# Esophageal Doppler Monitor (EDM) guided individualized goal directed fluid management (iGDFM) in surgery - a technical review

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**Abstract**

Esophageal Doppler Monitoring (EDM) is an easy to use, accurate and minimally invasive methodology for the optimization of Stroke Volume (SV). The predominant EDM device (CardioQ-EDM™) utilizes a nomogram incorporating age, weight and height which was generated by calibrating descending aortic blood flow velocity directly against total cardiac output (CO) as measured by thermodilution, thus negating the need to adjust for upper body flow for accurate measurement of aortic diameter. The velocity-time integral generated by each left ventricular contraction thus equates to SV. Extensive validation studies have shown EDM to be reliable in studies comparing it to simultaneous measurements made with a pulmonary artery catheter (PAC) and other reference techniques, both in absolute values and for following trends. Esophageal Doppler monitoring directly measures blood flow velocity in the descending thoracic aorta by the change in frequency (Doppler shift) of a fixed 4.02 MHz frequency ultrasound beam emitted from a probe placed in the esophagus of the patient. The probe can be placed orally or nasally, the latter approach being more comfortable in awake patients, for example when undergoing surgery with epidural anesthesia alone.

Fluid management can be thus individualized to the Frank-Starling curve to safely deliver intravenous fluids to optimize SV. This is facilitated by the additional and unique flow-based parameters offered by EDM, such as Stroke Distance (SD), Flow Time corrected (FTc), Mean Acceleration, and Peak Velocity (PV), not available on pressure-based systems. These parameters provide invaluable information on left ventricular preload, afterload and contractility which, when combined with SV, are highly effective in accurately identifying hemodynamic changes and guiding appropriate fluid and vasoactive drug treatment. Esophageal Doppler Monitoring is particularly useful in hemodynamically unstable patients where it can track changes and therapeutic responses on a beat-by-beat basis. By measuring flow in a major central vessel (the aorta), its accuracy is not affected by changes in peripheral arterial compliance, resistance and impedance.

Individualized Goal Directed Fluid Management (iGDFM) of intraoperative surgical patients guided by EDM has been proven in 9 prospective randomized clinical trials (RCTs) to significantly reduce complications, unplanned ICU admissions, hospital stay and costs. Patient populations include major abdomino-pelvic, cardiothoracic, orthopedic and trauma. Individualized Doppler Guided Fluid Management (i-DGFM) is the only outcome validated methodology. Intraoperative delivery of fluid has been suggested to be of greatest benefit in the first quarter of the operative period. It is evident that not only does the right amount of fluid need to be administered to optimize SV but that the timing of its delivery is of equal importance. Three separate meta-analyses have confirmed the benefit of perioperative Doppler-guided goal directed fluid management. The US Agency for Healthcare Research and Quality; the US Centers for Medicare & Medicaid Services; the UK National Health Service (NHS) Centre for Evidence based Purchasing; a subsequent UK NHS Health Technology Assessment; and the British Consensus Guidelines on Intravenous Fluid Therapy for Adult Surgical Patients have all endorsed the use of EDM-guided iGDFM to improve patient outcomes after surgery.

Being minimally invasive, the EDM has relatively few limitations. Caution should be applied in patients with pathology of the oropharynx/esophagus and undue force should not be applied during probe insertion. This is similar to practices with naso– and orogastric tubes. Esophageal Doppler Monitoring can now be performed in awake patients utilising the dedicated probes for this application. Accuracy in measuring absolute values of CO may be affected by patients undergoing epidural anesthesia or in those with body metrics outside the nomogram range, however fluid management can be achieved using SD changes as these will still be reliable.

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## Introduction

Patients undergoing moderate and major surgery can carry a significant risk of mortality and morbidity. The level of this risk is dependent on a number of factors, including: the length and severity of the surgery; the age of the patient; and the presence of co-existing disease. A high percentage of patients (one report of 63%) exhibit clinically significant fluid depletion pre-operatively.[1, 2] In 1988 Shoemaker demonstrated that patients who were unable to maintain adequate levels of oxygen delivery ($DO_2$) had higher levels of morbidity and mortality than those patients who received cardiovascular optimization while undergoing major surgery. [3] Since that time there have been a number of randomized controlled trials that have demonstrated reductions in morbidity, length of hospital stay and costs of treatment following perioperative SV optimization with EDM in various surgical procedures.[4-16]

## Hemodynamic Monitoring

It is the primary function of the cardiovascular system to maintain a stable metabolic state at both the organ and cellular level. This is achieved by the delivery of adequate amounts of oxygen and other substrates to meet the demands of metabolism, and the removal of metabolic waste products from all the cells of the body. Esophageal Doppler hemodynamic monitoring enables the assessment of left ventricular output contributing to the assessment of oxygen delivery.

In the 1930's it was suggested that the measurement of mean arterial blood pressure (MAP) would not necessarily give accurate assessments of circulating blood volume [17] and since the 1940's it has been acknowledged that CO may be significantly decreased without an associated fall in MAP.[18] From the late 1950's there have been a number of clinical studies reported where the authors have described an association between increased perioperative CO and increased survival following major surgery.[19-21]

It has been demonstrated that routine physical assessment alone, which includes the measurement of blood pressure (BP), heart rate (HR) and urine output, often fails to reveal the true hemodynamic status of the cardiovascular compromised patient. Several recent studies have demonstrated that clinicians were only able to accurately predict the hemodynamic status in approximately 50% of the patients monitored using physical assessment and clinical findings alone.[22-26] Many factors may contribute to these findings, most notably the physiological cardiovascular compensatory mechanisms. These mechanisms divert blood from the peripheral and splanchnic circulations in response to hypoperfusion and consequently often mask the true nature of blood flow. Typically, while a patient may have a significant decrease in circulating blood volume and an associated decrease in CO, the initial compensatory response of peripheral and splanchnic vasoconstriction will result in an increase in systemic vascular resistance (SVR) and thus the patient will have a relatively normal MAP. The effects of these compensatory mechanisms inhibit the ability of pressure-based monitoring systems to accurately assess the decrease in blood flow and oxygen delivery.

After the introduction of the PAC in the 1970's it became the primary technique used for monitoring the hemodynamic status of the critically ill patient. Use of the PAC was widespread with estimates of approximately 1 million catheters used in the United States in 1996 alone.[27] Despite this extensive use, an improvement in patient outcomes has not been demonstrated in a number of randomized clinical trials. Additionally, recent evidence would suggest that an increase in morbidity and mortality is associated with the use of the PAC.[28, 29.] These unfavorable outcomes may be associated with a lack of knowledge regarding the optimal use of the PAC among clinicians, reports of which have been well documented.[30-32] These findings, along with the known risks associated with the use of PACs, have resulted in declining use of the PAC and to clinicians seeking alternative less invasive hemodynamic monitoring techniques.

The minimally invasive nature of the EDM makes it a suitable method for hemodynamic assessment in the operating room. In contrast, traditional Fick based techniques, such as dye or thermodilution, are more difficult to apply in the intra-operative period due to their extended set up time, complex calibration requirements and the potential for drug interaction with the chemical agents used for calibration. The EDM is considered useful for most moderate to high-risk surgical patients who would not otherwise warrant the risk of the insertion of a PAC, arterial or central venous pressure (CVP) line.

