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Editorial

Practice Variation in Pharmacological Management During Cardiopulmonary Bypass: Is It Time for an International Expert Consensus?

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Practice variation remains a familiar feature of cardiopulmonary bypass (CPB). Differences in myocardial protection, temperature management, perfusion targets, haemodilution, transfusion thresholds, monitoring strategies, and pharmacological management continue to exist between institutions and even between clinicians [1,2,3]. Much of this variation is appropriate and reflects differences in patient characteristics, surgical complexity, institutional experience, and evolving evidence [1,2,3,4]. However, variation without a clearly defined rationale deserves closer examination.

One area that remains poorly defined is the administration of pharmacological adjuncts given through the CPB circuit. These include medications added to the prime, administered into the venous reservoir during bypass, incorporated into cardioplegia solutions, or delivered through the circuit to support patient management while on CPB [1,3,4]. Common examples include electrolyte replacement, antiarrhythmic agents, osmotic therapies, corticosteroids, anticoagulation adjuncts, vasoactive medications, antibiotics, and various cardioplegia strategies. Compared with anticoagulation, blood conservation, temperature management, and perfusion safety, there is limited structured guidance regarding pharmacological adjuncts administered through the CPB circuit. While many of these therapies are supported by varying levels of evidence, their routine use, timing, route of administration, and indications often remain institution-specific [1,2,3].

Although contemporary international guidelines address important aspects of the practice of cardiopulmonary bypass, including anticoagulation, the composition of the prime, myocardial protection, and perfusion safety, no dedicated multidisciplinary framework currently exists that specifically addresses pharmacological adjuncts administered through the CPB circuit.

This variation is recognized by everyone in the field of cardiothoracic surgery. A patient undergoing routine coronary artery bypass grafting in one institution may receive a significantly different combination of pharmacological adjuncts than a comparable patient treated elsewhere. In some centres, magnesium, calcium, lidocaine, corticosteroids, mannitol, sodium bicarbonate, or vasoactive agents are administered routinely through the CPB circuit. In others, these therapies are reserved for specific clinical indications or omitted entirely. Similar variation exists in myocardial protection, where blood cardioplegia, Del Nido, Buckberg, modified Del Nido, and crystalloid solutions continue to coexist in contemporary practice. Although these approaches have all been described in the literature, few have achieved universal acceptance across all patient groups or in surgical procedures [2,5].

This variation is not confined to differences between institutions but may also exist within the same cardiothoracic program. For example, following aortic unclamping, some clinicians or perfusion teams routinely administer magnesium, lidocaine, calcium, or combinations of these agents, whereas others administer only selected agents or reserve treatment until biochemical results or clinical findings indicate a specific need. Similarly, patients undergoing the same procedure, such as isolated coronary artery bypass grafting, may receive different cardioplegia strategies depending on the preference of the individual surgeon. This includes differences in the choice of the cardioplegic solution (e.g., Del Nido or Buckberg), induction protocols, maintenance dosing, and terminal warm reperfusion ("hot shot") techniques. Variations also extend to perfusion practice, particularly in the composition of the CPB prime. The use of albumin, heparin, mannitol, bicarbonate, and other pharmacological adjuncts may differ between perfusionists despite comparable patients and procedures. For example, although a large randomised trial comparing 4% al-

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bumin with Ringer acetate did not demonstrate a reduction in major adverse events, variation in the use of albumin-containing prime solutions continues across institutions, illustrating the differences between available evidence and routine clinical practice [6]. These examples are not intended to suggest that one approach is universally superior; rather, they highlight how routine pharmacological practice continues to be influenced by local protocols, clinician preference, and interpretation of the available evidence.

Volatile anaesthetic administration during CPB represents another area of variation in international practice. Some centres routinely administer volatile anaesthetic agents such as isoflurane or sevoflurane through the oxygenator to provide anaesthesia and potentially enhance myocardial protection, whereas others favour total intravenous anaesthesia throughout the period of cardiopulmonary bypass. Although current evidence has not established the consistent superiority of either approach, these differences in practice further illustrate the need for transparent, evidence-based pharmacological management pathways and clear documentation of institutional practices [7,8].

