100002 | Premier Journal of Cardiology 2025;2:100002

bleeding in surgical patients. The reason is that increased intracellular levels of cyclic adenosine monophosphate also inhibit adenosine diphosphate (ADP) and arachidonic acid (AA)-induced platelet aggregation.[16]

Haemodynamics in Off-Pump CABG

The degree of heart dislocation during off-pump coronary artery bypass grafting can significantly impact global cardiac output. The anterior and lateral ventricular walls exhibit greater displacement during systole and diastole compared to the septal and posteroinferior walls, which play a significant role in stroke volume. Surgical access to the left anterior descending artery is relatively straightforward, but operations on the posterior or lateral walls require displacing the heart from its pericardial cradle.[17] This cardiac displacement leads to a substantial increase in atrial pressures and a marked decrease in cardiac output.[18] During OPCAB, the heart is tilted vertically, with the apex at the highest point, causing the atria to be situated below the ventricles. This leads to higher filling pressures in the right and left atria than ventricular end-diastolic pressures, requiring higher-than-normal levels to sustain ventricular filling. Atrial size may increase by up to 50%, exceeding ventricular size.[19] Furthermore, diastolic dysfunction frequently occurs, characterized by the impaired ability of ventricles to relax and fill with blood during the diastolic phase of the cardiac cycle. This can lead to higher filling pressures and reduced cardiac output, further exacerbating the hemodynamic disturbances associated with off-pump CABG procedures.[20]

The stabilizer device immobilizes the anastomosis site, restricts local ventricular motion, and decreases dimensions. The location of the stabilizer, combined with the predominant contribution of the septal and posteroinferior walls to stroke volume, means that compression on the anterior and lateral walls has more serious hemodynamic consequences than on the posterior wall.[21]

Significant disturbances arise during lateral wall exposure for circumflex artery anastomosis, as the heart is lifted more extensively than in left anterior descending artery surgery. The vertical heart position also induces distortions in the mitral and tricuspid annuli, leading to increased mitral regurgitation.[3]

Milrinone Use During Off-Pump CABG

The challenges associated with off-pump CABG, such as impaired cardiac output, increased atrial pressures, and mitral regurgitation, have led to the use of Milrinone in this setting.

Jebeli et al. studied Milrinone in a randomized clinical trial for patients with myocardial dysfunction scheduled for CABG. Milrinone treatment was associated with better PAT results, increased LVEF, reduced serum creatine kinase concentration, and a lower incidence of atrial/ventricular arrhythmias compared to the placebo group.[16] Similar findings were observed in patients undergoing off-pump CABG by Hadadzadeh et al. comparing the use of intravenous Milrinone with placebo, showing that the patients receiving Milrinone had higher left ventricular ejection fraction, reduced serum levels of serum creatinine phosphokinase, and lower incidence of arrhythmia.[22] Omai et al. demonstrated improved cardiac index and lower mean pulmonary artery pressure in patients undergoing CABG with Grade 1 and 2 Mitral regurgitation.[3]

Milrinone has favorable impacts on patients with right ventricular dysfunction. In the study conducted by Jo et al. comparing the effects of Milrinone on right ventricular function, it was found to improve right ventricular ejection fraction significantly compared to the placebo.[23] Similar findings were corroborated by another study in patients on beta blockers undergoing CABG. Milrinone reduced the need for dopamine in these patients during posterior vessel grafting.[24]

Beyond its positive impact on cardiac contractility and relaxation, Milrinone directly elevated blood flow through the grafted mammary arteries following coronary artery bypass surgery. Lobato et al.[25] showed the differences in graft flow between Milrinone and epinephrine, with Milrinone yielding better graft patency and flow post-CPB.[25]