### The Doppler Principle

On the 25th May 1842, Christian Doppler presented a paper in Salzburg, in which he proposed that the velocity of a moving object is proportional to the shift in reflected frequency in an optical wave of known frequency.[33] The principle also applies to sound waves. The received frequency of sound or light waves emitted by or reflected from a moving object is proportional to the relative velocity between the object and the receiver.

Doppler's hypothesis was formulated in relation to light emitted by double stars and it was not until 1845 that Buys Ballot confirmed it empirically using sound waves.[34] The principle was finally revised by Edwin Hubble in 1929. For example, the pitch of the sound waves emitted by a car (object) moving towards you (receiver) will increase in frequency, while the pitch decreases in frequency as the car moves away from you. This is known as the Doppler effect. Today the Doppler effect is widely used to measure the speed of motor vehicles, predict atmospheric events, and calculate the distance of celestial bodies. Applying the Doppler principle to sound waves, technologies have been developed that can measure blood flow velocities and other related hemodynamic variables.[35]

The Doppler equation is as follows:

$$f_D = \frac{2\ v\ \ f_T\ \cos\theta}{c}$$

this can be rearranged to measure velocity as:

$$v = \frac{c\ f_D}{2\ f_T\ \cos\theta}$$

where v is the velocity of the red blood cells, c is the speed of the ultrasound waves through body tissues (1540 $m.s^{-1}$), $f_D$ is the Doppler frequency shift, $f_T$ is the transmitted frequency of the ultrasound and cos θ is the cosine of the angle of insonation between the sound beam axis and the direction of blood flow.

The esophagus is a convenient, minimally invasive access point, allowing ultrasound transmit and receive piezo-electric crystals to be located close to the descending aorta (Figure. 1). When using ultrasound Doppler to measure flow velocity, the angle of insonation is an important parameter (Figure 2). The angle of insonation is the angle between the Doppler ultrasound beam and the direction of blood flow in the vessel being examined. At large angles of insonation the errors in calculating blood flow velocity due to small errors in angle of measurement become unacceptably high (Figure 3). In fact, ultrasound directed at 90° to the flow path does not undergo a Doppler shift as the cosine of 90° is zero. At angles less than 45°, a 2° overestimation of the Doppler angle will give an over-estimation of the true blood flow velocity of less than 5%. The most commonly used EDM is designed to insonate at 45° with the probe shaft lying in the esophagus and parallel to the aorta and it is generally recommended that devices use an angle of

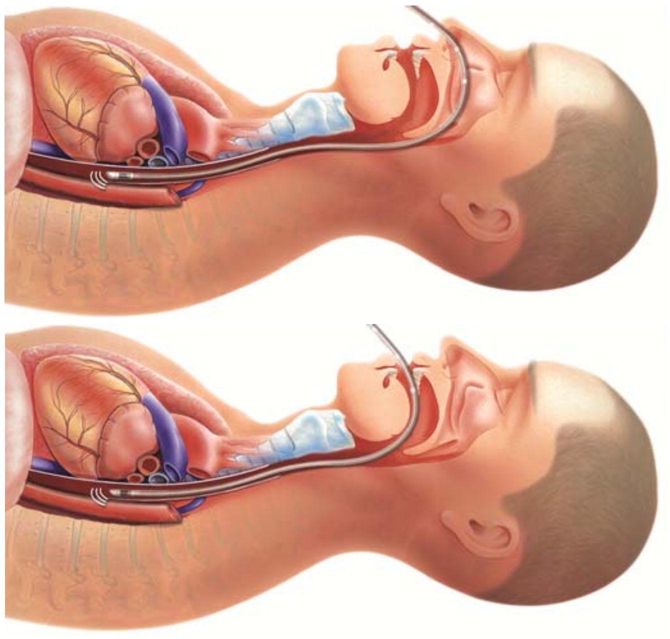

**Figure 1.** Nasal and oral positioning of esophageal probe in relation to the aorta

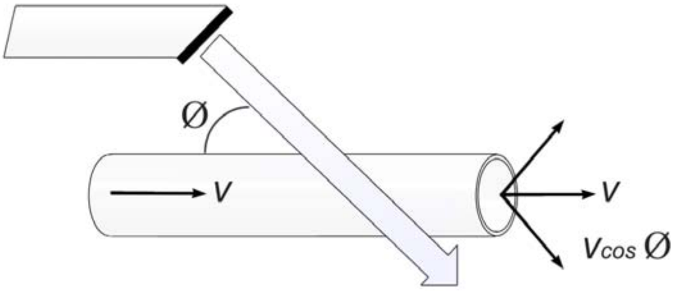


**Figure 2.** Derivation of the V cos θ component of velocity away from the transducer

insonation of <60°.

It was Satomura in 1957 and later Franklin in 1961 who were amongst the first to use the Doppler principle to measure red blood cell velocity in humans.[37, 38] Since that time Doppler velocimetry has become a commonly used technique in many different medical applications and is utilized for the measurement of aortic and peripheral blood flow and intracardiac flow patterns.

During the intraoperative period anesthetists can utilize

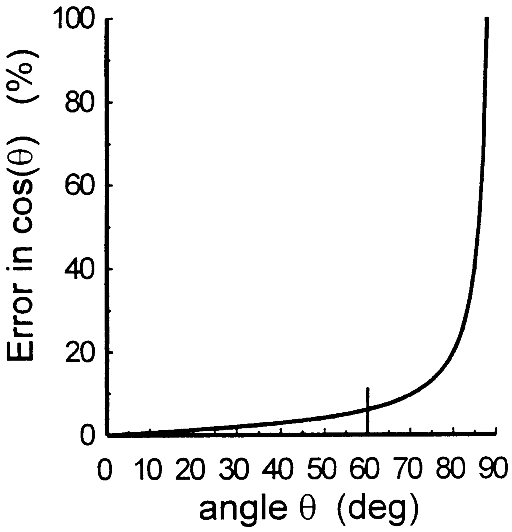


**Figure 3.** Potential for error due to a 2° uncertainty in the angle of insonation- redrawn from Cardiovascular and Haemodynamic Waveforms Explained - Oates 2008.[36]

EDM to measure descending thoracic aortic blood flow and derive CO. The EDM produces a velocity-time waveform that graphically displays the pulsatile blood flow in the descending thoracic aorta. This information can then be used as the basis for optimization of SV. Esophageal Doppler monitoring requires the insertion of a lubricated probe into the esophagus of a patient. The angled tip of the probe contains ultrasound crystal transducers (piezo-electric) that are oriented towards the descending thoracic aorta. Red blood cells within the blood stream possess a higher density compared to that of the surrounding plasma. This density difference acts as an 'acoustic impedance mirror' to reflect the ultrasound emitted from the stationary probe.[36] The shift in the frequency of the reflected ultrasound waves returned from the moving red blood cells is converted into a 'beat to beat' real-time display of blood velocity against time. The esophageal Doppler waveform not only provides for the derivation of CO, but also illustrates real-time changes in blood flow for qualitative assessment of preload, afterload, and contractility.