This variation is not necessarily problematic. Cardiothoracic surgery is inherently complex, and patient characteristics, surgical pathology, institutional experience, and clinician judgement all influence intraoperative decision-making. Variation driven by patient need has become an essential component of individualized care. This challenge arises when routine pharmacological practices persist primarily because they have always been used, rather than because there is a clearly defined indication or an evidence-based rationale for their use.

Variation driven by patient-specific factors should be encouraged, whereas variation based solely on historical practice or individual preference should prompt further analysis. As perfusion continues to evolve towards data-driven practice and continuous quality improvement, understanding why pharmacological adjuncts are administered through the CPB circuit may be just as important as deciding which agents are used.

This editorial does not advocate uniform pharmacological practice across all cardiothoracic surgery programs. Individual patient characteristics, operative complexity, clinician judgement, and institutional expertise will always require flexibility. Instead, we propose that routine pharmacological management should be guided by a transparent, evidence-based framework supported by periodic multidisciplinary review.

Not every pharmacological adjunct administered through the CPB circuit should become routine. Some therapies are appropriately indication-specific. Antithrombin III is reserved for selected patients with heparin resistance. Methylene blue may be considered in patients with vasoplegic syndrome or those judged to be at particularly high risk for developing this event. The choice of cardioplegia strategy depends on multiple factors, including the procedure performed, myocardial pathology, surgeon preference, and institutional experience. These differences are expected and, in many situations, are entirely appropriate [9,10,11,12].

However, the greater concern is how these pharmacological adjuncts become incorporated into standard clinical practice (Table 1). Across many institutions, pharmacological adjuncts administered through the CPB circuit, including cardioplegia solutions, electrolyte replacement, antiarrhythmic agents, osmotic therapies, acid-base modifiers, corticosteroids, anticoagulation adjuncts, antibiotics, and vasoactive medications, are often used according to long-established local practice rather than within a clearly defined pharmacological management pathway. The rationale for administration, timing, dosing, route of administration, and intended therapeutic objective may differ between clinicians even when managing similar patients undergoing similar procedures.

This distinction is more than semantic. Pharmacological adjuncts administered through the CPB circuit have the potential to influence myocardial protection, vascular tone, coagulation, inflammatory response, metabolic homeostasis, and postoperative recovery. The objective is therefore not to eliminate variation, but to ensure that pharmacological decisions are appropriate, evidence-informed, and aligned with clearly defined clinical objectives.

Variation in practices also affects education, quality improvement, and research. Differences in routine pharmacological management complicate the training of staff, introduce the element of confounding in multicenter studies, and make benchmarking between institutions more difficult when pharmacological strategies are poorly described [1,2,3].

Perhaps the most important question is not whether magnesium, lidocaine, calcium, methylene blue, or any other individual medication should be administered routinely. Instead, we should ask a simpler question: Do we have a clearly defined, evidence-informed rationale for administering each pharmacological adjunct through the CPB circuit?

1. Towards a Structured Approach

Recognizing variation in practice is only the first step. The more important question is how pharmacological management during CPB should be monitored within a contemporary cardiothoracic surgery program. The objective is not to replace clinical judgement with rigid protocols, but to ensure that routine pharmacological decisions are supported by data from peer-reviewed studies, which are regularly reviewed and adapted into practice as new, reliable evidence becomes available.

One practical solution would be the development of an institutional pharmacological management pathway for cardiopulmonary bypass. Similar structured pathways have

Table 1. Examples of international practice variation in pharmacological management during cardiopulmonary bypass and future consensus considerations.