Milrinone is usually administered at a 50 μg/kg bolus over 10 minutes, followed by a continuous infusion of 0.375–0.75 μg/kg/min for an immediate hemodynamic response.[26,27] However, a slow infusion protocol without bolus administration is superior regarding decreased incidence of hypotension.[28] Kwak et al. compared the effects of continuous Milrinone infusion at a rate of 0.5 μg/kg/min in a group of 29 patients with a group of 33 patients receiving normal saline infusion during off-pump CABG. Hemodynamic variables were recorded before, during, and after applying the tissue stabilizer. Continuous invasive blood pressure and ECG monitoring were done to detect hypotension and arrhythmia. Continuous cardiac output and mixed venous oxygen saturation were monitored with a thermodilution pulmonary artery catheter. The mean arterial pressure was maintained above 60 mm Hg with intravenous crystalloids of 1 – 1.5 l, norepinephrine infusion at 0.03 – 0.05 μg/kg/min, and head-down position during heart displacement. The infusion of Milrinone was associated with only a minor decrease in cardiac output.[29]

Advantages Over Other Inotropes

Compared to other inotropic agents like dobutamine or epinephrine, Milrinone offers several advantages in the perioperative setting. Milrinone is not dependent on beta-adrenergic receptor stimulation, which can be impaired in the setting of heart failure or patients receiving concomitant beta-blocker therapy.[30] Furthermore, Milrinone does not increase myocardial oxygen demand, an important consideration in the vulnerable post-cardiopulmonary bypass period.[31]

The vasodilatory effects of Milrinone can reduce afterload and preload, thereby improving cardiac output without significantly increasing myocardial oxygen consumption. Conversely, traditional catecholamine inotropes like dobutamine and epinephrine increase

Table 1 | Comparative Analysis of Inotropes

Parameter	Milrinone	Dobutamine	Levosimendan	Epinephrine
Mechanism	PDE III inhibitor	β-adrenergic agonist	Calcium sensitizer	α and β-adrenergic agonist
Effect on HR	Minimal	Increases	Minimal	Increases
Vasodilation	Moderate	Mild	Strong	Minimal
Oxygen Demand	No significant increase	Increases	No significant increase	Increases
Half-life	0.5–1 hour	Short	Long (~80 hours)	Short
Hypotension Risk	Moderate	Mild	High	Low
Arrhythmia Risk	Moderate	Moderate	Low	High
Beta-blocker Interaction	None	Reduced efficacy	None	Reduced efficacy

heart rate and myocardial oxygen demand, potentially exacerbating ischemia in the postoperative setting.[27]

Unlike levosimendan, it causes less reduction in systemic vascular resistance and profound hypotension.[32] It possesses a long half-life, whereas Milrinone has a relatively short half-life of 0.5–1 hour, facilitating easier dose titration and more rapid discontinuation if adverse effects occur.[33]

Comparative Analysis of Inotropes

The comparative analysis of inotropes summarizes in Table 1.

Discussion

The use of Milrinone in patients undergoing off-pump coronary artery bypass grafting has been extensively studied and has demonstrated several benefits. Milrinone can effectively alleviate the hemodynamic challenges associated with CABG, such as impaired cardiac output, elevated atrial pressures, and increased mitral regurgitation[27,34] in both on-pump and off-pump situations.

Through its positive inotropic and vasodilatory effects, Milrinone can sustain cardiac output and improve right ventricular function during surgical manipulation and displacement of the heart.

However, some caution is necessary when administering Milrinone, as the loading dose should be carefully titrated to avoid potential adverse impacts such as hypotension and arrhythmias.[35] Wesley et al. showed that it affected platelet activation at a plasma concentration of 300 ng/ml.

Despite promising results, there are certain limitations to validate and optimize the use of prophylactic Milrinone in off-pump CABG. There is a scarcity of well-designed, multicenter, randomized controlled trials that address the research gaps. Studies that focus on diverse patient populations, including high-risk groups with comorbidities, may provide further insights into the role of Milrinone in improving postoperative outcomes. Investigations into the impact of Milrinone on long-term survival rates, cardiac function, and quality of life post off-pump CABG are also limited.

