Point of view

Pulmonary artery catheterisation - A problem swept under the carpet?

Pulmonary artery catheterisation (PAC) by balloon flotation has been at the centre of modern intensive care practice since its introduction by Swan *et al* in 1970.[1] The addition of a balloon to the fluoroscopically guided catheter previously used by cardiologists for the diagnosis of congenital heart disease, changed the geographical area of PAC from the cardiac catheter laboratory to the intensive care unit (ICU).

It is important to note from a historical perspective, that the measurement of cardiac output by thermodilution in patients had in fact been introduced earlier, in 1966 by Branthwaite and Bradley at St. Thomas's Hospital in London.[2] They used a rigid, thermistor tipped catheter passed into the pulmonary artery under fluoroscopic control with a second injection catheter placed in the right atrium. Indeed, measurement of pulmonary artery pressure during general anaesthesia using these rigid catheters had been quite common place throughout the 1960s.[3] The achievement of Swan and Ganz was to bring the technique to the bedside through balloon flotation of a multi-lumen thermistor tipped catheter, so dispensing with the routine requirement for fluoroscopy. Subsequently, physicians working in the ICU throughout the developed world but particularly in North America pushed the boundaries of PAC so as to generate haemodynamic and oxygen transport data describing the course of critical illness rather than just sticking to the making of diagnoses, as their predecessors.[4]

Initially the use of PAC was limited to patients with acute myocardial infarction in whom it was used in a continuation of its previous role by allowing detection of papillary rupture, significant mitral regurgitation, and ventricular septal defect.[5] In the setting of acute myocardial infarction and congestive heart failure of any cause, its role expanded further to incorporate instances in which there was thought to be a significant dissociation between right and left heart function.[6] The explosion of ICU activity through the 1970s and 1980s – greater numbers of patients being admitted particularly after major surgery, more teaching and research and the emergence of intensive care as a discrete specialty within medicine – was accompanied by a concomitant rise in the use of PAC. The number of catheters used rose from a few thousand per annum worldwide in the mid 1970s to in excess of 2 million per year by 1997.[7] This was allowed by funding authorities without subjecting the new technique to rigorous testing that might have pre-empted some of the later divisive discussions.

The popularity of PAC lies in its ability to deliver physiological measurements (Table 1) that are thought to be important but otherwise unavailable to the ICU clinician.

Table 1. Physiological measurements from pulmonary artery catheterisation

Measured variables
Pulmonary artery pressure
Pulmonary artery occlusion pressure
Cardiac output
Mixed venous oxygen concentration
Calculated variables
Stroke volume
Systemic vascular resistance
Pulmonary vascular resistance
Coronary perfusion pressure
Oxygen delivery
Oxygen uptake

The assumption underlying this demand for 'more data' is that this physiological information is potentially useful and whilst there are the obvious complications associated with PAC (Table 2), these are sufficiently rare so as to be worth the risk. Yet this assumption is probably false.

Table 2. Complications from pulmonary artery catheterisation

Insertion and mechanical problems
Pneumothorax, subcutaneous emphysema,
Pleural cannulation with hydrothorax or haemothorax
Mediastinal malposition
Noninfective endocarditis
53% in one post mortem study (control 2.5%)[8]
Infective endocarditis
7% in the same post mortem study (control 0%)
Pulmonary artery rupture
Pulmonary artery thrombosis and embolism
Internal jugular vein thrombosis (up to 67%)[9]
Arrhythmias
Atrial
Ventricular ectopy
Ventricular tachycardia
Ventricular fibrillation

Firstly, studies both in Europe and North America now show that data collection and interpretation from PAC are seriously flawed even when performed by experienced ICU specialists.[10,11] Although the relevance of these observations has not been established in Australasia,[12] there is little reason to believe that the situation here is fundamentally different. Secondly, there is now in excess of 20 years documentation of serious side effects associated with PAC. Although the 4% mortality of one review [13] has not been confirmed, the individual risk benefit ratio has been inadequately assessed in too many cases.