Domain	Examples of current international practice variation	Potential consequences	Future consensus considerations
Priming solution and additives	Crystalloid-only prime, albumin-containing prime, blood prime, balanced electrolyte solutions, bicarbonate, mannitol, heparin, corticosteroids, electrolyte supplementation, or minimal-additive prime.	Variation in hemodilution, oncotic pressure, inflammatory response, anticoagulation exposure, renal protection strategies, and comparability of outcomes	Define evidence-informed recommendations for prime composition and additive use according to patient and procedural risk.
Anticoagulation adjuncts	Antithrombin supplementation, additional heparin, heparin in the CPB prime, or no heparin in the CPB prime	Variation in anticoagulation management and heparin resistance strategies	Standardised algorithms while allowing patient-specific clinical judgement.
Myocardial protection	Del Nido, Buckberg, blood cardioplegia, crystalloid cardioplegia, modified Del Nido	Variation in myocardial protection strategies for similar procedures	Develop consensus on reporting standards and procedure-specific recommendations while preserving surgeon discretion.
Cardioplegia delivery	Differences in induction dose, maintenance dosing, reinfusion intervals, and terminal warm reperfusion (‘hot shot’)	Limited comparability of myocardial protection techniques	Establish expert recommendations describing acceptable practice and key reporting parameters.
Reperfusion management	Routine magnesium, lidocaine, calcium, combinations of agents, or treatment guided by clinical findings after aortic cross-clamp removal	Variation in myocardial recovery and rhythm management following reperfusion	Define evidence-informed criteria for routine versus indication-specific pharmacological therapy.
Volatile anaesthetic administration during CPB	Isoflurane, sevoflurane delivered through the oxygenator, no volatile anaesthetic, or total intravenous anaesthesia	Variation in myocardial protection strategies, anaesthetic delivery, and potential organ protection	Develop guidance on indications, delivery methods, monitoring, and reporting of volatile anaesthetic administration during CPB.
Vasoactive therapies	Phenylephrine, metaraminol, norepinephrine, vasopressin, methylene blue	Different thresholds and prescribing practices for hemodynamic support	Develop multidisciplinary guidance on indications, timing, administration, and documentation.
Documentation and governance	Institution-specific protocols, clinician preference, or no formal pharmacological management pathway	Difficulties in education, benchmarking, audit, and multicenter research	Encourage institutional pharmacological management pathways with regular audit and periodic review.

Legend: Examples of contemporary international practice variation in pharmacological management during CPB. The table illustrates representative areas where practice differs between institutions, surgeons, anaesthesiologists, and perfusion teams, including CPB prime composition, myocardial protection, cardioplegia delivery, reperfusion management, volatile anaesthetic administration, vasoactive therapies, and documentation. It highlights opportunities for future international multidisciplinary collaboration and Delphi-based expert consensus to support transparent, evidence-informed pharmacological management while preserving appropriate clinical judgement and patient-specific care. CPB, cardiopulmonary bypass.

been implemented in areas such as management of anticoagulation, blood conservation, perfusion safety, and enhanced recovery programs [1,3,13]. Such a pathway would not prescribe identical treatment for every patient; rather, it would provide a transparent framework for defining routine pharmacological adjuncts, indication-specific therapies, determining prescribing responsibilities, administration through the CPB circuit, documentation requirements, and periodic review.

This pathway should remain sufficiently flexible to accommodate variations in patient complexity and evolving evidence. Therapies such as cardioplegia strategies, antithrombin III supplementation, or methylene blue administration may appropriately remain indication-specific, whereas other interventions may become routine within individual programs. The purpose of the pathway is therefore not uniformity, but clarity, transparency, and shared understanding across the multidisciplinary team.

Regular reviews will be necessary to ensure that established practices reflect contemporary evidence and should provide a structured process for evaluating new pharmacological therapies before they become routine.

Ultimately, the goal is not protocol-driven practice, but rather transparency. When pharmacological adjuncts

are administered through the CPB circuit, every member of the multidisciplinary team should understand why they are being used, when they are indicated, what outcome they are intended to address, and whether that objective has been achieved.

2. Implications for Practice, Education, and Research

The implications of variations in practice extend well beyond the operating room. At an institutional level, inconsistent pharmacological management makes it more difficult to educate new staff, onboard perfusionists from other centres, and evaluate clinical practice through audits and quality improvements. When routine medications are administered differently between clinicians without a clearly defined rationale, it becomes challenging to determine whether differences in practice reflect patient need, evolving evidence, or simply historical preference.