Artificial intelligence (AI) can revolutionize the administration of Milrinone in off-pump CABG. AI models can analyze continuous hemodynamic parameters (e.g., cardiac output, blood pressure, and heart rate) and predict patient-specific responses to Milrinone. Machine learning algorithms can predict individual patients' responses to Milrinone doses based on cardiac function, comorbidities, and intraoperative conditions.

AI-driven systems can continuously assess the hemodynamic status and adjust Milrinone infusion rates in real time. AI can consolidate data from electronic health records, intraoperative monitors, and laboratory results to comprehensively view patient status.

Artificial intelligence has the potential to revolutionize the administration of Milrinone in off-pump CABG. AI models could analyze continuous hemodynamic data and predict individualized patient responses to Milrinone.[36] Machine learning algorithms may predict patient responses to different Milrinone doses based on factors like cardiac function, comorbidities, and intraoperative conditions.[37] AI-driven systems could continuously monitor hemodynamic status and adjust Milrinone infusion rates in real-time. AI could consolidate data from electronic health records, intraoperative monitors, and laboratory results to provide a comprehensive assessment of patient status.[37]

Conclusion

In summary, the use of Milrinone in patients undergoing off-pump CABG has shown promising results in improving cardiac performance, reducing the need for additional inotropic support, and mitigating the hemodynamic disturbances associated with surgical manipulation of the heart. The current evidence supports the use of Milrinone as a valuable adjunct in managing patients undergoing off-pump coronary artery bypass grafting procedures.[27,31,33,38]

References

1 Kusu-Orkar T, Kermali M, Oguamanam N, Bithas C, Harky A. Coronary artery bypass grafting: Factors affecting outcomes. J Cardiac Surg. 2020;35(12):3503. https://doi.org/10.1111/jocs.15013

2 Rocha B, Amador R, Maltes S, Cunha G, Mateus C, Aguiar C, et al. CAD in kidney transplant recipients: A real-world assessment pre-ISCHEMIA-CKD. Euro Heart J. 2022;43:2619. https://doi.org/10.1093/eurheartj/ehac544.2619

3 Omae T, Kakihana Y, Mastunaga A, Tsuneyoshi I, Kawasaki K, Kanmura Y, et al. Hemodynamic changes during off-pump coronary artery bypass anastomosis in patients with coexisting mitral regurgitation: Improvement with milrinone. Anesth Analg. 2005;101:2–8. https://doi.org/10.1213/01.ane.0000155262.37491.6a

4 Torracca L, Schreuder JJ, Quarti A, Ismeno G, Franzè V, Alfieri O. Acute effects of beating heart coronary surgery on left ventricular performance. Ann Thorac Surg. 2002;74(4):S1348–52. https://doi.org/10.1016/s0003- 4975(02)03973-5

5 Levy JH, Bailey JM, Deeb GM. Intravenous milrinone in cardiac surgery. Ann Thoracic Surg. 2002;73(1):325. https://doi.org/10.1016/s0003-4975(01)02719-9

6 Levy JH, Ramsay JG, Bailey JM. Pharmacokinetics and pharmacodynamics of phosphodiesterase-III inhibitors. J Cardiothoracic Anes. 1990;4:7–11. https://doi.org/10.1016/0888-6296(90)90226-6

7 Shipley JB, Tolman D, Hastillo A, Hess ML. Milrinone: Basic and clinical pharmacology and acute and chronic management. Am J Med Sci. 1996;311:286–91. https://doi.org/10.1016/s0002-9629(15)41723-9

8 Yano M, Kohno M, Ohkusa T, Mochizuki M, Yamada J, Kohno M, et al. Effect of milrinone on left ventricular relaxation and Ca^{2+} uptake function of cardiac sarcoplasmic reticulum. Am J Physiol Heart Circ Physiol. 2000;279:H1898–905. https://doi.org/10.1152/ajpheart.2000.279.4.h1898

9 Young RA, Ward AC. Milrinone. A preliminary review of its pharmacological properties and therapeutic use. Drugs. 1988;36:158–92. https://doi.org/10.2165/00003495-198836020-00003

