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Multimodal monitoring (MMM) in the perioperative period

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ABSTRACT

Routine anaesthesia monitoring until the mid-1980s often consisted of just a finger on the pulse, primitive ECG and intermittent blood pressure (MAP) measurement using a cuff and aneroid gauge or mechanical oscillotonometer. Then in quick succession an explosion of new monitors was introduced including pulse oximetry (SpO2), end tidal carbon dioxide (EtCO2) and anaesthetic agent monitoring as well as automated non-invasive blood pressure (NIBP) machines. These were all routinely in place in many hospitals by the late 1980's, but then progress came to a halt with no advances in routine anaesthetic monitoring for over 25 years.
This paper concentrates on three classes of non- or minimally invasive monitors which have become additionally available in the last 10 to 15 years and if used in combination their potential impact on improving outcome following surgery in high risk patients:

1. Monitors which calculate stroke volume (SV, and thus cardiac output, CO) from a standard radial arterial line (e.g. LiDCO, UK), oesophageal probe (Deltex, UK), ECG pads or even from the finger
2. Monitors which assess the degree of cortical suppression (e.g. BIS, Medtronic, USA) produced by anaesthetics thus potentially allowing the administrator to "fine tune" anaesthesia for individual patients
3. Monitors which assess tissue oxygenation, usually of the brain (e.g. Invos, Medtronic, USA)

If used together they provide complementary information which should improve perioperative haemodynamic management and outcome and form part of a multi-modal monitoring (MMM) strategy which is the subject of this article.

Key words: cardiac output, minimally invasive, tissue oxygenation, depth of anaesthesia multi-modal monitoring

WHAT'S WRONG WITH CURRENT MONITORING STRATEGY?

A recent UK survey reported that "The low mortality rate of GA (0.06% or one in 1718) during surgery is notable" and that "Many patients are scared of anaesthesia and this figure can only be reassuring for them". With mortality rate so low during anaesthesia what can be gained from adding additional monitors for a multimodal monitoring (MMM) strategy? (1)
However, the authors then added:
"This low mortality rate is in marked contrast to the report by EUSOS of an overall 4% or one in 25 mortality rate for in patient elective major surgery in Europe" (2)
They went on to comment that "these differences (80 fold difference in immediate and intermediate mortality) highlight the potential impact advances in perioperative care by anaesthetists, surgeons and intensivists might have on overall mortality rates after surgery". There is an urgent need to close the gap between the very low immediate perioperative mortality indicated above to the whole perioperative period and accept that poor management of the intra-operative course may start the "time bomb ticking" and lead to complications and mortality further down the line.

THE INCREASINGLY HIGH-RISK SURGICAL POPULATION

It was estimated that 1 million of the estimated 3 million operations carried out in the UK NHS in 2013 as part of the above survey were on patients aged over 65. (1) In a recent Australian and New Zealand study, 5% of patients over 70 died within 30 days of surgery. (3) The "Reason" study investigators commented that "strategies are needed to reduce complications and mortality in older surgical patients". Strategies and protocols need to be guided by monitors not "recipe books" and we need to individualise patient care. (4) Anaesthetists must recognise that deficiencies in intraoperative management may not produce immediate mortality but are deleterious for long-term patient outcome. Multimodal monitoring (MMM) as described in the article is an attempt to reduce those complications and overall mortality after high risk surgery, especially in the elderly.

NEW MONITORING TECHNOLOGY AND ITS USE IN THE OPERATING ROOM.

