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ORIGINAL RESEARCH

Additional hemodynamic measurements with an esophageal Doppler monitor: a preliminary report of compliance, force, kinetic energy, and afterload in the clinical setting

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Abstract The esophageal Doppler monitor (EDM) is a minimally-invasive hemodynamic device which evaluates both cardiac output (CO), and fluid status, by estimating stroke volume (SV) and calculating heart rate (HR). The measurement of these parameters is based upon a continuous and accurate approximation of distal thoracic aortic blood flow. Furthermore, the peak velocity (PV) and mean acceleration (MA), of aortic blood flow at this anatomic location, are also determined by the EDM. The purpose of this preliminary report is to examine additional clinical hemodynamic calculations of: compliance (C), kinetic energy (KE), force (F), and afterload ($TSVR_i$). These data were derived using both velocity-based measurements, provided by the EDM, as well as other contemporaneous physiologic parameters. Data were obtained from anesthetized patients undergoing surgery or who were in a critical care unit. A graphical inspection of these measurements is presented and discussed with respect to each patient's clinical situation. When normalized to each of their initial values, F and KE both consistently demonstrated more discriminative power than either PV or MA. The EDM offers additional applications for hemodynamic monitoring. Further research regarding the accuracy, utility, and limitations of these parameters is therefore indicated.

Keywords Esophageal Doppler monitor · Volume status · Contractility · Afterload · Compliance · Force · Kinetic energy · Velocity · Acceleration

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1 Introduction

The esophageal Doppler monitor (EDM) has become well-established as a safe and reliable means of assessing cardiac output (CO), and intravascular volume status, in the clinical settings of both the operating room and critical care unit [1–4].

The EDM graphically displays and calculates, in real time, the velocity of *distal* thoracic aortic blood flow. Note that the velocity and acceleration of *proximal* aortic blood flow have been shown to correlate with measurements of left ventricle (LV) contractility [5–9]; including ejection fraction (EF) and the time rate change of pressure, dP/dt [10, 11]. This relationship could be extrapolated to distal thoracic aortic blood flow.

Additional quantitative evaluations, of LV contractility, may also be possible by determining the amount of kinetic

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energy (KE) and force (F) associated with each cardiac cycle. These measurements are readily estimated using existing EDM technology [12].

Moreover, total systemic vascular resistance index ($TSVR_i$) [13] and systemic compliance (C) can also be examined, both continuously and in real time, with the EDM [12]. These require simultaneous measurement of blood pressure. Whereas knowledge of either hematocrit (Hct), or hemoglobin (Hb), is necessary for KE and F calculations *(q.v.)*.

The purpose of this preliminary paper is to report EDM-based examination of the above parameters; utilizing data from patients either undergoing surgery or who were in an ICU setting. These measurements are then assessed with respect to each individual's clinical condition.

The EDM probe is placed, either orally or nasally, in patients whose trachea is intubated. It can also be used with patients receiving general anesthesia with an appropriate laryngeal mask airway.[1] Nasal placement in awake patients has also been described [14, 15]. After proper focusing, the velocity of blood flow in the distal thoracic aorta is then displayed (Fig. 1).

Stroke distance within the distal thoracic aorta (SDa), is determined in real time by the EDM. This is accomplished using numerical integration of the measured velocity, $v(t)$, throughout the period of LV ejection. This time period is referred to as the flow time (FT).[2] Specifically, this integral represents the area under the velocity versus time curve; from the opening of the aortic valve until its closure [16]:

$$SDa = \int_0^{FT} v(t)dt. \tag{1}$$

Stroke volume, within the distal thoracic aorta, (SVa), is then calculated:

$$SVa = A \cdot SDa \tag{2}$$

where A represents the cross sectional area of the distal thoracic aorta. It can also be directly measured using M-mode ultrasound. However, this feature is not available in current commercially-manufactured EDMs.