The use of PAC has undoubtedly added to our understanding of the patho-physiological mechanisms playing some role in the development of critical illness, for example, pulmonary oedema developing in the context of low hydrostatic pressures or the haemo-dynamic disturbances associated with sepsis. For the experienced user, it does provide some insight into the level of intra-vascular filling, tissue perfusion and ventricular performance. However, the measurements are not absolutes and are often dependent on variables secondary to mechanical ventilation or intrinsic lung disease (intra-thoracic pressure, vascular compliance, cardiac contractility) the significance of which is not fully understood and hence tends to be ignored. An important issue is the capacity for errors in the measurement of both pulmonary arterial occlusion pressure (PaoP)[14] and cardiac output [15] by PAC (Table 3).

Table 3. Potential pitfalls in pulmonary artery catheterisation measurements and calculations

Pulmonary artery occlusion pressure
Mitral stenosis
Mitral regurgitation
Left ventricular compliance abnormalities
Respiratory/ventilatory cycle dependent
Pressure differences between lung zones
Right ventricular overload
Pericardial constriction
Cardiac output
Respiratory/ventilatory cycle dependent
Tricuspid regurgitation
Catheter position

With the continuing advent of new technologies the ICU clinician is now able to obtain cardiac output, measures of the adequacy of intra-vascular filling and tissue perfusion in other more reliable ways (Table 4). These methods of monitoring touch on areas that were previously unique to PAC and therefore used to justify its continuing role. Whilst the substitution of PAC by these new, less invasive forms of monitoring may be viewed as appropriate,[23-26] we are in danger of missing an important point.

Table 4. New diagnostic and monitoring tools in the intensive care unit

Doppler echocardiography[16]
Transoesophageal echocardiography[17]
Transpulmonary thermodilution[18]
Gastric tonometry[19]
Carbon dioxide rebreathing cardiac output[20]
Lignocaine metabolism[21]
Impedence plethysmography[22]
Serum lactate[21]

The use of PAC has generated controversy for many years, with questions raised concerning safety, interpretation and the unfettered use of a highly invasive piece of apparatus. These questions have touched not only on our use of PAC but on our understanding of the data it generates and our ability to turn this into beneficial (for the patient) changes in management. If assessments of our use of data from new technological advances are to be valid, to what do we compare them, and by what methods?

The Evidence Based Medicine Critical Care Group[27,28] have described certain criteria that should be used in regard to the introduction of new technology. Firstly, any new technology should provide new data that would otherwise be unavailable. Secondly, the new data should provide an insight into the presence or severity of disease. Thirdly, the new data must be integrated into the care process. Fourthly, and perhaps of most importance, this use of new data should favorably alter the outcome. Next, the economic consequences of the use of the new technology need to be considered. The final and somewhat questionable criterion relates to any increase in health care worker confidence arising from the use of the new technology. Over the last 30 years, several if not all of these points have been used as a justification for PAC (Table 5) but times have moved on in relation to this relatively aged

Table 5. Pulmonary artery catheterisation justification

- Cardiac output and filling pressure data otherwise unavailable[29]
- Insight into the pathophysiology of low pressure pulmonary oedema[30]
- Data integrated into the care of patients[29]
- Favorable outcome from using the data[31]

(and perhaps dangerous) technology. Arising from the Connors study[32] substantial questions have been leveled at the continued use of PAC. Rightly so, given the breadth of evidence that shows that PAC derived data may be flawed and can now also be derived by other means. There is evidence that PAC data is misused or not even collected post insertion.[33] Insight into the disease process and prognosis can be gained by other means. Even with sub-group analysis, there is little evidence of improved outcome with PAC. The increased costs associated with PAC use are without obvious benefit. And finally, should instilling confidence in the health care worker be an endpoint in itself? PAC has a strong and vocal support group who, without compelling evidence (freely admitted by the Consensus Conference of 1997),[4] continue to advocate its use in all manner of situations sometimes quoting studies over 20 years old when clearly practices and patients have changed.

