BJA

British Journal of Anaesthesia, 135 (4): 840–843 (2025)

doi: 10.1016/j.bja.2025.07.047
Advance Access Publication Date: 14 August 2025
Editorial

EDITORIAL

Goal-directed perioperative haemodynamic therapy: need for a modern perioperative care loop

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This editorial accompanies: Perioperative Quality Initiative consensus statement on goal-directed haemodynamic therapy by Edwards et al., *Br J Anaesth* 2025:135: 547–560, doi: 10.1016/j.bja.2025.05.033

Summary

Using GRADE and modified Delphi methods, international experts in haemodynamic management from the Perioperative Operative Quality Initiative (POQI) group presented an updated consensus statement on goal-directed haemodynamic therapy. They do not recommend routine use of goal-directed haemodynamic therapy for major abdominal surgery, or fixed low-dose infusions of inotropes. They recommend goal-directed haemodynamic therapy only in specific settings such as during cardiopulmonary bypass, after cardiac surgery, and for hip fracture surgery, all with a low level of evidence. This approach has implications for future perioperative research.

Keywords: cardiac output; fluid therapy; goal-directed haemodynamic therapy; inotropes; perioperative medicine

Goal-directed haemodynamic therapy (GDHT) describes haemodynamic treatment strategies using titrated fluids, vasopressors, and inotropes to achieve predefined haemodynamic targets.[1] GDHT was proposed as a strategy to reduce organ dysfunction and postoperative complications with three mechanisms: (i) improve cardiac output and oxygen delivery for tissue perfusion,[2] (ii) decrease haemodynamic stress, using early titration of fluids to prevent extreme variations in both cardiac output and blood pressure, and (iii) reduce the systemic inflammatory response by stable haemodynamic perioperative care.

In a recent issue of the *British Journal of Anaesthesia*, Edwards and colleagues[3] presented the updated consensus statement for perioperative GDHT that was drafted during the last Perioperative Quality Initiative (POQI) consensus conference. The POQI is an international multidisciplinary nonprofit organisation that organises consensus conferences on clinical topics related to perioperative medicine. International clinicians with expertise in perioperative fluids, haemodynamic monitoring, and therapies used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) and modified Delphi methods, with non-anonymous voting. Key take-home messages include that routine use of GDHT was not recommended for patients undergoing major elective abdominal surgery, and that low-dose inotrope infusions used in some GDHT protocols should be avoided. Use of GDHT, however, was recommended in certain settings including for cardiopulmonary bypass, after cardiac surgery, and during hip arthroplasty. These changes in guidance require further explanation.

The lack of benefit of goal-directed haemodynamic therapy in recent clinical studies

Since the first study in 1988,[2] >100 randomised studies have been performed in diverse populations with different monitoring devices, haemodynamic targets, and therapeutics. Although certain systematic reviews and meta-analyses have

DOI of original article: 10.1016/j.bja.2025.05.033.

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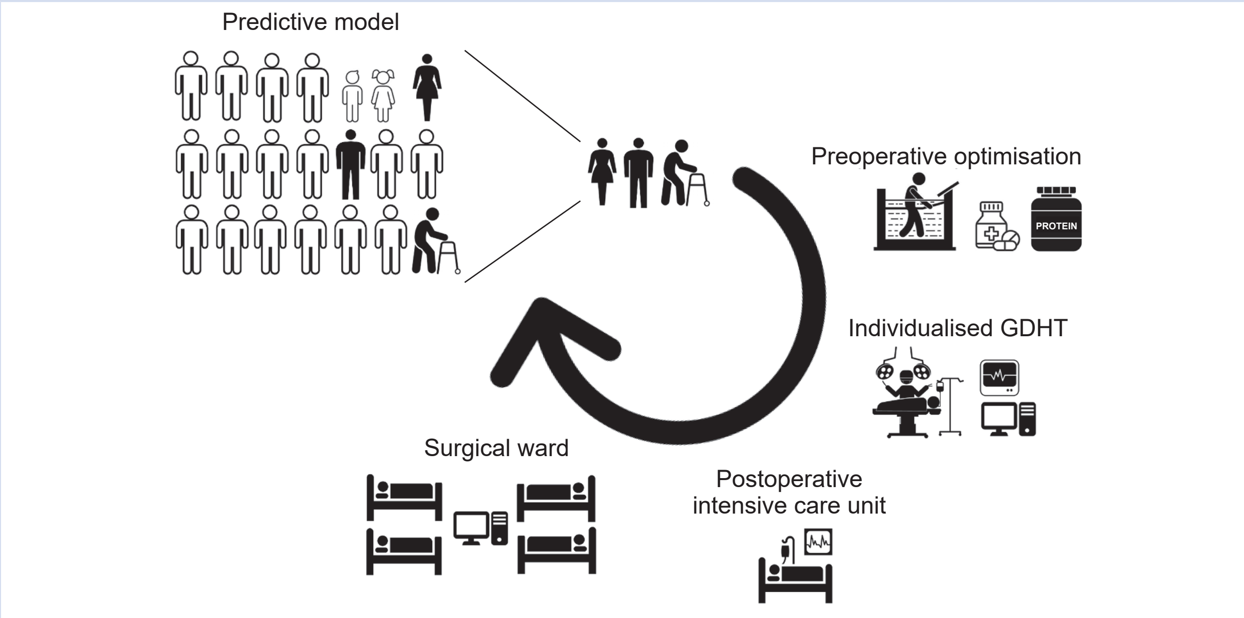

