Deltex Medical: Evaluation pathway submission – APPENDIX E

Oesophageal Doppler monitors measure changes in central vascular blood velocity directly. Other Cardiac Output monitors typically measure peripheral arterial blood pressure. As such Pulse Pressure Wave Analysis or Pulse Contour Analysis based devices are distinctly different in their mode of operation to Oesophageal Doppler Monitors and cannot be considered as equivalent.

Comparison of ODM to PPWA technologies

Patient benefit from Pulse Pressure Waveform Analysis (PPWA) technologies

Deltex Medical defines PPWA technologies as those that measure pulse pressure and use mathematical algorithms to extrapolate pressure data into flow metrics: these include the calibrated/recalibrated devices PICCO and LidcoPlus as well as those that claim no calibration/recalibration to be necessary (FloTrac and LidcoRapid).

Deltex Medical is aware of four published outcome studies using PPWA during surgery, two conducted with calibrated PPWA the other with uncalibrated PPWA. The first found that PPWA (PICCO) led to more fluid being given but found no changes in: organ perfusion; organ performance; mortality; length of ICU stay; length of hospital stay. The authors compared their results to the positive outcomes using ODM and speculated that PPWA was not sufficiently sensitive to guide fluid management. The second, a pilot study (LidcoPlus) reported no outcome benefits and noted increased length of hospital stay in the PPWA group (5.5 days) with more than twice as many PPWA than control patients in hospital on day 15. The third (FloTrac, manufacturer funded study) reported a significant reduction in complications and a four day median reduction in total hospital stay; only patients admitted to ICU post-operatively were included and there was no reduction in ICU stay. The fourth (Flotrac) reported reductions in complications post-operatively, but no reductions in mortality, ICU stay or length of hospital stay: analysis of those patients treated in accordance with protocol showed a one day reduction in length of hospital stay but not ICU stay.

The one published ICU outcome study, of which Deltex Medical is aware, has reported benefit from PPWA (via LidcoPlus). Patients haemodynamically managed in ICU for eight hours post-operatively were found to have statistically significant reductions in complications and length of hospital stay, but not length of ICU stay.

The results of this study have not been replicated. The results of a larger similar RCT were presented in October 2009. The primary outcome goal of this RCT was “Reduction in post-operative complication rates associated with the use of Goal Directed Therapy”, however the study found “there were no significant differences in morbidity, mortality or hospital stay”. This later data may raise concerns over the confounding results of the earlier trial, where patient randomisation was carried out by members of the study team only when surgery was complete and the fluid management protocol to address hypovolaemia allowed additional fluid to be administered by a member of the study team “if there was strong clinical suspicion of persistent hypovolaemia” (i.e. fluid could be administered in the intervention group even where PPWA indicated none was required); however Deltex Medical has not undertaken an objective assessment of any of the RCTs referred to in this section and has, for the purposes of its economic model, assumed the results to be reproducible.

Discussion

The benefits of ODM-guided fluid management have been shown during abdominal, general, orthopaedic and cardiac surgery and also post-operatively in both cardiac and trauma surgical patients. The patient management strategies are summarised in Table 1:

| Table 1 |
|---------|--------|-----|---|----|---|
| RCT     | Surgery type | Setting | SV change | FTC | CVP |
| Mythen⁷  | Cardiac     | Intra-op | >0%         | -  | Yes |
| Sinclair⁸ | Orthopedic  | Intra-op | 10%         | Yes| -   |
| McKendry⁹ | Cardiac     | Post-op ICU * | 10%         | Yes| -   |
These studies have been assessed in a number of meta-analyses and systematic reviews\cite{6,17,18,19,20,21}. The results of other RCTs and audits using ODM are summarised in Deltex Medical’s RCT and Audit database\cite{22}.

Table 1 indicates that the metrics critical to the ODM fluid management protocols are:

- Stroke Volume: most commonly to intervene if a change is greater than a cut-off point of 10%, and not intervene for a change of less than 10%; and
- Flow Time corrected: most commonly used as an indicator or ‘gatepost’ re vascular filling if the patient is within a pre-determined targeted range of FTc values.

To extrapolate ODM trial results to PPWA, it would be necessary to demonstrate that PPWA:

- Measures FTc or a validated equivalent; and
- Detects changes in SV sufficiently accurately to allow safe intervention based around a cut-off point of 10% (i.e. that a 10% change represents a genuine underlying change in the patient’s haemodynamics and that a change of less than 10% represents a genuine absence of underlying change).