So what about the Connors study? It is difficult to criticize such a large (n = 5735 critically ill patients), prospective cohort study performed by such an eminent group of bio-statisticians and epidemiologists other than to say that it was not randomized and controlled. More importantly it does not support the 'pro PAC' prejudice of the intensive care establishment! The significance of the increased odds ratio for 30 day mortality associated with PAC in the first 24 hours of ICU admission (1.24, 95%CI 1.03-1.49) and the increase in hospital costs (mean increase $13600) depends primarily upon the matching of cases through the use of a propensity score. Whatever one's views of this method of matching, the sensitivity analysis emphasizes that any missing covariant would have to increase the risk of death by six times for a true beneficial effect of PAC to be misrepresented as harmful. The arguments against accepting the conclusions of the Connors study are multiple and have been examined in depth before. The most pertinent have been related to the prevalence of the use of Shoemaker's 'supra-normal' goal direct therapy (GDT) during the period of study 1989-1994.[34] The Support Investigators studied nine specific diagnostic groups, none of which were included by Shoemaker in his original studies and hence in which GDT would not be indicated. Again, turning to the oft-quoted study of Hayes *et al*,[35] it is clear that high doses of vasoactive drugs can be detrimental in some groups of patients. The softest conclusion from the Connors study would be that it is the use of the PAC data that was being brought into question and not PAC itself. It is interesting to note however, that when presented with suggestions of the deleterious effects of PAC, intensive care specialists the world over have acted as if they had heard some unpleasant gossip about a close and trusted friend. They seemed to regard the allegations as 'vile slander' and have continued to use PAC ignoring the evidence and missing the point. Comments about 'shooting the messenger' and 'bad workmen blaming their tools' are all very well and while inappropriate fluid and vasopressor therapy may have contributed to the excessive death rate in the PAC group, brushing the problem under the carpet is not the answer! Better technologies now exist to obtain the information that we need to manage the vast majority of patients with critical illness and it is not clear that anyone actually needs a 'yellow snake'. As they say in some parts of the world "Vorsprung dürch tecknik"! (*Advancement through technology*).

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High-risk non-cardiac surgery - is supranormal oxygen delivery the answer?

The peri-operative management of the high-risk surgical patient has evolved considerably over the last twenty years. For example, elective surgery after myocardial infarction, previously deferred for up to six months, can now proceed in four to six weeks unless a stress test reveals that further myocardium is at risk.[1] Peri-operative beta-blockade can improve outcomes in patients with established coronary artery disease or significant risk factors for coronary artery disease who are undergoing non-cardiac surgery. Here beta-blockade reduces myocardial ischaemic episodes both in the operating room and during the first post-operative week, and lowers mortality and cardiac event rates over the following two years.[2,3] More recently, impressive in-hospital reductions in cardiac deaths and non-fatal myocardial infarction have been achieved using beta-blockade in high-risk patients undergoing major vascular surgery.[4]

Despite progress, there is still controversy concerning the best and most cost-effective management of the broader categories of high-risk surgical patients, defined as those who suffer a high mortality in the peri-operative period due to any combination of major surgery and single or multisystem disease. Over the last eight years British researchers have produced data supporting the pre-operative admission of all such patients to intensive care units for the induction and maintenance of supranormal whole-body oxygen delivery (supranormal goal-directed therapy).[5,6] Evidence has been advanced that this approach improves morbidity and mortality as well as reducing costs.[7] Consequently a longstanding debate on the manipulation of haemodynamic and oxygen transport patterns in high-risk surgical patients has been carried over into the new millennium. This paper critically evaluates current evidence for peri-operative supranormal goal-directed therapy.

Peri-operative 'tuning' to normal cardiovascular end-points

In the 1980's there were some reports of improved post-operative outcomes after pre-operative insertion of pulmonary artery (PA) catheters and optimisation of cardiovascular variables to normal (rather than supranormal) endpoints.[8,9] Subsequent studies of this more conventional type of peri-operative 'tuning' have been few, and mainly in the area of vascular surgery. One investigation in 1991 showed a benefit from 'tuning' in peripheral limb-salvage arterial surgery.[10] Importantly, there was an extra control group without automatic PA catheter insertion. Protocol patients had fewer intra-operative adverse events, less cardiac morbidity and a lower rate of early graft occlusion. In contrast, two later investigations of 'tuning' prior to elective peripheral vascular and aortic surgery failed to show any benefit.[11,12] However, although these were prospective randomised controlled trials, both were low power single centre studies. Furthermore, neither had a non-PA catheter control limb.