The Esophageal Doppler Monitor manufactured by Deltex Medical (Figure 4) utilizes a disposable probe, which emits continuous wave ultrasound. Ultrasound is emitted by one transducer in the probe tip, while another transducer, also in the probe tip, continuously receives the ultrasound reflected by the moving blood (Figure 5). A proprietary nomogram is contained in the software of the EDM to convert the measured descending thoracic aortic blood flow velocity into total left ventricular SV. The research for the nomogram was performed by Prof. Mervyn Singer of University College London, and it uses the patient's age, weight, and height to generate a

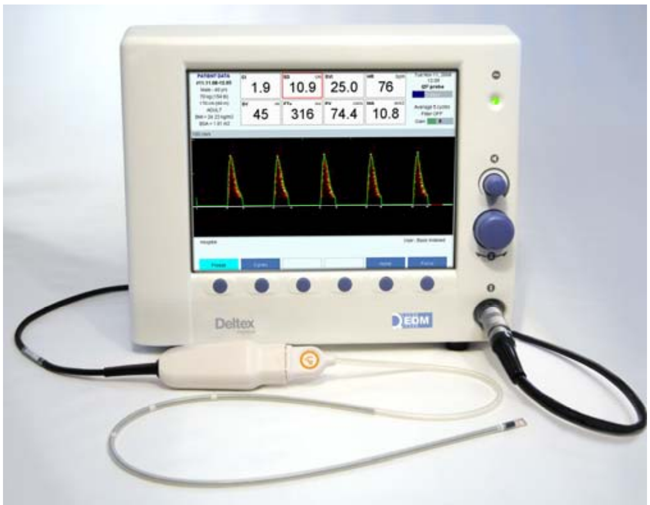


**Figure 4.** CardioQ-EDM™ Esophageal Doppler Monitor.

conversion factor and does not rely upon any other measurement.[39]

There are some mis-understandings in the literature as to how EDM derives the total CO while measuring flow only in the descending aorta. [40, 41] Approximately, 30% of blood flow leaves the aorta before this point to feed arteries supplying the heart, brain and limbs. [42] Some reviews have made assumptions that EDM monitors make a 70:30 correction to derive the total CO. [40,41] This is not strictly accurate as the manufacturers have taken different approaches to derive the total CO. [42,43] The

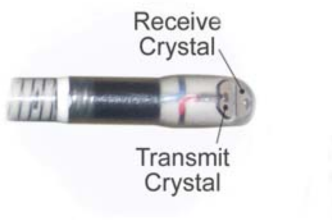


**Figure 5.** Receive and transmit ultrasound piezo-electric crystals

Hemosonic 100 device (formerly marketed by Arrow International, Reading, Pennsylvania, USA) utilizes M-mode echo to measure descending thoracic aortic diameter directly, and then uses a calibration factor to extrapolate this value to an estimate of total left ventricular SV. M-mode measurement of the aortic diameter may potentially introduce large discrepancies, as an 8% error in diameter measurement during systole (e.g. 2 mm variation from a true 25 mm diameter) will generate an approximate 16% error in cross-sectional area. In comparison the CardioQ-EDM (Deltex Medical, Chichester, UK) incorporates a nomogram created by 'calibration' of total left ventricular SV as measured by the PAC against descending aortic blood flow velocity and SD as measured by the EDM.

**Table 1 Studies correlating EDM with alternative methodologies for Cardiac Output measurement – primarily the Pulmonary Artery Catheter (PAC)**

| Author | Compared to: | Population | n-data points | r | Bias/ Precision |
|---|---|---|---|---|---|
| Shaw* | PAC | Critical Care | 10/14 | 0.91 ($r^2$) | 0.11/0.72 |
| Seoudi* | PAC | Critical Care | 15/187 | 0.89 | NR |
| Di Corte* | PAC | Perioperative | 34/160 | 0.77 | NR |
| Tibby* | PAC | Paediatric | 100/198 | 0.88 ($r^2$) | NR |
| Hersey* | Surface Echo | Paediatric | 12 | 0.8 | NR |
| Madan* | PAC | Critical Care | 14/118 | 0.6 | NR |
| Kincaid* | PAC | Critical Care | 7/36 | 0.79 | NR |
| Valtier* | PAC Fick | Critical Care | 46/138 53 | 0.95/0.95 | 0.24/NR |
| LeFrant* | PAC | Critical Care | 49/320 | 0.89 | NR |
| Guzzetta* | PAC | Perioperative CABG | 19/127 | 0.65 | ±2.9 |
| Cuschien* | PAC | Critical Care | 10 | 0.85 ($r^2$) | NR |
| | Fick | | | 0.81 ($r^2$) | |
| | PAC vs Fick | | | 0.72 ($r^2$) | |
| Cariou† | ABF vs | Critical Care | 20/80 | 0.8 | NR |
| Bernardin† | ABF vs | Critical Care | 22/60 | 0.92 | NR |
| Klein† | ABF vs | Perioperative | 48/171 | 0.9 | NR |
| Loik* | PAC | Critical Care | 13/24 | 0.74 ($r^2$) | 0.125/1.18 |
| Catogni* | PAC | Preop CPB | 14/40 | N/A | -0.235 |
| | | Postop CPB | 14/41 | | 0.074 |
| Nakatsuka* | PAC | Perioperative Liver transplant | 7 | 0.96 | 0.296 |
| Sorohan* | PAC | Periop CPB | 50/354 | 0.91 | +0.2/0.5 |
| Carrion* | Fick | Perioperative | 15 | 0.72 | NR |
| Carcellar* | PAC | Critical Care | 15/176 | 0.78 ($r^2$) | 0.196/2.188 |
| Klotz* | PAC | Aortic Surgery | | | |
| | | Pre-clamp | 6/75 | 0.84 | -0.96/NR |
| | | Post-clamp | 6/55 | 0.79 | -1.51/NR |
| | | Post-clamp | 6/65 | 0.76 | -1.47/NR |
| LeFrant* | PAC | Critical Care | 11/85 | 0.93 | NR |
| Belot* | PAC | Critical Care | 44/127 | 0.86 | NR |
| Muchada† | ABF vs | Perioperative | 21/300 | 0.97 | NR |

*CardioQ-EDM Deltex Medical † Hemosonic Arrow International, ABF=Aortic Blood Flow, CPB= Cardiopulmonary bypass, NR=Not Reported, PAC=Pulmonary Artery Catheter, Table redrawn from Turner 2003 [67].