The portion of the CO that flows within the distal thoracic aorta, COa, is then found:

$$COa = HR \cdot SVa \tag{3}$$

where HR refers to heart rate. Total cardiac output (CO) is linearly proportional to COa [17]. CO is then calculated by the EDM using an integral nomogram incorporating the patient's age, height and weight [18]. Furthermore, CO can be calculated on an "instantaneous" or "beat-to-beat" basis.

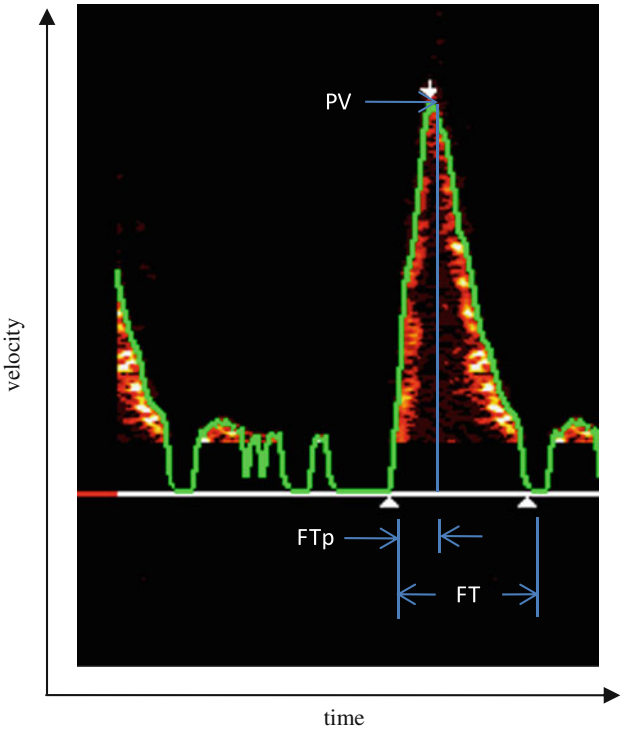

Fig. 1 The EDM waveform depicts the velocity, $v(t)$, of distal thoracic aortic blood flow versus time. Peak velocity (PV), flow time (FT), and flow time to peak velocity (FTp) are also illustrated

Also illustrated in Fig. 1 is peak velocity (PV), measured in cm/s, and flow time to peak velocity (FTp). Using these terms, mean acceleration (MA), measured in m/s^2, is then defined as:

$$MA = \frac{PV}{FTp}. \tag{4}$$

Corrected flow time (FTc) is another EDM term. Note that it resembles Bazett's formula [19] which mathematically "compensates" the ECG's QT interval to a heart rate of 60 bpm [20]:

$$FTc = \frac{FT}{\sqrt{CT}} \tag{5}$$

where CT (cycle time) is the time from the beginning of one cycle to that of the next. This is equivalent to the R-to-R interval found on the electrocardiogram:

$$RR = \frac{60}{HR}. \tag{6}$$

Currently, SV is emerging as the most frequently-used parameter to clinically assess intravascular fluid status [21, 22]. FTc has also been used [23], however, this term is relatively non-specific as it is directly affected by changes in afterload [24, 25]. Furthermore, ventilator-induced

[1] The EDM probe can be used with those laryngeal mask airways which have an esophageal port.

[2] Flow time (FT) is also referred to as left ventricle ejection time (LVET).

variations in both PV and SV accurately correlate with fluid responsiveness [26, 27].

The purpose of this paper is to report the use of the EDM for hemodynamic measurements of force (F), kinetic energy (KE), and compliance (C). In addition, a method of assessing afterload, total systemic vascular resistance index ($TSVR_i$), is also examined. It should be noted that $TSVR_i$ ignores the minimal contribution of central venous pressure (CVP) to afterload. Previous research has preliminarily demonstrated that $TSVR_i$ correlates well with SVR_i [13]. Furthermore, changes in $TSVR_i$ clinically correlate with changes in SVR_i [13]. Thus, $TSVR_i$ appears to be a reasonable "surrogate" for SVR_i in clinical afterload assessment.