Peri-operative 'revving' to hyperdynamic cardio-vascular end-points

An association between flow patterns and survival post high-risk non-cardiac surgery was first reported by Clowes and Del Guercio in 1960.[13] In the seventies and eighties, Shoemaker and colleagues drew further attention to differences in haemodynamic and oxygen transport patterns of surviving versus non-surviving patients undergoing major non-cardiac surgery.[14-17] They showed that patients who spontaneously achieve supranormal degrees of oxygen delivery and consumption are more likely to survive. From this they formed the hypothesis that an induced peri-operative hyperdynamic state is protective. To test this hypothesis, a list was constructed of patient-specific and surgery-specific factors defining those with increased peri-operative risk[18] (Table 1). Patients fulfilling one or more of these criteria were shown to suffer an overall mortality of 23-33%. According to Shoemaker, this could be reduced to 4% when fluids and vasoactive drugs were titrated to achieve supranormal haemodynamic and oxygen transport patterns (cardiac index > 4.5 L/min/m^2, oxygen delivery > 600 mL/min/m^2, oxygen consumption > 170 mL/min/m^2).[18]

A related concept also prevalent in the eighties was that of pathologic supply dependency of oxygen consumption.[19] In normal tissues, oxygen consumption is independent of supply unless oxygen delivery is reduced below the anaerobic threshold.[20] Studies of the relationship between whole-body oxygen delivery and consumption in sepsis,[21,22] in the acute respiratory distress syndrome [23, 24] and also in surgical patients[25] revealed apparent oxygen supply dependency at normally adequate delivery levels. Some took this to imply that organs in these individuals were suffering from a covert oxygen debt.[26] To correct this debt it was theorised that supranormal goal-directed therapy ought to be extended from Shoemaker's high-risk surgical group to a wider ICU population. An influential study of the time was that of Edwards and colleagues,[27] in which 29 patients with septic shock were subjected to the goal-directed approach. Their mortality of 52% compared favourably with that of historical controls.

Table 1. The Shoemaker criteria defining high-risk surgical patients

1. Previous severe cardiorespiratory illness (acute myocardial infarction, chronic obstructive pulmonary disease, stroke, etc)
2. Extensive ablative surgery planned for carcinoma; e.g. oesophagectomy and total gastrectomy, prolonged surgery (> 8 hr)
3. Severe multiple trauma, e.g. > 3 organs or > 2 systems, or opening of 2 body cavities.
4. Massive acute blood loss (> 8 units), blood volume < 1.5L/m^2, haematocrit < 20%.
5. Age over 70 years and evidence of limited physiological reserve of one or more vital organs.
6. Shock, mean arterial pressure < 60 mm Hg, CVP < 15 cm H_2O, and urine output < 20 mL/hr.
7. Septicaemia, positive blood culture or septic focus, white blood count >13,000, spiking fever to 101^{O}F for 48 hr, and haemodynamic instability.
8. Respiratory failure, e.g. PaO_2 < 60 mm Hg on F_IO_2 > 0.4, venous admixture > 30%, mechanical ventilation needed > 48 hr.
9. Acute abdominal catastrophe with haemodynamic instability, e.g. pancreatitis, gangrenous bowel, peritonitis, perforated viscus, gastro-intestinal bleeding.
10. Acute renal failure (blood urea nitrogen > 50 mg/dL, creatinine > 3 mg/dL)
11. Late vascular disease involving aortic disease

These results seemed sufficiently encouraging at the time to make supranormal goal-directed therapy a popular and widely supported practice.[28]

Since then three factors have led to a questioning of the twin concepts of pathologic oxygen supply dependency and supranormal goal-directed therapy in critical illness. The first was the likelihood that many apparent cases of supply dependency were merely due to mathematical coupling of variables common to the calculation of both oxygen delivery and oxygen consumption (i.e. cardiac output and arterial oxygen content).[29] In fact it was possible on the one hand to demonstrate pathologic supply dependency when oxygen consumption was determined by the reverse Fick method, and its simultaneous absence on the other using direct measurement of oxygen consumption.[30] Second, it was realised that vasoactive agents themselves can cause a dose related increase in oxygen consumption (the calorigenic effect),[31,32] creating the false impression of supply dependency. The third factor has been the publication of at least five separate studies, all of which failed to show any survival benefit attributable to supranormal goal-directed therapy. Two were of patients with severe sepsis or septic shock.[33,34] Three were of patients with a wider range of diagnoses,[35-37] and included a large multicentre trial. Mortality was actually increased in the goal-directed cohort of one of these studies.[36]

One suggestion was that intervention after the insult (as was the case in all five studies) is always too late.[38] This became the fall-back position for those advocating the pre-operative institution of supranormal goal-directed therapy, a practice now supported by two further single-centre trials, both originating from the United Kingdom. The trial by Boyd and colleagues was performed on 107 patients at St George's Hospital in London,[5] and that of Wilson and colleagues on 138 patients undergoing surgery at York District Hospital.[6] Both trials used recruitment criteria similar to those of Shoemaker (Tables 2 and 3), but interventions were focussed solely on augmenting oxygen delivery. Cardiac index and oxygen consumption were not primary endpoints. In both studies, fluid loading was first employed to optimise preload, and then vasoactive drugs were administered.