In this way any fluctuation of the aortic diameter is implicitly included in the calculation and as calibration is against total cardiac ejection there is no 70:30 proportioning required. [42]

**Accuracy of esophageal Doppler monitoring**

The reliability of the technology is widely supported with a large body of evidence demonstrating its accuracy for the measurement of CO when compared to the "clinical standard" methodology of the PAC (Table 1) .[44 -66] The Esophageal Doppler Monitor measures blood flow velocity by highly accurate spectral analysis of the frequency-shifted (Doppler) signal. This real-time spectrum displays the distribution of red blood cell velocities at any given point in time. The EDM automatically traces the maximum velocity of the spectrum and, by calculating the area under this maximum-velocity curve during systole, a beat-to-beat value for SD is given, which is the distance a column of blood moves in the aorta during systole. This is shown graphically in Figure 6.

The calibration nomogram built-in to the device's software is accessed by entering the patient's age, weight and height data. From this the EDM calculates the SV using the measured SD. Since the machine automatically calculates the patient's HR from the spectrum, it can also provide a beat-to-beat measurement of CO (SV x HR). The nomogram was constructed by correlating EDM measurements of SD against simultaneous SV measurements made by PAC thermodilution, over a wide range of patients of differing ethnic origins varying in age, weight and height.[39]

The accuracy of the SD calculation is dependent on the precision of both the velocity measurement (typically ± 0.25

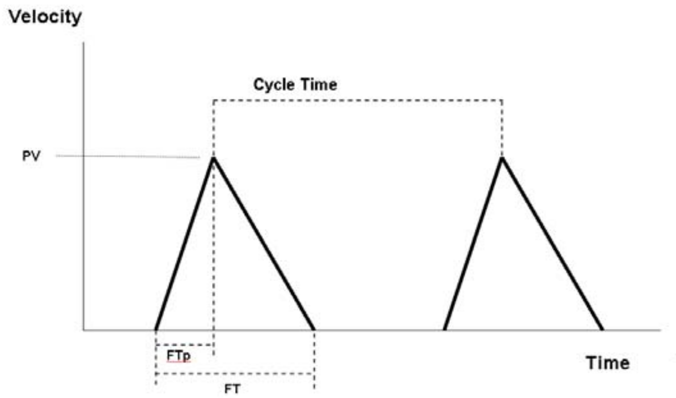


**Figure 6.** Stylized waveform of Velocity/Time display
PV is the Peak Velocity measured during systole (in $cm.s^{-1}$).
Flow Time (FT) is the time of systolic aortic blood flow (in ms).
Flow Time to peak (FTp) is the time from the beginning of systole to the point when PV is detected (in ms).
Cycle time is the time between identical successive points of the systolic waveform (in ms).

$cm.s^{-1}$) and the flow-time measurement (± 3 ms). Ultimately, the accuracy of the spectral analysis is dictated by the accuracy of the quartz crystal clocks (typically ± 0.005%). Repeatability for a known spectrum is better than ± 1% for the measurements of SD, PV, FT and HR, upon which all other calculations are made.

Conversion of the SD into SV is dependent on the accurate measurements made of PV, FT and FTc. The HR is also recorded by the monitor. The adult EDM nomogram contains extensive patient data for patients from 16 to 99 years of age, 30 to 150 kg in weight and 149 to 212 cm in height. Once the nomogram is accessed, the EDM monitor will continuously display the selected hemodynamic parameters.

**Probe Placement and Focusing**

The insertion of a disposable esophageal Doppler probe is similar to the placement of an oro/naso-gastric tube and usually takes an average of 2-3 min. [68,69] Both clinicians and nursing staff, depending on the protocols of individual institutions, may perform this simple procedure. Patients are usually sedated, however recent publications have described a protocol for placement of esophageal Doppler probes in awake patients using a new more flexible probe.[70, 71]

Probes are inserted orally to a depth of approximately 35-40 cm from the incisors, or nasally to a depth of approximately 40-45 cm from the nasal septum. In either case this will place the tip of the probe in the region of the 5$^{th}$ or 6$^{th}$ thoracic vertebrae. At this level the esophagus is typically parallel with and approximately 1cm from the descending thoracic aorta. The probe is manipulated by the operator adjusting depth and rotational position by using small movements until the characteristic descending thoracic aortic waveform shape is visualized and the distinctive Doppler "whip crack" sound associated with aortic blood flow is heard. An EDM is not a "hands free" continuous monitor and a degree of refocusing will be required, particularly if the patient is moved significantly. Esophageal Doppler monitors do however offer continuously available, minimally invasive data.

Focusing the ultrasound beam into a position that maximizes the waveform display is straightforward. The blood flow velocity profile in the descending thoracic aorta is distinctive in that it differs from that typically found in most vessels. Due to the proximity of the heart and its pulsatile pumping action the flow velocity profile in the descending aorta is referred to as "plug flow". Unlike a typical parabolic velocity profile where the flow is largest in the centre of the vessel and decreases to zero at the wall, in plug flow the peak velocity of flow is present across a large part of the internal diameter of the vessel [72] (Figure 7). An optimal pitch and a sharp visual image can therefore be accepted as evidence of correct probe positioning. As a result focusing on the peak flow in the aorta is considerably easier than would at first be thought. Additionally the ultrasound beam is approximately 5 mm in width and the large aortic luminal diameter results in a "go/no-go" focusing result. The probe may require occasional adjustment to ensure an optimal signal. These adjustments typically take a few seconds.

**Waveform and Parameters**

The waveform provides valuable clinical information. The real-time waveform displayed on the monitor is the integral of the velocity of the blood passing the tip of the probe. A normal waveform will be triangular in shape (Figure 8). The peak of the triangle represents the PV detected during systole. The upslope of the triangle depicts the acceleration of blood as it is ejected down the descending thoracic aorta at the beginning of systole. The area under the velocity-time waveform is the SD. Stroke distance is the distance a column of blood will travel down the aorta with each left ventricular contraction.

Any change in the left ventricular output will cause a proportional change in the descending thoracic aortic blood flow, which will in turn cause a change in the size and shape of the waveform. This assumes fixed proportionality of upper and lower body blood flow and that the aortic diameter remains

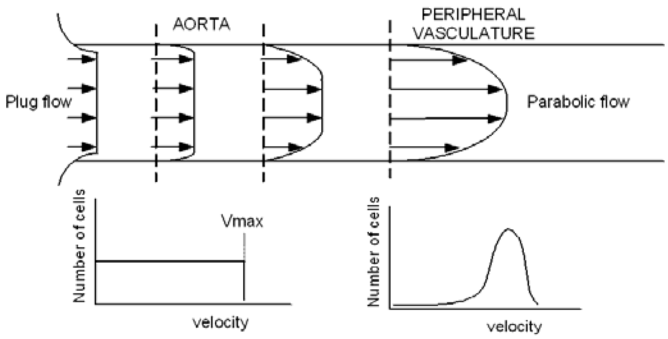


**Figure 7.** Vascular fluid dynamics – Peak Velocity flow profiles Redrawn based on Caro et al [72]

constant during the period of the measurements. An increase in flow will result in the waveform increasing in size and consequently the area under the curve will also be increased. Conversely when left ventricular output is decreased, the blood flow decreases and the area under the curve will be less. This demonstrates a proportional relationship between SV and the area under the systolic portion of the waveform. The velocity-time waveform display provides real-time information on changes in blood flow and left-ventricular function. Examination of the shape and size of the waveform can be used to identify specific hemodynamic changes.