2 Methods

All patients were either within an intensive care unit, or an operating room, of University College Hospitals NHS Foundation Trust, London, UK. IRB approval was deemed unnecessary as all data were obtained during routine clinical care in both a purely observational and anonymous manner. No additional interventions were performed outside of standard clinical settings. Thus, this study was classified as a "service evaluation."

All patients were receiving either general anesthesia, or sedation, with standard monitoring of blood pressure, ECG, HR, and pulse oximetry. In addition, a Deltex esophageal Doppler monitor (EDM) was routinely used to collect SV, HR, PV, and MA data (Deltex Medical, Chichester, UK).

The EDM ultimately determines stroke volume (SV) by initially measuring SDa. Equation (2) yields SVa which is proportional to the product of A and SDa. Thus, SV is proportional to SVa:

$$SV \propto SVa. \tag{7}$$

The mass (M_{sv}), in kilograms, of the calculated SV, is then found:

$$M_{sv} = \rho \cdot SV \tag{8}$$

where ρ is blood density; which can be determined using either hemoglobin (Hb) or hematocrit (Hct) (see Appendix 1).

Force, in Newtons, associated with LV contractility, is determined as:

$$Force = M_{sv} \cdot MA. \tag{9}$$

A global measure of hemodynamic compliance, C, can also be obtained [28]:

$$C = \frac{SV}{PP} \tag{10}$$

where PP represents pulse pressure:

$$PP = (SBP) - (DBP). \tag{11}$$

SBP and DBP refer to systolic and diastolic blood pressures, respectively.

Afterload can also be assessed using $TSVR_i$. As previously stated, inclusion of the measurement of central venous pressure (CVP) may not be necessary to clinically evaluate afterload [13]:

$$TSVR_i = \frac{MAP}{C_i} \cdot 80 \tag{12}$$

where C_i represents cardiac index (i.e. cardiac output divided by body surface area), $TSVR_i$ denotes TSVR corrected for body surface area, and MAP represents mean arterial blood pressure. This can be determined using either a non-invasive blood pressure cuff or an invasive arterial catheter [29]:

$$MAP = \frac{1}{3}(SBP) + \frac{2}{3}(DBP). \tag{13}$$

The constant 80 allows $TSVR_i$ to be expressed with units of dyne s cm^{-5} m^{-2}. This dimension is commonly referred to as "resistance units."

Kinetic energy (KE) is defined as the work done by the LV in propelling the M_{sv} from a position of rest, or zero velocity, to its PV:

$$\text{Kinetic Energy} = \frac{1}{2}(M_{sv}) \cdot (PV)^2. \tag{14}$$

The derivation of KE is shown in Appendix 2.

2.1 Discriminative analysis

Normalization, of the primary data, was accomplished by dividing each particular parameter's set of data by its own initial value. This process yields *dimensionless* numerical information. A subsequent comparison, of the relative sensitivity of each parameter, can then be made. Thus, a normalized parameter, which is more sensitive, would be spread over a greater dimensionless data range and would also have a greater dimensionless statistical variance. This increase in a parameter's response to either physiologic and/or pharmacologic changes is also referred to as an increase in its discriminative power or discriminative ability.

However, normalized data, being non-random, cannot be assessed using traditional statistical analysis [30]. Use of a *bootstrapping* statistical technique enables determination of statistical significance under these circumstances [31].

Using Fisher F-test type statistics, this particular bootstrap test was developed based upon the *ratio* of two sample variances. As an example, the sample variance of the normalized data, for both MA and F, is expressed as a ratio; with MA as the denominator and F as the numerator. Since F and MA are dependent, and both of their sample

sizes are small, their original data distribution is then assumed to be bivariate normal with a non-zero correlation.

Using large sample theory, the above Fisher F-test type statistics were then analyzed to assess when both the numerator and denominator would have the same distribution. This analysis then generates the null hypothesis. Specifically, this would occur when the magnitude of the coefficient of variation would be the same for both the populations of MA and F. Note that the magnitude of the coefficient of variation represents the population standard deviation divided by the corresponding magnitude of its mean: $\sigma/|\mu|$.