Table 2. The St George's Hospital criteria for high-risk patients

Surgery > 90 minutes plus one or more of;

1. Previous severe cardiorespiratory illness (e.g. acute myocardial infarction, COPD, stroke)
2. Extensive surgery planned for carcinoma (e.g. oesophagectomy, gastrectomy, cystectomy)
3. Acute massive blood loss (> 8U)
4. Age > 70 years with limited physiological reserve in one or more vital organs
5. Septicaemia (positive blood cultures or septic focus)
6. Respiratory failure (PaO_2 < 8 kPa on an F_IO_2 > 0.4 or mechanical ventilation > 48 hr)
7. Acute abdominal catastrophe with haemodynamic instability (e.g. pancreatitis, perforated viscus, peritonitis, gastrointestinal bleed)
8. Acute renal failure (urea > 20 mmol/L, creatinine > 260 μmol/L
9. Late stage vascular disease involving aortic disease

In the St George's study,[5] all patients were admitted to intensive care pre-operatively for the insertion of PA catheters and monitored fluid loading, whereas in the York study only protocol patients were treated in this way.[6] After fluid loading, the inodilator dopexamine was used in the protocol group to achieve supra-normal oxygen delivery. In the York study there was an additional group of patients given adrenaline instead of dopexamine.[6] The York study reported control mortality rates consistent with that predicted by the POSSUM score ('Physiological and Operative Severity Score for

Table 3. The York District Hospital criteria for high-risk patients

Major elective surgical procedures in general surgery, vascular surgery or urology and one or more of;

Surgical admission criteria
1. Repair of aortic or common iliac aneurysm
2. Planned resection of upper gastrointestinal malignancy
3. Anterior resection
4. Cystectomy

Medical criteria
1. Ischaemic heart disease
2. Myocardial infarction in past 5 years
3. Congestive cardiac failure
4. Cerebrovascular disease
5. Hypertension
6. Peripheral vascular disease
7. Obstructive airways disease
8. Pulmonary embolus
9. Chronic renal insufficiency
10. Diabetes mellitus with end organ damage
11. Long term systemic steroid therapy

the enUmeration of Mortality and morbidity').[39] In both investigations there was a dramatically reduced mortality in the protocol groups (St George's; 22% to 6%, York; 17% to 3%). Importantly, the group receiving adrenaline shared in the reduced mortality.[6] Post-operative complications ranging from those of a specific surgical nature to sepsis to system-specific complications were also less in the dopexamine groups of both studies, but adrenaline was not associated with any reduction in complications.

An editorial accompanied the publication of the York study. One of the writers was a principle researcher in the St George's study. The editorial led with the sub-caption, 'Optimising oxygen delivery before surgery does work; now we have to implement it'.[40] This dogmatic statement was particularly confronting for large sections of the surgical and critical care community who did not practice peri-operative supranormal goal-directed therapy. We will therefore consider in more detail whether it can be regarded as a definitive pronouncement, or whether closer scrutiny casts doubt on the assertions of these editorialists.

In fact there are major problems with both British studies, many of which also apply to Shoemaker's original work. Firstly, both were single-centre studies, and were by necessity unblinded. In the St George's study an attempt was made to keep the surgeons and anaesthetists in the operating room unaware of the group allocations, although the practicalities of this attempt at blinding must have been difficult at best. However, it was not possible to blind either the care-givers or the patients in the pre-operative and post-operative phases of either study. Surgeons and anaesthetists were also not blinded in the York study. The possibility of unintentional bias due to lack of blinding was thus significant, particularly if the protocol limb was the one favoured by the investigators. It has been estimated that in the absence of double-blinding, reports of treatment efficacy increase by 17%.[41] In trials of this nature, it is difficult to see how such a problem can be overcome.