Greater transparency also benefits research. Contemporary studies frequently compare outcomes between institutions, yet the pharmacological management of CPB is rarely described in sufficient detail to allow meaningful comparisons. Variations in cardioplegia strategies, electrolyte replacement, antiarrhythmic agents, corticosteroids, anticoagulation adjuncts, vasoactive medications, and other pharmacological therapies administered through the CPB circuit may all influence perioperative outcomes but often remain unreported. Improving the consistency and documentation of these interventions would strengthen future multicenter research and facilitate more meaningful benchmarking [2,12].

Many aspects of perfusion practice have been addressed through evidence-based guidelines, standards of care, and expert consensus statements. Pharmacological management during cardiopulmonary bypass represents a similar opportunity for international collaboration. A logical first step would be an international multidisciplinary survey to characterise current practices and identify areas of agreement, uncertainty, and genuine variation. These findings could subsequently inform a formal Delphi-based expert consensus involving perfusionists, cardiothoracic surgeons, cardiac anaesthesiologists, pharmacists, and intensivists. Rather than promoting universal treatment protocols, such a consensus could provide an evidence-informed framework describing routine pharmacological adjuncts, indication-specific therapies, and areas where evidence remains insufficient to support recommendations. This process would also identify priorities for future research and support institutions in developing transparent, evidence-based pharmacological management pathways while preserving appropriate clinical judgement [2,14].

3. Looking Ahead

Pharmacological management during CPB has evolved gradually over decades, often through clinical experience, institutional learning, and adaptation to new evidence. This process has undoubtedly improved patient care. At the same time, it has also resulted in considerable variation between centers in the pharmacological adjuncts administered through the CPB circuit. Some of this variation reflects differences in patient populations, surgical practice, and available evidence. Some reflects institutional philosophy, whereas some persists because established practices are rarely revisited.

Periodically reviewing these practices should be viewed as a sign of a mature and high-performing perfusion service rather than a criticism of historical practice. Every pharmacological adjunct administered through the CPB circuit should have a clearly understood purpose, an agreed indication, and a mechanism for periodic review. Equally important, medications that are no longer supported by evidence should be reconsidered, while emerging therapies should be evaluated within a structured framework before becoming routine practice.

The conversation should therefore move beyond the question of which pharmacological adjuncts should be administered during CPB. A more important question is whether every institution has a transparent, multidisciplinary process for deciding why, when, and how those therapies are used.

4. Conclusion

Practice variation is an inevitable feature of modern cardiothoracic surgery, and not all variation should be eliminated. Individualized patient care will always require flexibility, clinical judgement, and adaptation to complex operative scenarios. However, routine pharmacological management during cardiopulmonary bypass should be guided by more than tradition alone.

Pharmacological adjuncts administered through the CPB circuit represent an important but comparatively under-discussed component of perfusion practice. Whether these include cardioplegia strategies, electrolyte replacement, antiarrhythmic agents, corticosteroids, anticoagulation adjuncts, antibiotics, vasoactive medications, or other therapies, their use should be supported by a clearly defined rationale, consistently documented, and periodically reviewed against emerging evidence.

The objective is not to achieve identical practice between institutions. Rather, it is to ensure that variation is intentional, evidence-informed, and centred on the needs of the patient. Developing institutional pharmacological management pathways represents a practical first step towards improving transparency in the administration of pharmacological adjuncts through the CPB circuit. We believe that the time is right for an international multidisciplinary survey followed by a formal Delphi-based expert consensus. Such a survey would identify practices that are universally accepted, those that remain controversial, and those where high-quality evidence is lacking. These findings could then

inform an evidence-based expert consensus while preserving appropriate individual clinical judgement. Such an initiative would not seek to eliminate appropriate clinical variation but rather provide an evidence-based framework to support institutional practice, strengthen multidisciplinary collaboration, facilitate research, and ultimately improve patient care.

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SPB conceived the editorial, conducted the literature review, drafted the manuscript, and critically revised its intellectual content. AA, AG, IR, SS, and GB contributed to the critical interpretation of the literature and intellectual development of the editorial, critically reviewed and edited the manuscript, and provided substantive comments. All authors have approved the final version of the manuscript and agree to be accountable for the accuracy and integrity of the work. All authors contributed to editorial changes in the manuscript.

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