The alternate hypothesis is defined when the true magnitude of the coefficient of variation, of the population within the numerator, is greater than that of the denominator. *In this example, the true coefficient of variation of F is greater than that of MA.*

Independent and identically distributed (iid) bootstrap samples, of size n, are then created. *Note that in the case of F and MA, $n = 7$.* These bootstrap samples are computer-generated to be iid bivariate normal; with mean values equivalent to the corresponding mean values of the original data samples.

The bootstrap sampling distributions also reflect the null hypothesis by maintaining equal magnitudes of their coefficient of variation. Note that the common magnitude of the coefficient of variation is estimated by taking the simple average of the two individual original sample estimates. This is accomplished using the form: $(s/|\bar{x}|)$.

The variance, of each of the bootstrap samples, is the square of the mean of the original data sample multiplied by the square of the common estimate of the coefficient of variation.

The correlation of the bootstrap samples is equivalent to that of the original data. This is accomplished using Pearson's correlation.

One thousand bootstrap samples were then generated using a computer. The percentage of bootstrap F-test type statistic values, which exceeded the original data-based F-test type statistic values, was computed as the *p* value of the test.

It should be noted that an upper-tailed test statistic is equivalent to a lower bound confidence interval. Therefore, one can be assured that a 99.8 % lower-bound confidence interval, based upon the Fisher F-test type test statistic, will stay above 1 when the tests are significant at an alpha = 0.002. Whereas such a lower-bound confidence interval will contain 1 when the corresponding tests are not significant.

3 Results

These four patient cases illustrate how EDM-based measurements of F, KE, $TSVR_i$ and C may be clinically useful.

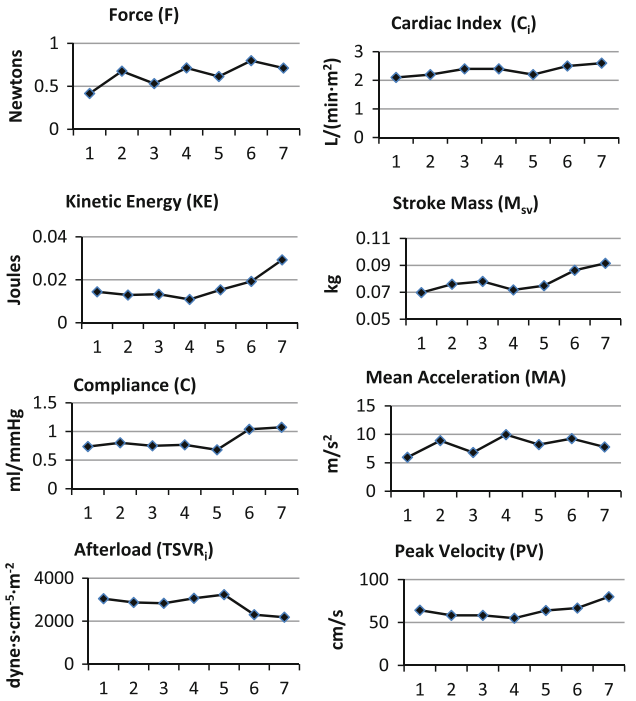

Fig. 2 Patient 1 received a significant colloid bolus throughout the entire time period; 1 through 7. This caused an overall net increase in M_{sv}. A reduction in the continuous infusion of norepinephrine, during observations 6 and 7, yielded a decrease in $TSVR_i$ and an increase in C, F and KE. This decrease in afterload also contributed to an increase in M_{sv}

Furthermore, F and KE appear to have more discriminative power than either MA or PV.

3.1 Patient 1

An elderly male (ASA 4[3]) was mechanically ventilated in an ICU following a middle cerebral artery infarct. The patient was receiving an infusion of intravenous (IV) norepinephrine at a rate of 0.08 μg/(kg min) until the last two measurements; when it was reduced to 0.06 μg/(kg min). This is shown in Fig. 2 occurring during time periods 6 and 7. In addition, the patient also received a total of 750 ml of IV colloid for the duration of the entire observation.