Secondly, although each study used slightly different recruitment criteria (Tables 2 and 3), in both cases the defining characteristics of high-risk patients were broad in the extreme. The net was thus cast very widely as in the Shoemaker studies (Table 1), with criteria so lacking in specificity that undetected baseline differences between control and protocol limbs could easily have been present. Thirdly, the York researchers reported control mortality rates similar to those predicted by the POSSUM index. Since the POSSUM index has been shown to over-predict mortality in some other hospitals by approximately twofold (and for those at lowest risk by more than sevenfold),[42] control mortality rates should perhaps have been lower. A further criticism is that protocol patients in both studies may merely have received 'glorified pre-operative fluid loading'. Certainly, in neither investigation was it possible to raise oxygen delivery consistently in the protocol groups to the stated goal (> 600 mL/min/m^2), and interestingly when oxygen consumption was measured in the St George's study it was scarcely affected.[5] However, in both studies the fluid loading prior to theatre was significantly greater in the protocol group, particularly in the York study where the treatment group received a mean of 1500 mL of extra pre-operative fluid.[6]

Next, was the benefit attributed to the protocol merely due to extra 'care and attention' rather than the specifics of the protocol? This is a particular possibility in the York study, where control patients were managed along normal hospital lines, often outside of intensive care. Even in the St George's study, a protocol designed to create and maintain a state of supra-normal oxygen delivery would have required continual monitoring of output and adjustment of input. This could have had spin-offs for the protocol patients solely from the need for constant re-evaluation. Any protocol mandating repeated assessments and adjustments might have achieved the same results. For example, rather than focussing on supranormal oxygen delivery it might have been equally successful to aim for a urine output of 200 mL/hr for the entire peri-operative period while maintaining conventional cardiovascular targets and optimal hydration.

Furthermore, protocols requiring pre-operative placement of PA catheters across the board need careful assessment. Reports of the negative effects of PA catheterisation include evidence (admittedly based on retrospective analysis) for a detrimental effect in acute myocardial infarction.[43,44] There is stronger evidence (prospective cohort study) that the use of PA catheterisation in the first 24 hours in ICU patients with any of 9 major disease categories increased 30 day mortality, mean length of stay and mean cost per hospital stay. This was particularly so in the post-operative group.[45] Of course there are problems with this study (the well-known Connors study) which include whether or not there was true matching of PA catheter versus control groups using a 'propensity factor'. Nevertheless, to use an example closer to home, a 1990 audit of 410 elective aortic aneurysm repairs at an Australian teaching hospital[46] revealed that 2 of the 22 deaths were directly attributable to the peri-operative insertion of PA catheters. One death was from PA rupture, and the other from carotid artery injury causing stroke (personal communication, P Walker). Other directly attributable PA catheter deaths have also been reported.[47,48]

Yet surprisingly there was no reported catheter-related morbidity let alone mortality in either of the British studies, although only the St George's paper makes specific mention of this. At the very least this implies zero complications of central venous access in over 200 insertions, an almost unique performance as immediate complication rates well above zero are usually described even under relatively ideal conditions.[49] Given that the negative effects of PA catheters are likely to exceed those of gaining central venous access (for example just taking into account arrhythmias and catheter sepsis), the lack of reported catheter complications in these studies becomes even more striking.[50]

Other criticisms can be made and questions raised. Specific immuno-modulatory, anti-inflammatory or gut-vasodilatory effects of dopexamine unrelated to oxygen delivery need to be considered.[51,52] Haemoglobin concentrations were maintained by blood transfusion at 120 g/L in the St George's study and 110 g/L in the York study. Current evidence does not support such an aggressive transfusion policy in the broader intensive care context at least outside of the operating room, and even points to a possible detrimental affect in younger less critically ill patients.[53] Also the recruitment criteria of the American and both British studies included patients with significant ischaemic heart disease (Tables 1-3). Two prospective randomised placebo-controlled trials support improved outcomes for such patients if acute peri-operative beta blockade is established and maintained.[2-4] One trial was of very high-risk patients, and reductions in the in-hospital mortality rate were dramatic.[4] Yet acute beta-blockade as a primary intervention goes against the whole philosophy underpinning the goal-directed approach, as it is more likely to reduce rather than increase peri-operative oxygen delivery.

In summary, there are more questions raised by these studies than answered. Suffice it to say, the case for the deliberate peri-operative establishment of supra-normal oxygen delivery in high-risk surgical patients has not yet been established.

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