The EDM has the facility to store 'snapshots' of patient data at various stages of therapy. A "snapshot" captures the image of the waveform and a display of all twelve of the monitors recorded parameters. Snapshots are a useful adjunct to the assessment of hemodynamic changes in the patient as treatment proceeds.

Esophageal Doppler monitoring enables several measured and derived parameters to be assessed. Three of the primary measurements are, SD, FT, and PV. It is important to note that

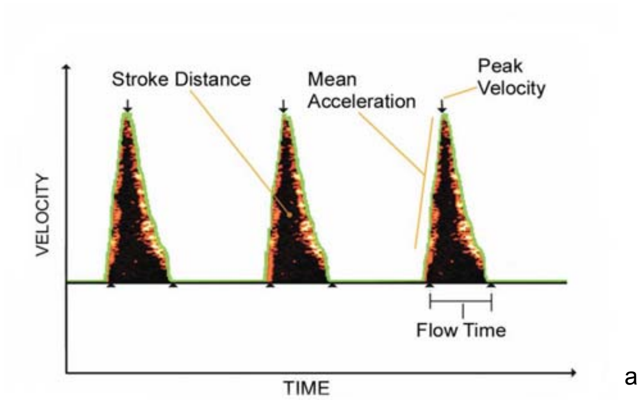


**Figure 8.** Waveform displaying Stroke Distance, Peak Velocity, Mean Acceleration and Flow Time measurements

true measurement of SV and CO does not exist. Therefore the absolute value of SV and CO may be subject to some imperfection. This holds true for all technologies providing these parameters. However with the EDM it is extremely easy to identify a high, adequate, or low cardiac output state. Trending of the derived parameters is of greater clinical value and is extremely useful in guiding therapies.[42]

### Stroke Volume and Cardiac Output

The area under the systolic portion of the waveform is defined as SD (Figure 8). The SV is calculated from the measured SD and a calibration constant derived from the nomogram. CO is then calculated by multiplying the SV by the HR.

### Preload

Preload is understood clinically as the degree of ventricular filling such that a low preload equates with under filling due to for example, hypovolemia or an obstruction in the circulation (e.g. pulmonary embolus) whereas an excessive preload is associated with intravascular fluid overload. The width of the base of the waveform represents the systolic ejection time and is expressed as FTc. This is the measured flow time corrected for HR in the same way as the Q-T interval of an ECG is corrected. This is achieved using Bazett's equation.[73] The measured FT (Figure 8) is divided by the square root of the cardiac cycle time thus adjusting the heart rate to 60 bpm. This results in one corrected cardiac cycle per second. Normally systole is approximately one-third of the cardiac cycle at a heart rate of 60 bpm, (i.e. a third of a second). The FTc is displayed on the EDM in milliseconds (ms) and a number in the region of 330 ms to 360 ms is considered normal. However in patients undergoing regional or general anesthesia there may be cases when their SVR is altered by the anesthetic agents. Consequently caution should be observed in using FTc alone to assess hypovolemia in surgical patients. SV and SD are the preferred index for guiding and monitoring hemodynamic optimization.

The FTc is inversely correlated with the systemic vascular resistance and can be expressed as:

$$\mathrm{FTc} \;\; \alpha \;\; \frac{1}{\mathrm{SVR}}$$

Therefore a narrow waveform base (<330 ms) is an indicator of vasoconstriction, of which hypovolemia is the commonest cause.

Studies have reported that changes in FTc are as good or better than pulmonary artery wedge (or occlusion) pressures for indicating changes in preload.[74 - 77] Flow time corrected has also been reported as useful in predicting fluid responsiveness particularly when used in conjunction with other clinical information and CVP measurements. [79] Pulmonary artery occlusion pressure is still widely used to assess intravascular volume status, despite it having been shown to be a relatively poor indicator of preload.[79, 80]

### Contractility

Contractility is the inotropic status of the myocardium. The PV measured by the amplitude of the waveform, is a marker of contractility. Contractility decreases with age from typically 90 to 120 $cm.s^{-1}$ in a 20 year old to 30 to 60 $cm.s^{-1}$ in a 90 year old. In a hypo-contractile state such as left ventricular dysfunction, the waveform will appear dampened with decreased amplitude, resulting in a low PV. If the left ventricle is stimulated with a positive inotrope, the amplitude of the waveform will increase. Mean Acceleration, the average acceleration of blood from the start of systole to detected PV, is also a marker of contractility and can be used to guide inotropic therapy.

### Afterload

The afterload is the resistance or 'load' against which the heart has to eject blood. It affects the relationship between the width and amplitude of the waveform. An increase in afterload may be noted by a simultaneous reduction in both the FTc and PV, resulting in a narrow waveform with decreased amplitude. This may be seen with any condition causing vasoconstriction, e.g. hypovolemia, flow obstruction, excess vasopressor, hypotension or hypothermia. A reduction in afterload will result in an increase in amplitude (increased PV) and a widening at the base (increased FTc), as the left ventricle has less resistance to pump against. It is important to remember that any changes in the size of the waveform represents proportional changes in SD and therefore SV.

### Individualized Goal Directed Fluid Management

Enhanced Recovery After Surgery (ERAS) programs are gaining increasing importance. The challenge to the modern clinician is the improvement of patient care combined with a reduction in hospital costs.[81-83] While many ERAS programs are still in their infancy and yet to fully introduce the complete package of possible care management initiatives, major advances have been made in numerous centers within Europe. Colorectal surgery has been a leading discipline in the implementation of fluid management as a major component of enhanced recovery and many have reported significant improvements in patient outcome and reductions in costs.[84– 87]

Individualized Goal Directed Fluid Management is based on optimization of SV. Thus, in its simplest form iGDFM is achieved through the administration of fluid, most often a colloid, guided by an algorithm to enhance SV without the risk of fluid overload. Numerous authors have developed algorithms based on the measurement of SV, CVP, and FTc.[4 -16]

These algorithms utilise the Frank-Starling law, which describes the relationship between left ventricular SV and left ventricular end diastolic volume (Figure 9). The Frank-Starling law states that: "Within limits, the greater the heart muscle is stretched during filling, the greater will be the force of contraction and the greater the quantity of blood pumped into the receiving vessels".

When a colloid challenge is given to a patient who has a low left ventricular end diastolic volume, a significant rise in SV is expected. Conversely if the patient has a high left ventricular end diastolic volume, little or no increase in SV is expected for the same challenge volume. A typical perioperative SV optimization algorithm is shown in Figure 10. As described earlier, the calculation of SV by an EDM is based on the highly accurate measurement of SD. Because SV is SD multiplied by a constant provided by the built-in calibration nomogram of the EDM, SD and SV are directly related. Stroke Distance is a useful parameter for guiding therapy in any circumstance where the patient parameters are outside the nomogram limits (e.g. due to obesity), during periods of aortic cross clamping, or where epidural use alters the upper/lower flow proportionality. Stroke Volume Index (SVI) may also be used if preferred, which is SV normalised to body surface area.