However, all studies to date comparing PPWA to ODM, of which Deltex Medical is aware, have shown that Stroke Volume Variation (SVV) is not equivalent to FTc, that differences between consecutive SV readings on individual patients of substantially greater than 10% occur and indicated that PPWA regularly reports changes in the opposite direction to ODM\cite{29,30,31,32}. Other studies comparing PPWA to reference cardiac output technologies other than ODM have also shown sufficiently large differences to indicate that PPWA may not be able to detect reliably such small haemodynamic changes as ODM or identified specific issues with PPWA\cite{33,34,35,36,37,38,39,40,41,42,43,44,45,46,47,48,49,50,51,52,53,54,55,56,57,58,59,60}.

These findings suggest that PPWA devices may not detect underlying changes in SV of 10% sufficiently reliably to allow clinician intervention without frequent recalibration; further they may report changes in SV of over 10% which do not reflect underlying changes.

Deltex Medical’s analysis suggests that as SV is calculated differently between ODM and PPWA, (ODM being based on a direct measurement of circulating blood whereas PPWA is based on direct measurement of pulse pressure and estimation of arterial compliance) it may not be appropriate to use PPWA in managing treatment for patients during surgery where the patient’s haemodynamic status might be expected to change frequently due to factors such as moving the patient, administering or changing levels of anaesthetic agents, administering fluids, administering vaso-active drugs and patient bleeding or pain receptor activity.

Further studies need to be undertaken either to validate use of PPWA to measure changes in SV (during treatment of specific groups of patients) in surgery and ICU and to compare the values of SV obtained from PPWA and ODM in patients whose haemodynamic status is changing rapidly.

For the purposes of comparative effectiveness research in the UK, Deltex Medical considers that uncalibrated/unrecalibrated PPWA should be considered as a comparator technology to ODM during surgery as it is currently being used as a substitute for ODM in a number of NHS hospitals. Deltex Medical believes such use inappropriate based on the available evidence.
Deltex Medical does not believe that calibrated PPWA devices are valid comparators to ODM in surgery as they are not regularly used in this setting.
References


6. UK trials register www.controlled-trials.com/ISRCTN94850719


18. Phan TD, Ismail H, Alex Heriot AG, Ho KM. Improving Perioperative Outcomes: Fluid Optimization with the Esophageal Doppler Monitor, a Metaanalysis and Review. jamcollsurg,2008.08.007.


Systematic review of the clinical effectiveness and cost-effectiveness of oesophageal Doppler monitoring in critically ill and high risk surgical patients: see status at www.ncchta.org/project/1633.asp

Cost effectiveness of oesophageal Doppler monitoring for colorectal surgery. Contact MD Blasco Amaro JA Health Technology Assessment Unit (Unidad de Evaluacion de Tecnologias Sanitarias, UETS) Lain Enralgo Agency, Public Health System of Madrid, Madrid, Spain 28013


Maintenance of cardiac index within normal range during surgery is associated with mortality reduction in patients undergoing large urological surgery: contact Kula R, Szturz P, Sklenka P, Tichy J, Chylek V, Sukenik P, Neiser J Department of Anaesthesia and Intensive Care, University Hospital Ostrava, Czech Republic.

Delteux Medical RCT & Audit database (submitted as Appendix to submission)

Jonas M, Fennell J, Mills E. Intra-operative goal directed optimization of high risk surgical patients using pulse wave analysis. ASA 2007, abstract 104


Lees NJ, Singer M. Measurement of cardiac output using the Vigileo/Flotrac system and oesophageal Doppler: a comparison in mechanically ventilated critically ill patients. ESICM 2009 abstract 0037


Ceconi M, Favcett R, Grounds M, Rhodes A. A prospective study to evaluate the accuracy of...
pulse power analysis to monitor cardiac output in critically ill patients. BMC Anesthesiology 2008, 8:3
42 Cooper ES, Muir WW. Continuous cardiac output monitoring via arterial pressure waveform analysis following severe hemorrhagic shock in dogs. Crit Care Med 2007; 35:1724-1729
46 de Wilde RBP, Schreuder JJ, van den Berg PCM, Jansen JRC. An evaluation of cardiac output by five arterial pulse contour techniques during cardiac surgery. Anaesthesia. 2008; 62 (8) , 760–768
57 Marque S, Cariou S, Chiche JD, Squara P. Comparison between FloTrac-Vigileo and Bioreactance, a totally non-invasive method for cardiac output monitoring. Critical Care 2009, 13;R73
58 Eleftheriadis S, Galatoudis Z, Didilis V, Bougioukas I, Schon J, Heinze H, Berger K-U, Heringlake M. Variations in arterial blood pressure are associated with parallel changes in FlowTrac/Vigileo(R) - derived cardiac output measurements: a prospective comparison study Critical Care 2009, 13;R179