Fig 1. Proposed modern perioperative care loop to improve perioperative care. A predictive model using biomarkers and artificial intelligence could help improve identify high-risk surgical patients who require GDHT. These patients could also benefit from preoperative optimisation including physical prehabilitation, drugs optimisation, and nutritional support. During surgery, GDHT could be proposed with individualised mean arterial pressure and cardiac output adapted to tissue perfusion and using technology-assisted delivery of fluid management. GDHT could be used during the early postoperative period in the intensive care unit specifically in patients with a high risk of oxygen debt. The nursing supervision could be followed in the surgical ward, with artificial intelligence and predictive models that could help caregivers to detect patient deterioration earlier. Finally, the monitoring and acquisition of data could help improve the predictive model and perioperative care loop. These approaches require further study to confirm feasibility and effectiveness. GDHT, goal-directed haemodynamic therapy.

attempted to summarise these complex results, their conclusions were biased by the inclusion of small trials with heterogenous interventions and outcomes.[4]

Two large recent multicentre randomised studies, performed in major abdominal surgery used a simple GDHT algorithm with fluid loading and dobutamine during surgery and for 4–8 h after surgery.[5,6] These studies concluded that GDHT did not reduce postoperative complications in this setting.[5,6] Moreover, dobutamine was associated with an increased incidence of acute cardiac events within 24 h, especially tachyarrhythmias.[6] These results are the reason that the POQI consensus statement does not recommend routine GDHT in patients undergoing major elective abdominal surgery (strong recommendation) or the routine inclusion of fixed low-dose inotrope infusions in GDHT protocols (strong recommendation).

These recent negative results do not support the initial encouraging studies. Postoperative complications were high in both studies (incidence of ~50% in the iPEGASUS trial for moderate or severe postoperative complications, and of 23% in the OPTIMISE 2 trial for postoperative infections), and properly administered GDHT did not reduce them. Firstly, dobutamine showed a negative benefit–risk balance because of an increase in the incidence of arrhythmias. Secondly, routine clinical care has changed since the first published study showing that fluid loading and vasopressor infusion were similar in the control and GDHT groups. Recent large studies have encouraged anaesthesiologists to give more fluids and take into account the importance of mean arterial pressure in routine practice.[7,8] Better and more comprehensive perioperative cardiovascular risk assessment, along with improved management of perioperative medical therapies such as aspirin, statins or beta-blockers, could strengthen the care provided to control groups in recent studies compared with earlier studies since 1980s.[9] Moreover the enhanced recovery after surgery (ERAS) programme obviated the isolated effect of GDHT, which explains why patients in the control group were already optimised.[10]

Expected clinical utility of goal-directed haemodynamic therapy for specific patients and perioperative settings

The POQI only recommends considering use of GDHT in specific settings, in particular during cardiopulmonary bypass, after cardiac surgery, and during hip fracture surgery, with a moderate quality of evidence.[3]

The POQI recommends using goal-directed perfusion to maintain global oxygen delivery (DO_2) $\geq$280 ml min^{-1} m^{-2} or >300 ml min^{-1} m^{-2} during cardiopulmonary bypass.[11,12] The two randomised controlled studies mentioned as evidence show that this strategy only reduces stage 1 of postoperative acute kidney injury and does not benefit other postoperative complications.[11,12] The latter explains the weak quality of evidence for this recommendation during cardiopulmonary bypass. The level of evidence is also moderate for the POQI recommendation to use GDHT after cardiac surgery, probably because of the limited number of recent studies evaluating GDHT in this setting with a high risk of postoperative complications.