There have been very little advances in routine intraoperative monitoring in anaesthesia in the last 30 years since the clinical introduction of the pulse oximeter in 1984. Even in the latest trials, the addition of flow monitoring to routine monitoring does not appear to have had much benefit as far as either reduction in mortality or complications are concerned, and it is still around 5% in the elderly surgical population. (3, 5, 6) Although there is now evidence to suggest that the use of individual new monitors

can influence outcome, it will only be their combination that will radically improve the perioperative management on outcome of high-risk surgical patients. (7, 8)
Blood Pressure and Flow monitoring as part of a multimodal monitoring strategy
Most anaesthetists will try and maintain mean arterial pressure (MAP) during surgery within about 20% of the pre-induction value. What is the evidence that low MAP is harmful? A recent retrospective study from the Veterans Administration (VA) system in the USA showed that a systolic, mean or diastolic pressure less than 70, 50 or 30 mmHg respectively for more than 5 minutes was associated with a roughly 3 fold increase in 30 day mortality. (9)

USING FLUIDS TO MAINTAIN MAP

Intraoperative fluid management is still influenced by the ground breaking paper from Shires et al from Dallas published in 1961 in the Annals of Surgery. (10) The investigators used a triple indicator dilution technique which suggested that there was a profound loss of functional extracellular fluid during major surgery, later nicknamed "third space", which could amount to up to 15ml.kg-1 body weight hr-1 during major surgery This volume of balanced salt solution (e.g. Hartmann's solution) to replace this "loss" would be equivalent to 24 hours total body water requirements and 6 days Na+ requirement in a 3 hour procedure!
Interestingly, recent papers and reviews have confirmed that "there is no convincing evidence supporting the existence of the non-anatomical third space loss neither in haemorrhagic shock nor in surgery of any kind". (11-14) This highlights another problem. Third space loss does exist in conditions such as septic shock, anaphylaxis and burn injury and it is important to distinguish fluid and flow requirements in elective surgery in contradistinction to haemodynamic changes in the intensive care unit where sepsis may well be a serious problem. Reviews of fluid management often mix up these two completely different scenarios and thus cause unnecessary confusion! The dangers of excessive fluids and volume overload have recently been re-iterated by Marik. e.g. pulmonary oedema and increased extravascular lung water, impaired oxygenation, altered pulmonary and chest wall mechanics, increased work of breathing, myocardial oedema etc. The list is long. (15)

USING VASOACTIVE AGENTS TO MAINTAIN MAP

It is very easy to restore MAP to "normal" using vasoactive agents such as metaraminol, phenylephrine or noradrenaline. (16) However, MAP may then be maintained by increasing systemic vascular resistance (SVR) rather than CO and DO2.

CARDIAC OUTPUT CHANGES FOLLOWING INDUCTION AND MAINTENANCE OF ANAESTHESIA

Introduction
MAP fall following induction of anaesthesia is often ascribed to peripheral vasodilation with a fall in SVR. Kamenik and Petrun, using the LiDCO rapid (LiDCO, UK), were able to demonstrate that the fall in MAP following BIS (Medtronic, USA) targeted induction using either propofol or etomidate was mainly due to a fall in CO and not due to a fall in SVR). (17)
Why does MAP and CO fall during anaesthesia? Experiments using propofol in dogs showed that it produced an increase in venous capacitance due to venodilation (not peripheral arteriolar vasodilation), which we feel a key feature of anaesthesia that has been very little recognised. (18, 19) Following venodilation the fall in MAP is due not only to falling preload, SV and CO with a consequent reduction in oxygen delivery (DO2) but also due to a shift of volume out of the arterial tree into the dilated venous compartment. (19) This mimics hypovolaemia. The question is whether we should maintain venous capacitance with liberal fluids or by administration of a venoconstrictor? Phenylephrine, in low dose infusion commenced pre-induction, with the effect monitored by the LiDCOrapid (see later), can maintain venous tone (without increasing SVR), venous capacitance SV, CO and MAP without the need for liberal fluid administration. (20) It seems that liberal fluid replacement in surgery (see above) was simply given historically to overcome the effects of increase in venous capacitance rather than a true loss of functional extracellular fluid. This excess fluid can lead to complications in the later postoperative period. (15)
Post induction measurement of CO greatly underestimates the true resting CO/DO2 and therefore any intervention which is supposedly designed to "optimise stroke volume" (whatever that means) rather than maintain pre-induction CO/DO2 will be flawed and may result, as above, in unnecessary excess fluid and Na+ administration without improving outcome in high-risk patients _ENREF_15. (6,15)