10 Colucci WS. Myocardial and vascular actions of milrinone. Eur Heart J. 1989:10(Suppl C):32–8. https://doi.org/10.1093/eurheartj/10.suppl_c.32

11 Tejerina T, Sesin J, Delgado C, Tamargo J. Effect of milrinone on contractility and 45Ca movements in the isolated rabbit aorta. Eur J Pharmacol. 1988;148:239–46. https://doi.org/10.1016/0014-2999(88)90569-9

12 Rocci ML, Wilson H. The pharmacokinetics and pharmacodynamics of newer inotropic agents. Clin Pharmacokinet. 1987;13:91–109. https://doi.org/10.2165/00003088-198713020-00002

13 Chong L, Satya K, Kim B, Berkowitz R. Milrinone dosing and a culture of caution in clinical practice. Cardiol Rev. 2018;26(1):35–42. https://doi.org/10.1097/crd.0000000000000165

14 Fleming GA, Murray KT, Yu C, Byrne JG, Greelish JP, Petracek MR, et al. Milrinone use is associated with postoperative atrial fibrillation after cardiac surgery. Circulation. 2008;118(16):1619–25. https://doi.org/10.1161/circulationaha.108.790162

15 Holmes JR, Kubo SH, Cody R, Kligfield P. Milrinone in congestive heart failure: Observations on ambulatory ventricular arrhythmias. Am Heart J. 1985;110(4):800–6. https://doi.org/10.1016/0002-8703(85)90460-0

16 Jebeli M, Ghazinoor M, Mandegar MH, Rasouli MR, Eghtesadi-Araghi P, Goodarzynejad H, et al. Effect of milrinone on short-term outcome of patients with myocardial dysfunction undergoing coronary artery bypass graft: A randomized controlled trial. Cardiol J. 2010;17(1):73–8. Available from: http://europepmc.org/abstract/MED/20104460

17 Sabik JF. Off-pump coronary revascularization: Operative technique. Cardiac Surg. 2006;11:90–104. https://doi.org/10.1053/j.optechstcvs.2006.06.002

18 Chassot P, der Linden PV, Zaugg M, Mueller XM, Spahn DR. Off-pump coronary artery bypass surgery: Physiology and anaesthetic management. Br J Anaesth. 2004;92(3):400–13. https://doi.org/10.1093/bja/aeh064

19 George SJ, Al-Ruzzeh S, Amrani M. Mitral annulus distortion during beating heart surgery: A potential cause for hemodynamic disturbance—A three-dimensional echocardiography reconstruction study. Ann Thorac Surg. 2002;73(5):1424–30. https://doi.org/10.1016/s0003-4975(02)03406-9

20 Biswas SS. Changes in systolic and diastolic function during multivessel off-pump coronary bypass grafting. Eur J Cardiothorac Surg. 2001;20(5):913–7. https://doi.org/10.1016/s1010-7940(01)00932-0

21 Verma S, Fedak PWM, Weisel RD, Szmitko PE, Badiwala MV, Bonneau D, et al. Off-Pump Coronary Artery Bypass Surgery. Lippincott Williams & Wilkins. 2014. https://doi.org/10.1161/01.cir.0000120292.65143.f5

22 Hadadzadeh M, Hosseini SH, Mostafavi-Pour-Manshadi SMY, Naderi N, Meybodi ME. Effect of milrinone on short term outcome of patients with myocardial dysfunction undergoing off-pump coronary artery bypass graft: A randomized clinical trial. Acta Med Iran. 2013;51(10):681–6.