Patients are challenged with 200 mL of fluid (colloid) over 5 minutes. Following the challenge the result is monitored using an EDM. If the SD or SV increases 10% or more this indicates that the patient's left ventricular end diastolic volume is not optimal and that a further colloid challenge should be delivered.

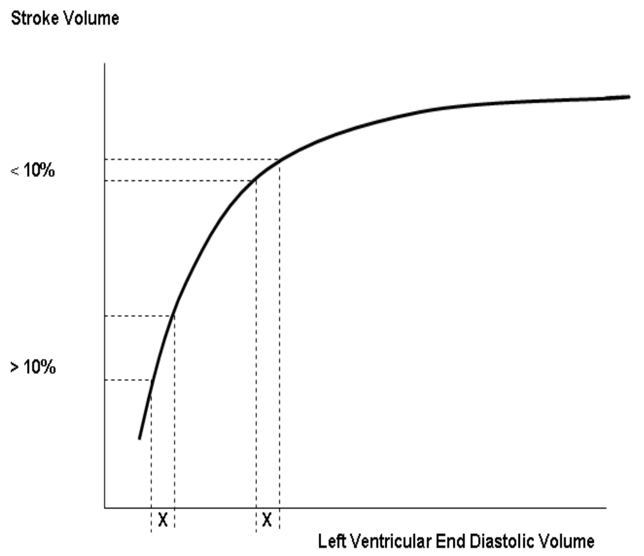


**Figure 9.** Frank-Starling Curve

Fluid challenges are repeated until the change in SD or SV as monitored by the EDM is less than 10%. A change of less than 10% either suggests the left ventricular end diastolic volume has been optimized or that the patient is losing fluid at a rate equal to or greater than that of infusion. Stroke Distance or SV are then monitored and if a decrease of 10% or more is observed or if there is excessive fluid loss then a further colloid challenge is given. Fluid challenges given as part of perioperative SV optimization are additional to the normal fluid

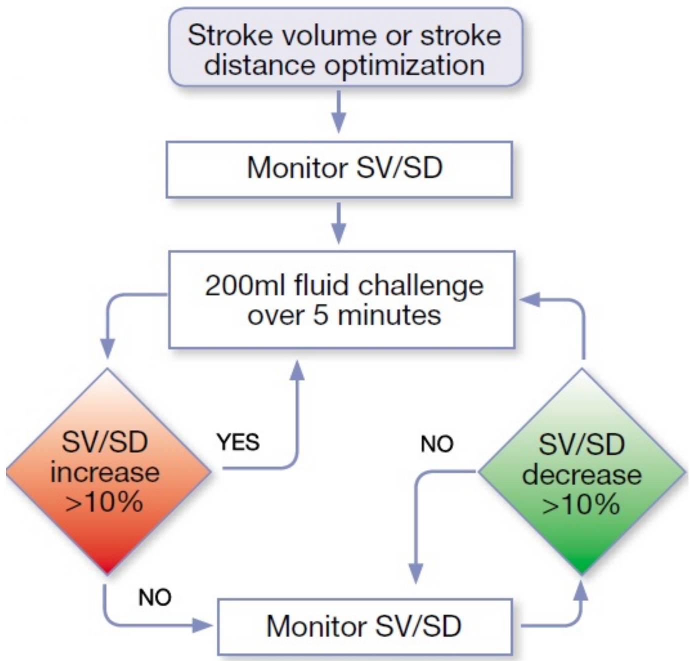


**Figure 10.** Typical perioperative Stroke Distance or Stroke Volume

maintenance. A number of algorithms have utilised FTc as an indicator of hypovolemia. Flow Time corrected is often used as an indicator of hypovolemia and fluid responsiveness, however during anesthesia the vasodilatory effects of anesthetic agents should be considered. Anesthetics and other vasoplegic agents may create a decrease in left ventricular afterload such that the baseline FTc may be elevated above the normal range of 330 ms to 360 ms. Clinicians need to be aware of these effects and to take other parameters into consideration so as not to rely solely upon single parameters for fluid management.

It is recommended therefore that SD, SV or SVI be used as the primary guiding parameter for individualized Doppler guided fluid management.

**Clinical Application**

Esophageal Doppler monitoring may be used in many clinical settings, including the operating room, the intensive care unit (ICU), the post-anesthesia recovery unit and the emergency or trauma department. Many patient groups will benefit from the use of EDM including those undergoing surgery, particularly moderate to high-risk patients, patients with large volume blood loss, the elderly, critically ill patients with an unstable hemodynamic status and those at risk of hypoperfusion or fluid overload due to inadequate left ventricular function.

In the context of EDM as applied to surgery, esophageal Doppler monitoring has been proven to be beneficial in patients undergoing operations of longer than 1 hour duration and/or where the surgery involves entry into a body cavity or during orthopedic surgery.[4-16] Table 2 summarises the surgical criteria for use of EDM as reported in the literature. The EDM is also useful in detecting changes that might otherwise go unnoticed. The hemodynamic data can also guide the titration of vasopressors and inotropes as well as fluids.

In recent years SV optimization using the EDM has been used to enhance $DO_2$ in the perioperative period. Hypovolemia is a significant contributor to tissue hypoxia. Any degree of hypovolemia jeopardizes oxygen transport and increases the risk for tissue injury or death.

Dubniks, in a thesis entitled “Aspects of Fluid Therapy” stated that hypovolemia implies a reduced circulating blood volume and is one of the most common reasons of circulatory instability in surgical and critically ill patients.[89] Hypovolemia can be absolute or relative. Absolute hypovolemia is the result of hemorrhage, external or internal fluid losses. Internal fluid losses due to increased microvascular permeability is a common reason for hypovolemia in critically ill patients suffering from sepsis, shock or systemic inflammatory reaction syndrome. Relative hypovolemia can result from vasoplegia, which can be caused by pharmacologically induced vasodilation during anesthesia.[90-94] Dubnik further states that hypovolemia leads to reduced venous return and inadequate cardiac preload, decreased CO and insufficient oxygen

| ASA Grade | Anerobic threshold mL/min/kg | Body cavity exposed/ penetrated | Orthopedic surgery |
|---|---|---|---|
| 2 or more [4,5,7,11,12,14,15] | <13.9 [88] | Yes [4,7,12,14,15] | Yes [5,11] |

**Table 2.** Summary of criteria for use of EDM in surgery

delivery to the tissues. The decrease in circulating volume triggers activation of the baroreflex originating from stretch receptors in the central veins, the right atrium, in the carotid sinus and in the aortic arch. This leads to an increase in sympathetically mediated vasomotor tone in venous system aimed to preserve central blood volume, cardiac preload, CO and MAP. Unloading of the arterial baroreceptors results in arterial vasoconstriction, which is selective to maintain perfusion in the vital organs such as the brain and the heart. Simultaneously, however, it will result in hypoperfusion in regional beds, such as the splanchnic area, skin, and muscle.[89,95,96] The consequences of decreased oxygen delivery and impaired microcirculatory flow are tissue hypoxia and oxygen debt [97] which, if not corrected early,[98] leads to cell damage, organ dysfunction, multiple organ failure (MOF), and death.[94, 95, 97, 99]