Recommendation to add flow monitoring
In 2011 the National Institute of Health and Care Excellence (NICE) in the UK recommended the addition of flow monitoring using Doppler (Oesophageal Doppler, Deltex UK) technology for a distinct group of high-risk surgical patients undergoing particular surgical operations. (21) Even then, the guidance was questioned and argued over in editorials. (22, 23)

Update on circulatory physiology during anaesthesia.
Distinguishing between venodilation and vasodilation and the role of the intact endothelial glycocalyx layer (EGL) in controlling fluid exchange in the tissues has important implications for surgical fluid management19. Excess fluids and Na+ to replace non-existent "third space loss" are not only unnecessary but may actually damage the EGL directly by compression and distortion and also lead to an increase in atrial natriuretic peptide (ANP) which itself damages the layer. The implication is that "third space loss" may actually be precipitated by excess fluids!

Does the use of flow monitoring on its own when added to conventional monitoring improve outcome and reduce mortality?
In a recent Cochrane collaboration review entitled "Perioperative increase in global blood flow to explicit defined goals and outcomes after surgery", the investigators noted that using this strategy there was no decrease in mortality and length of stay was decreased on average by only one day. (24) There were reductions in complications which accounted for the reduction in length of stay. However, the investigators concluded "the balance of current evidence does not support widespread implementation of this approach to reduce mortality but does suggest a complications and duration of hospital stay are reduced". The Optimise trial, also did not reduce a composite outcome of complications or 30 day mortality. (5) A recent editorial concluded that SV optimisation/maximisation provides "no marginal benefit in aerobically fit patients having elective surgery within

a contemporary enhanced recovery pathway". (25)

Conclusion
It is clear that there has not been as much benefit as expected in particular there has been no effect on mortality reduction versus current practice and mortality remains unacceptably high. What is the way forward?

THE ROLE OF INDIVIDUALISED HAEMODYNAMIC THERAPY.

In a review of perioperative haemodynamic therapy the authors stated that "once an individualised approach will be identified, the terms of liberal, restrictive and supranormal values could eventually be replaced by adequate haemodynamic support that fits every patient's own needs". (4) The question is, can we identify a better individualised approach to further improve outcomes and in particular reduce mortality in this high risk patient group?
The goal should be directed towards avoiding the build-up of oxygen debt as this has been shown by Shoemaker et al to contribute to poor outcome. (26) MMM can be used to assess and maintain DO2 as close to the pre-induction level as possible during surgery and into the immediate postoperative period, thereby avoiding the build-up of oxygen debt. Lack of oxygen debt at the end of the procedure means that goal directed therapies (GDT) intended to increase DO2 by fluids and inotropes in HDU/ICU and thus repay debt5 or bring DO2 values up to pre-induction levels are no longer necessary and indeed may not benefit the patient anyway. (27)

CEREBRAL AND TISSUE OXYGEN MONITORING AS PART OF THE MMM STRATEGY

"The proper management of brain oxygenation should be one of the principal endpoints of all anaesthesia procedures yet the brain remains one of the least monitored organs during clinical anaesthesiology". (28) Near infrared technology (NIRS) using a reflectance technique can be used to measure cerebral tissue oxygenation to a depth of about 2.5 cm below the measuring electrodes which are usually placed on the forehead. Regional brain oxygen saturation (rSO2 or ScO2) also reflects overall tissue rather than arterial oxygen saturation or Spo2 as is assessed with a pulse oximeter. (29) Cerebral rSO2 is venous weighted with a characteristic value in healthy patients of around about 70% and is similar to jugular venous oxygen saturation. A detailed consideration of this technology is outside the scope of this chapter so the reader is referred to excellent reviews. (28-30) These monitors work best as trend monitors rather than absolute monitors emphasising the importance of getting a pre-induction value in elective patients.(28)
Apart from those neurological conditions where brain oxygenation is obviously suspect, for example carotid endarterectomy, many operations on the elderly may lead to reductions in rSO2 and poor outcome. (31-33) The problem is to define suitable interventions if rSO2 diminishes by more than about 10% from starting value. A MMM strategy which maintains flow and DO2 almost always insures that rSO2 will remain at or above the pre-induction level. (34)