During periods 6 and 7, an increase in M_{sv}, F, and KE resulted from the combined effects of both the additional fluid load and afterload reduction. As expected, a prominent drop in $TSVR_i$ also occurred during the latter two observations; this was accompanied by an increase in C. This afterload reduction also "allowed" for a greater SV to be ejected.

[3] The American Society of Anesthesiologists (ASA) physical status classification system is summarized in Appendix 3.

3.2 Patient 2

A middle-aged male (ASA 3E) was undergoing emergency surgery for a posterior cervical decompression. Figure 3 illustrates, during periods 1 through 8, that the patient received volume resuscitation. This is observed with an increase in M_{sv}. This was followed by deliberate hypotension which was achieved primarily by an increase in the concentration of the inhalational anesthetic agent for periods 9 and 10. After refocusing of the EDM probe, period 11, metaraminol was then administered to increase blood pressure.

Figure 3 demonstrates that, prior to EDM probe refocusing, there was a net increase in M_{sv} as well as an associated increase in C, KE, and F. This occurred as a result of an increase in fluid volume during periods 1 through 8.

Deliberate hypotension, from the increase in concentration of inhalational anesthetic agent, produced a further reduction in F and KE during periods 9 and 10.

Following refocusing, administration of metaraminol then yielded a decrease in C, KE, and F with an associated increase in $TSVR_i$ as seen during periods 12 through 16. This increase in afterload also resulted in a decrease in M_{sv}.

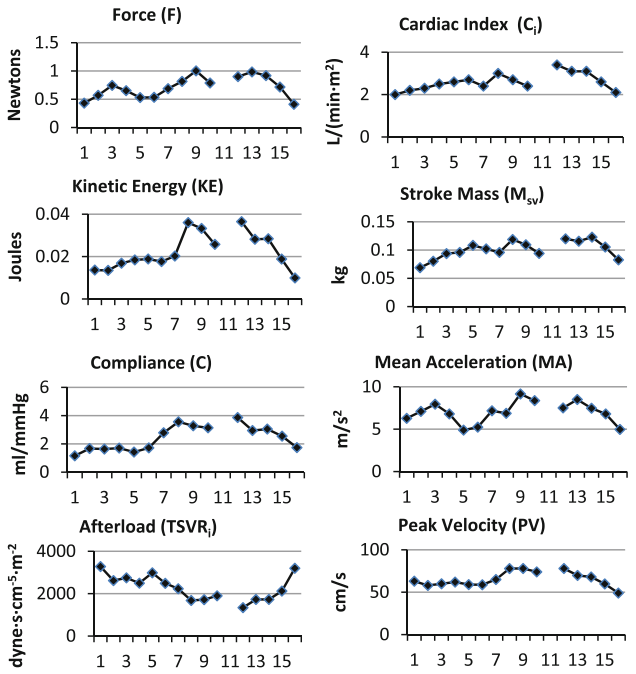

Fig. 3 Patient 2 was initially given volume loading during periods 1 through 8 and deliberate hypotension from period 9 through 10. This resulted in a drop in $TSVR_i$ and an increase in C, F and KE. Following this, the gap in the data, period 11, represents refocusing of the EDM probe. Subsequently, metaraminol was administered which increased $TSVR_i$ and decreased C, F and KE. This is observed during periods 12 through 16. M_{sv} also decreased concomitantly from the effect of metaraminol

This is in contradistinction to the effect of afterload reduction; as observed with patient 1.

3.3 Patient 3

A middle-aged male (ASA 2) was undergoing revision laminectomy and dural repair. The patient initially received IV colloid and crystalloid resuscitation during periods 1 through 13. A 40 cm H_2O Valsalva maneuver was then administered, during period 14, to assess dural integrity.