23 Jo HR, Lee WK, Kim YH, Min JH, Chae YK, Choi IG, et al. The effect of milrinone infusion on right ventricular function during coronary anastomosis and early outcomes in patients undergoing off-pump coronary artery bypass surgery. Korean J Anesthesiol. 2010;59(2):92–8. https://doi.org/10.4097/kjae.2010.59.2.92

24 Kim J, Ham BM, Kim YL, Bahk J-H, Ryu H-G, Jeon Y-S, et al., Prophylactic milrinone during OPCAB of posterior vessels: Implication in angina patients taking β-blockers. Eur J Cardiothorac Surg. 2003;24(5):770–6. https://doi.org/10.1016/s1010-7940(03)00393-2

25 Lobato EB, Urdaneta F, Martin TD, Gravenstein N. Effects of milrinone versus epinephrine on grafted internal mammary artery flow after cardiopulmonary bypass. J Cardiothorac Vasc Anesth. 2000;14(1):9–11. https://doi.org/10.1016/s1053-0770(00)90047-8

26 Feneck RO. Intravenous milrinone following cardiac surgery: II. Influence of baseline hemodynamics and patient factors on therapeutic response. J Cardiothorac Vasc Anesth. 1992;6(5):563–7. https://doi.org/10.1016/1053-0770(92)90098-r

27 Kikura M, Sato S. The efficacy of preemptive milrinone or amrinone therapy in patients undergoing coronary artery bypass grafting. Anesth Analg. 2002;94(1):22–30. https://doi.org/10.1097/00000539-200201000-00005

28 Baruch L, Patacsil P, Hameed A, Piña IL, Loh E. Pharmacodynamic effects of milrinone with and without a bolus loading infusion. Am Heart J. 2001;141(2):266–73. https://doi.org/10.1067/mhj.2001.111404

29 Kwak YL, Oh YJ, Shinn HK, Yoo K, Kim S, Hong Y. Haemodynamic effects of a milrinone infusion without a bolus in patients undergoing off-pump coronary artery bypass graft surgery. Anaesthesia. 2004;59(4):324–31. https://doi.org/10.1111/j.1365-2044.2004.03659.x

30 Francis GS, Bartos JA, Adatya S. Inotropes. J Am Coll Cardiol. 2014;63(20):2069–78. https://doi.org/10.1016/j.jacc.2014.01.016

31 Wright EM, Sherry KM. Clinical and haemodynamic effects of milrinone in the treatment of low cardiac output after cardiac surgery. Br J Anaesth. 1991;67(5):585–90. https://doi.org/10.1093/bja/67.5.585

32 Vyas CK, Kumar R, Sharma N, Verma I, Saiyed A. A comparative study of hemodynamic effects of levosimendan and milrinone in patients undergoing off-pump coronary artery bypass grafting. Acad Anesthesiol Int. 2020;5(1):131–6.

33 Das P, Skoyles J, Sherry KM, Peacock JE, Fox P, Woolfrey SG. Disposition of milrinone in patients after cardiac surgery. Br J Anaesth. 1994;72(4):426–9. https://doi.org/10.1093/bja/72.4.426

34 Lobato EB, FloreteOG, Bingham H. A single dose of milrinone facilitates separation from cardiopulmonary bypass in patients with pre-existing left ventricular dysfunction. Br J Anaesth. 1998;81(5):782–4. https://doi.org/10.1093/bja/81.5.782

35 Hilleman DE, Forbes WP. Role of milrinone in the management of congestive heart failure. DICP. 1989;23(5):357–62. https://doi.org/10.1177/106002808902300501

36 Gaizo JD, Sherard C, Shorbaji K, Welch B, Mathi R, Kilic A. Prediction of coronary artery bypass graft outcomes using a single surgical note: An artificial intelligence-based prediction model study. PLoS One. 2024;19(4):e0300796. https://doi.org/10.1371/journal.pone.0300796

37 Vlaar APJ, Myatra SN, Jung C. Artificial intelligence to enhance hemodynamic management in the ICU. Intensive Care Med. 2024. https://doi.org/10.1007/s00134-024-07752-6

38 Butterworth JF, Hines R, Royster RL, James RL. A pharmacokinetic and pharmacodynamic evaluation of milrinone in adults undergoing cardiac surgery. Anesth Analg. 1995;81(4):783–92. https://doi.org/10.1097/00000539-199510000-00022