Consideration of the role of cerebral oximetry in cardiac surgery where its clinical applicability is greatest is outside the scope of this article. However, the jury is out on it's true role but several studies have indicated possible benefits. (35-37)

My own experience with this monitoring technology amounts to nearly 1000 cases. These mainly include high-risk cases with an average ASA class of 3 or above, long duration where the build-up of oxygen debt will potentially be a problem and in the elderly population (average age 68) where oxygen debt is likely to cause most problems. Maintaining tissue oxygenation as assessed by the cerebral oximeter should lead to a reduction of oxygen debt and complications. (30) A recent review even suggests that cerebral and tissue oximetry should become the standard monitor of the future. (38)

DEPTH OF ANAESTHESIA MONITORING AS PART OF THE MMM STRATEGY

The figure indicates why monitoring the effect of the anaesthetic on cortical suppression is important for high-risk patients and may not be as important for fit and healthy patients. Looking along the x-axis from left to right, increasing anaesthetic concentration will inevitably lead to cardiovascular depression and decreased DO2. This obviously has implications for build- up of oxygen debt, complications in the post-operative period and poor outcome. It also is likely to produce neuronal toxicity as the concentration of anaesthetic increases. (39) On the other hand, moving from right to left along the x-axis, too little anaesthetic obviously gives one a risk of patient explicit recall and also we may lose the benefits of anaesthetic neuronal protection. So, there is a balance to be struck. The red curve indicates a low risk patient where the target anaesthetic concentration is rather broad and the implications of a small clinical misjudgement of the depth of anaesthesia (as indicated by the shallowness of the curve) means that not too much harm will likely come to the patient.

This is not the same situation in the elderly or high-risk patient in whom it is usually assumed that the amount of anaesthetic required is less and too light anaesthesia will lead to the patient waking up and moving around whereas a slight increase to deepen the anaesthetic may result in profound cardiovascular depression. All anaesthetists have observed this in their practice! However, 10 years' experience with the BIS monitor in high-risk patients, especially the elderly, have shown that some older patients require much more anaesthetic than others and indeed there is up to a fourfold variation in propofol anaesthesia requirement. (34) This variation cannot be predicted by clinical signs alone.

EXCESSIVE DEPTH OF ANAESTHESIA IS HARMFUL

This technology is now recommended by the National Institute of Health and Care Excellence (NICE) in the UK for high-risk patients and the latest Recommendations for Standards of Monitoring during Anaesthesia and Recovery 2015 from the Association of Anaesthetists of Great Britain and Ireland (AAGBI) include depth of anaesthesia monitoring during total intravenous anaesthesia when neuromuscular blockers are used. (40) Evidence shows that BIS guided anaesthesia decreases post-operative delirium and cognitive decline (POCD) and in the USA it is now recommended to reduce the incidence of delirium in older patients. (41-43)

USE OF COMBINED BIS AND CEREBRAL OXIMETRY TO REDUCE THE INCIDENCE OF POCD

In a cohort study and nested randomised controlled trial of high risk elderly patients undergoing major abdominal and orthopaedic surgery, using combined technology of BIS and cerebral oximetry as interventions, investigators were able to show a profound reduction in the intervention group in POCD. (44) Of interest was the fact that maintaining the BIS in the "normal" range (40-60) i.e. not too deep and not too light led to significantly lower levels of S100 B, an indicator of neuronal damage, in the intervention group.

Should we use a MMM strategy in high-risk patients?