It is important to also recognize that this covert tissue hypoxia in various organ beds may not be detected by conventional means because BP may frequently remain stable. Hamilton-Davies evaluated commonly measured cardiovascular parameters after removing 25% of circulating volume from healthy volunteers, and found no significant changes.[100] Price reported similar findings in that a 40% reduction in splanchnic blood volume resulted from only a 10-15% reduction in blood volume of healthy volunteers. This further demonstrated that systemic circulation was maintained at the expense of the splanchnic bed.[101] Fluid therapy aimed at restoring and maintaining circulating blood volume is, therefore, an important part of the complex circulatory management of perioperative patients. [89]

Esophageal Doppler monitoring can be used to correct hypovolemia in the patient who may be at risk. In an observational study, EDM has been shown to detect subsequent complications in the critically ill.[102] The goal of the study was to compare esophageal Doppler parameters with standard hemodynamic variables (MAP, CVP, HR, arterial base-deficit, and urine output) used to predict complications after cardiac surgery. The results showed that EDM monitoring of SV was the best marker for predicting post-operative complications during the initial postoperative period. Furthermore, those patients who developed complications received less volume in the first four hours postoperatively. Several studies have demonstrated that intraoperative SV optimization guided by EDM significantly improves outcomes as evidenced by a decreased length of hospital stay ranging from 30-40%.[4 -16] These studies were performed in a wide range of surgical populations, such as cardiac, orthopedic, colorectal and general surgery. All of the studies used similar algorithms to guide volume administration as previously described (Figure 10). These same studies have indicated that esophageal Doppler guided intraoperative SV optimization resulted in improvement in patient outcome, as measured by reduction in postoperative morbidity, reduction in time spent in the intensive care unit and overall hospital stay.[4 -16] These improvements also present the possibility of significant cost, equipment and resource savings.

Mythen et al in 1995 were the first to demonstrate that perioperative expansion of plasma volume using a colloid reduced the incidence of gastric hypoperfusion and directly associate this with improved outcome and reduction of major complications. Only 7% of patients in the flow-based esophageal Doppler guided fluid management group showed gastric hypoperfusion as measured by tonometry by pHi <7.32 compared to 56% in the control group.[4]

Noblett et al. has indicated that it is not necessarily the amount of fluid that is the determining factor in improved outcomes but the timing of the fluid optimization within the operative period.[15] This study also reported that no differences were found in the overall volume of fluid administered between their two study groups. However, the intervention group had higher FTc, SV, CO and cardiac index (CI) at the end of the procedure; 46% of the fluid boluses, accounting for more than 50% of additional protocol volume given in the intervention group, were administered within the first quarter of the operating time. This suggests that the early delivery of fluid challenges in the intraoperative period, rather than the overall fluid volume was significant in optimizing cardiovascular parameters.[15]

It has long been established that one of the initial responses to a reduction in circulating volume is the redirection of blood away from the splanchnic bed in favor of more vital organs. The gut mucosa is particularly susceptible to hypoxia. Gut mucosal hypoperfusion may lead to bacterial translocation, endotoxemia and the activation of inflammatory cascades, all of which may contribute to the systemic inflammatory response after surgery.[103,104]

Peak systemic inflammatory cytokine (IL-6) levels have been shown to be reduced in fluid optimized patients, suggesting that individualized Doppler guided fluid management with early achievement of a higher SV may have reduced the systemic inflammatory response to surgical trauma.[15] Perioperative vasoconstrictors may affect splanchnic blood flow and oxygen supply/uptake ratios.[105-107]

Early achievement and maintenance of a normovolemia reduces splanchnic hypoperfusion, reduces inflammatory mediator release and has beneficial effects on patient outcome. It is apparent that, although excess fluid administration may lead to complications, the inadequate treatment of occult hypovolemia is also a factor in postoperative morbidity. Further, all studies validating the outcome benefits of iDGFM utilized fluids rather than crystalloid solutions.[4-16] While the arguments over the pros and cons of fluid selection are outside the scope of this review, it is evident that fluid management is essentially the right amount of the right fluid at the right time.

Hemodynamic monitoring is rarely available in the emergency or trauma department, yet this is where many critically ill patients are often admitted. Clinicians must rely on assessment skills; along with all other clinical findings to assess the hemodynamic status of the patient and make appropriate treatment decisions. However, predicting hemodynamic status without the aid of additional monitoring is quite challenging and often inaccurate. The goal of a study done in a large urban emergency department was to determine how well physicians could accurately predict hemodynamic parameters. The study showed that the agreement between the physician and an EDM (CardioQ-EDM, Deltex Medical) was 48% for volume status, 50% for CO, 39% for contractility, and 48% for afterload, requiring a change in therapy in approximately 40% of the cases.[108] Rivers et al. reported that early goal-directed therapy in the emergency department, requiring hemodynamic monitoring, results in reduced morbidity, mortality, and hospital costs.[98] These findings suggest that EDM may also have a role to play in the emergency department, allowing for early and accurate assessment of patient hemodynamic status, leading to more appropriate and timely interventions.

Chytra et al. have reported on trauma patients in a RCT. Eighty multiple trauma patients with blood loss of more than 2,000 mL admitted to the ICU were randomly assigned to the protocol group with the EDM monitoring (Hemosonic 100, Arrow International Reading, Pennsylvania, USA) and to the control group. Fluid resuscitation in the Doppler group was guided for the first 12 hours of ICU stay according to the protocol based on data obtained by esophageal Doppler, whereas control patients were managed conventionally. Fewer patients in the EDM group developed infectious complications 15 (18.8%) versus 28 (34.1%). Intensive care stay in the Doppler group was reduced from a median of 8.5 days to 7 days, and hospital stay was decreased from a median of 17.5 days to 14 days. [16]

Latterly as the clinical evidence from RCTs utilizing EDM has expanded, meta-analyses have been published.[109-112] Two of these meta-analyses have specifically examined the evidence for use of EDM-guided fluid management in abdominal surgery.[109,110]

Abbas and Hill analysed data from five RCTs which had recruited 420 patients undergoing major abdominal surgery. The patients had received either intravenous fluid treatment guided by EDM or fluid administration according to conventional parameters. Their analysis showed a reduced hospital stay in the EDM treatment group. Overall, there were fewer complications and ICU admissions, and less requirement for inotropes in the EDM treatment group. Return of normal gastro-intestinal function was also significantly faster in the EDM treatment group. [109]

Walsh et al. investigated the potential of intraoperative fluid therapy guided by esophageal Doppler to improve post-operative outcome. Their search identified four RCTs comparing Doppler-guided intraoperative fluid management to standard practice in patients undergoing major abdominal surgery. Analysis of the 393 patients demonstrated fewer postoperative complications and shorter hospital stays where EDM was used to guide fluid management. [110]