The POQI recommendation to consider the use of GDHT in patients with hip fracture to reduce perioperative complications has a low quality of evidence. Although this older population has numerous comorbidities associated with a high risk of postoperative complications and mortality, they have not been regularly monitored in clinical practice,[13] and randomised controlled studies are lacking to assess the benefits of GDHT to reduce morbidity and mortality in this setting. The POQI group presented a before and after study with encouraging results,[14] but this is not sufficient to strongly recommend GDHT in routine clinical practice for this population. In addition to patients with hip fracture, large clinical studies are needed to assess GDHT in high-risk patients with comorbidities compared with control groups following ERAS programmes.[15]

Implications for future perioperative research

Future research should focus on each stage of the perioperative path (Fig. 1.).

Preoperative period

During the preoperative period, it is important to identify patients at high risk of major adverse cardiac events (MACE). On the one hand, implementation of large, continuously updated databases powered by artificial intelligence could improve preoperative assessment of patients at high risk of postoperative MACE. In a complementary approach, recent studies have shown that preoperative cardiovascular biomarkers might help classify patients into biologically distinct subgroups with varying risks of postoperative MACE. Notably, recent findings have identified distinct sub-phenotypes in patients undergoing major noncardiac surgery by using biomarkers such as N-terminal pro-brain natriuretic peptide, renin, aldosterone, and angiotensin-converting enzyme 2, which are associated with risk of MACE.[16,17] This exploratory mechanistic analysis suggested that effective preoperative suppression of the renin–angiotensin–aldosterone system was associated with a lower risk of MACE compared with non-responders.[16] These models could enhance perioperative risk stratification with more precise identification of high-risk patients, supporting targeted preoperative evaluation and perioperative management strategies. Integrating such biomarker-based sub-phenotyping with clinical data and artificial intelligence-driven predictive modelling could refine patient selection for specific interventions and improve clinical outcomes. Although use of cardiovascular biomarkers for perioperative sub-phenotyping appears promising for optimising preoperative risk stratification to identify high-risk patients who might benefit from GDHT, this strategy must first be validated in clinical trials.[17]

The preoperative period could also be used for patient prehabilitation with optimisation of medications, nutritional support, and exercise.[18] The rationale is that impaired functional capacity, especially critical oxygen consumption (VO_2) <10.9 ml kg^{-1} min^{-1}, was independently associated with increased in-hospital and 90-day mortality after major abdominal surgery.[19] Some clinical trials have shown that supervised activity prehabilitation programmes not only enhanced functional reserve, but also decreased postoperative complications and enhanced overall quality of life.[18] However current evidence is limited because of heterogeneous protocols, endpoints, study population, and type of surgery. This approach should therefore be further evaluated in large well-designed, adequately powered clinical trials.

Intraoperative period

During surgery, more individualised approaches could have more clinical benefit than providing GDHT with standardised cardiac output and mean arterial pressure values to all patients. It could be more appropriate to adapt haemodynamic targets to individualised parameters,[20] such as adapting the mean arterial pressure to cerebral autoregulation monitoring,[21] or cardiac output to tissue metabolism or the VO_2:DO_2 ratio. However, despite a clear physiological rationale, there are no studies confirming the benefit of a strategy using individualised DO_2 targeted haemodynamic therapy, the central-to-arterial carbon dioxide gap or respiratory exchange ratio between CO_2 production and O_2 consumption.[22–24] Further studies are needed to confirm these approaches.

Implementation of GDHT protocols remains low and protocol compliance among anaesthesiologists is suboptimal during surgery, explaining the negative results of some studies of GDHT. Results of a recent randomised study were encouraging in showing that semi-automated goal-directed fluid therapy, using real-time haemodynamic monitoring and closed-loop algorithms, improved cardiac output and microcirculation using sublingual microvascular flow compared with standard clinician-led management.[25] These technology-assisted systems aim to reduce variability in care by continuously guiding fluid administration based on stroke volume or cardiac output targets. While early results are promising, particularly regarding microvascular perfusion, these approaches require further validation before widespread adoption.

Postoperative period

In the EUSOS study, postoperative mortality frequently occurred for patients not admitted to an intensive care unit after surgery.[26] This point emphasised that GDHT could be used not only during surgery, but also during the early postoperative period, specifically in the intensive care unit, for patients at high risk of oxygen debt.[26] For patients in standard wards, remote monitoring with artificial intelligence and predictive models could help detect patient deterioration earlier, reducing mortality, sepsis, and length of stay with an increase in ICU transfers.[27]

In conclusion, GDHT should be redefined with more individualised targets and used throughout the perioperative period. Further studies of both physiological and technological approaches are needed to improve and adapt GDHT for specific high-risk patients. These future challenges must also take into account important implementation constraints, such as equipment costs and staffing needs.

Declaration of interest

The author declares that they have no conflict of interest.

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