One of the highest risk patient categories that are dealt with on a routine basis are those elderly patients who suffer a proximal femoral fracture. Recent guidelines suggest that monitoring of cardiac output, depth of anaesthesia and cerebral oxygenation should be considered alongside a basic monitoring setup in this high-risk group.(45)

Does the MMM strategy make a difference to outcome in high-risk surgery

An observational case series in 120 very high-risk patients undergoing major peripheral vascular surgery suggests benefits of reduction in 30 day mortality (only 0.8%) and amputation rate (2% at 1 year) as well as reduced requirement for postop HDU/ICU (8%) using the MMM strategy. (34)

It is crucial that future randomised controlled trials using flow monitoring should use the MMM approach mentioned above with efforts made to have appropriate levels of cortical suppression and maintain pre-induction values of CO and DO2 to within 10 to 15% of baseline. The technique of SV maximisation and GDT to a population-based target of 600 ml.m-2 BSA should be abandoned. (46) In addition, future trials should recognise that third space loss does not occur in elective major surgery and thus patients should only receive minimal maintenance fluid in addition to replacement of obvious volume losses, a point recognised in the Optimise trial protocol but not in other recent trials. (5, 6, 47)

THE FUTURE

It should become routine practice to use a MMM strategy to try to maintain perioperative DO2 to minimise build-up of oxygen debt as a key for successful outcomes in high-risk surgical patients. This is achievable now with the monitoring technology available. The recent arrival of finger-based non-invasive and continuous blood pressure monitoring with provision for converting the waveform into flow means that in the future all high risk patients could benefit from this strategy. (48)

CONCLUSION

MMM has advantages for the anaesthetist, the patient and the healthcare system. It pinpoints very clearly the physiological changes associated with anaesthesia and surgery from pre-induction to post anaesthesia care unit. It allows intervention strategies to be more focused and physiologically appropriate and allows a more rational approach to intraoperative haemodynamic management. As we get greater insight into intraoperative physiological change in our patients we can individualise management using strategies designed and centred on minimising the build-up of oxygen debt and thus this should improve outcome. The burgeoning of the elderly high-risk patient population mandates a new perioperative anaesthetic management strategy alongside ERAS. It would appear that MMM reduces the requirement for expensive HDU and ICU facilities and may decrease hospital length of stay and therefore reduce the cost of perioperative care by reducing patient morbidity and mortality.

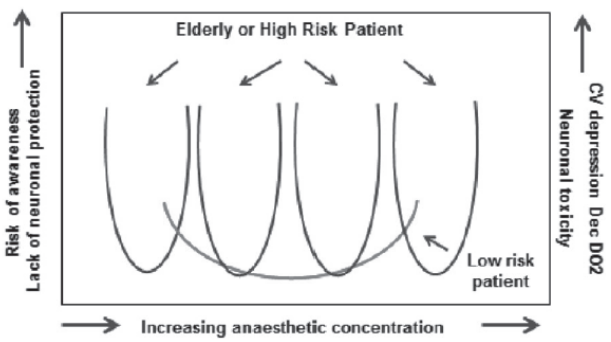

Figure 1. the x axis indicates that increasing anaesthetic concentration from low to high has an effect on the risk of awareness and lack of neuronal protection if the concentration is too low (left y axis) or on the other hand excessive cardiovascular depression and risk of neuronal toxicity in the concentration is too high (right y axis).

The low-risk patient is indicated by the red line which suggests that there is a wide margin of safety when choosing a suitable anaesthetic concentration and the risk of harm is minimal. This is indicated by the shallowness of the curve. On the other hand, with an elderly or high-risk patient, the implications for getting it wrong as indicated by the blue curves are much greater (steeper curves) and there is a much narrower margin of safety. Conventional wisdom suggests that most elderly or high-risk patients need very little anaesthesia as

indicated by the left-hand blue curve. However, there is a wide spectrum of anaesthesia requirements in the elderly or high-risk patient which means that they may require even more anaesthetic than the low-risk patient. Use of a cortical suppression monitor allows us to adjust for these differences and administer the correct amount of anaesthesia for the individual high risk patient.
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