Phan et al. have conducted a meta-analysis of the use of EDM across all clinical settings. Nine clinical trials were included in the analysis, seven using EDM in surgery and two in ICU. The primary outcome of this meta-analysis was length of stay (LOS) in hospital, defined as the number of postoperative days in an acute care hospital setting. Use of the EDM resulted in a significant reduction in LOS of 2.34 days. The group also analysed the colorectal surgery studies separately and concluded that LOS was reduced by 2.17 days in this subset. They concluded that using EDM to guide intraoperative IV fluid therapy increased the administration of intraoperative IV colloid fluid, and reduced length of hospital stay, time to resume full oral diet, and postoperative morbidity or complications. [111]

Hamilton et al. have reported a meta-analysis of 7 studies totalling 618 patients. The meta-analysis showed that there was no significant difference in mortality between control and treatment groups. However there was a significant reduction in the length of hospital stay for patients receiving Doppler guided fluid management of 2.98 days. [112]

The NHS for the UK and the Centres for Medicare and Medicaid (CMS) for the USA have commissioned Health Technology Assessments (HTA) to examine the value of wider introduction of EDM-guided fluid management. In the USA the Emergency Care Research Institute (ECRI) reported their HTA findings to Agency for Healthcare Research and Quality (AHRQ) in 2007 (Figure 11). [113] The findings resulted in CMS revising their financial coverage of ultrasound diagnostic procedures to include EDM for ventilated patients in the ICU and surgical patients with a need for intraoperative fluid optimization. [114]

The National Institute for Health Research (NIHR) released its systematic review of the RCTs published on the use of EDM in January 2009 (Figure 12). The UK review was based on the systematic review conducted by the AHRQ with supplementary evidence from additional studies identified in a web-based search. The effectiveness of EDM was compared with standard care, use of PACs, pulse contour analysis monitoring and lithium or thermodilution cardiac monitoring. Data were extracted on mortality, LOS overall and in critical care, complications and quality of life. The HTA compared EDM with conventional clinical assessment and reported that EDM is likely to be cost-effective since the initial cost of EDM is compensated by reduced complications and shorter length of stay in hospital. The report assessed the potential economic impact of EDM for surgical patients under the Quality Adjusted Life Year (QALY) methodology used by the National Institute for Health and Clinical Excellence (NICE). The analysis showed EDM to be both more effective and less costly under virtually every scenario modelled and that the NHS would need to spend between £642 and £4,441 extra on each additional survivor of surgery before EDM would no longer be considered cost effective. The report concluded that available evidence indicated that the addition of EDM-guided fluid administration to CVP monitoring plus conventional assessment during surgery resulted in fewer major and total complications, a shorter LOS and possibly fewer deaths. Pooled estimates for all outcomes showed a statistically significant difference in favor of the EDM group. [115]

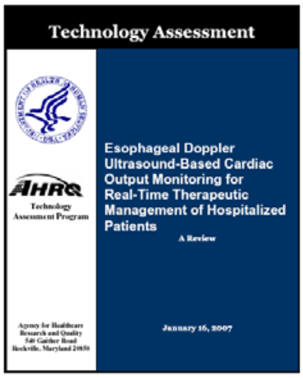


**Figure 11.** AHRQ HTA 2007

In parallel with the preparation of the NIHR HTA report the NHS Centre for Evidence-based Purchasing (CEP) utilized the results to make recommendations for patients undergoing high-risk surgery (Figure 13). The CEP concluded that compared with CVP monitoring plus conventional clinical assessment, addition of EDM guided fluid administration probably results in fewer deaths, fewer complications, and shorter length of hospital stay. CEP also concluded that the cost of EDM is likely to be offset by reductions in both complications and LOS. [116]


**Figure 12.** NIHR HTA 2009

The British Consensus Guidelines on Intravenous Therapy for Adult Surgical Patients (GIFTASUP) were released for dissemination to members of participating professional bodies late in 2008 (Figure 14). The guidelines were developed on behalf of BAPEN Medical; the Association for Clinical Biochemistry; the Association of Surgeons of Great Britain and Ireland; the Society of Academic and Research Surgery; the Renal Association; and the Intensive Care Society. The guidelines represent the latest clinical thinking on fluid management and contain a number of recommendations for IV fluid management with EDM. Each recommendation has been given an evidence level grade from 1-5 in accordance with the Oxford Centre for Evidence-based Medicine Levels of Evidence, with a score of 1a representing the highest possible level of supporting clinical evidence. In the context of EDM recommendation 14 was based on level 1a evidence for abdominal surgery and level 1b for orthopedic surgery. Recommendation 14 is solely based on evidence from studies using EDM.


**Figure 13.** Centre for Evidence-based Purchasing report 2008

Recommendation 13: *In patients undergoing abdominal surgery, intraoperative treatment with intravenous fluid to achieve an optimal value of stroke volume should be used where possible as this may reduce postoperative complication rates and duration of hospital stay.*

Further recommendations at Evidence level 1b also apply to optimization of SV. The beneficial effect is likely to relate to the early tailoring of fluid administration to the requirements of the individual patient rather than the blanket administration of extra fluid.

Recommendation 13: *In patients undergoing some forms of orthopaedic surgery, intraoperative treatment with intravenous fluid to achieve an optimal value of stroke volume should be used where possible as this may reduce postoperative complication rates and duration of hospital stay.*

Orthopaedic surgery: Evidence level 1b

Recommendation 14:
*Patients undergoing non-elective major abdominal or orthopaedic surgery should receive intravenous fluid to achieve an optimal value of SV during and for the first eight hours after surgery. This may be supplemented by a low dose dopexamine infusion.*

Evidence level 1b

The recommendations also call for wherever possible that preoperative or operative hypovolemia should be diagnosed by flow-based measurements. The clinical context should also be taken into account as this will provide an important indication of whether hypovolemia is possible or likely.[117]

## Limitations

Esophageal Doppler monitoring can be used in both awake and sedated patients but as with the use of naso- or orogastric tubes, or any other tube/probe placed into the esophagus, caution or special consideration should be given to patients where there may be an increased risk of bleeding, trauma or misplacing of the tube/probe. There may be circumstances where signal acquisition is not possible or very difficult due to coarctation of the aorta or during use of intra-aortic balloon pumps or in patients with thoracic aortic aneurysms. Users need to be aware that under epidural anesthesia the proportionality of upper and lower body flow may alter, in these circumstances relative changes can be monitored using Stroke Distance. Additionally where patients fall outside the nomogram limits (i.e. obese) or during periods of cross clamping of the aorta; SD changes can be used to guide fluid management.


**Figure 14.** GIFTASUP 2009

## Conclusions

An Esophageal Doppler Monitor provides real-time flow-based measurements and visualization of blood flow from the left side of the heart. Individualized Doppler guided fluid management (iDGFM) is a minimally invasive method of optimizing SV with a very low risk to the patient. The procedure requires significantly less insertion time than current standard methodologies, carries less risk of complications than invasive technologies requiring arterial catheter insertion. Current evidence from randomized clinical trials, meta-analyses and systematic reviews suggests that iDGFM to achieve SV optimization offers the potential for cost savings, decreased complications, decreased nursing and physician time, decreased hospital length of stay, and improved patient outcomes.

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