Figure 4 demonstrates a slight increase in M_{sv} with the initial volume load. A noticeable increase in $TSVR_i$ occurred with the Valsalva maneuver. There were also simultaneous concomitant falls in M_{sv}, F, KE, and C.

3.4 Patient 4

A middle-aged male (ASA 4E) was undergoing emergency surgery for an external ventricular drain. The patient received 750 ml of IV colloid (hydroxyethyl starch) during the procedure.

As a result of the fluid loading, an increase in M_{sv} was observed with an associated increase in PV. In addition, increases in both F and KE were noted while $TSVR_i$ decreased (Fig. 5). These were observed from time period 1 through 6.

Interestingly, C initially increased but then remained essentially unchanged. This occurred as the increase in M_{sv}

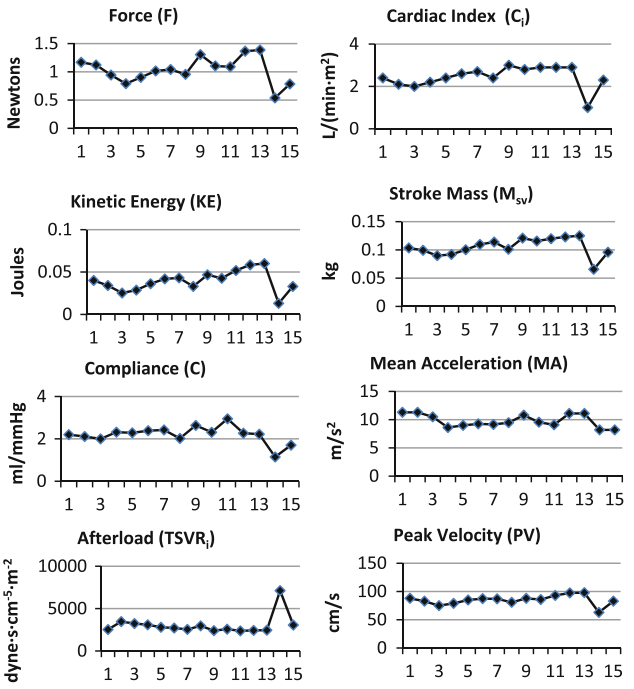

Fig. 4 Patient 3 received a Valsalva maneuver during period 14. An increase in $TSVR_i$ was noted as well as a drop in C, KE and F. A reduction in M_{sv} also occurred

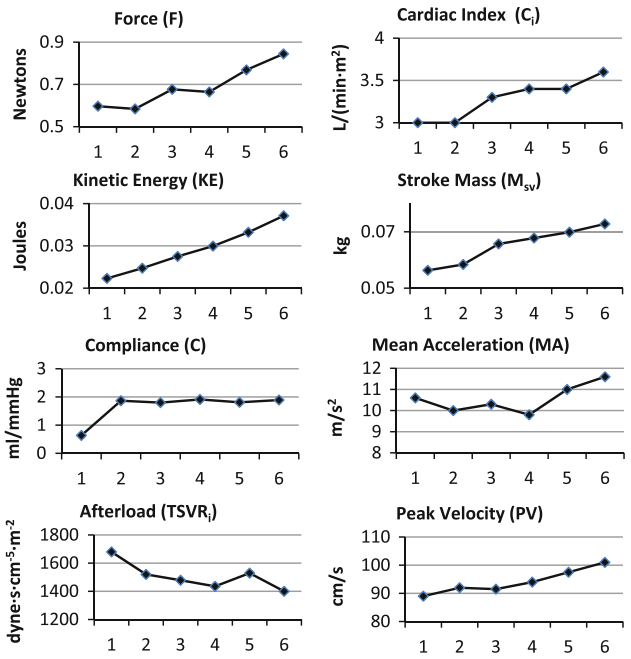

Fig. 5 Patient 4 required emergency neurosurgery. During the procedure, 750 ml of IV colloid was administered. From period 1 through 6 there was a steady increase in M_{sv} and an increase in F and KE. $TSVR_i$ also decreased with the associated increase in volume

was accompanied by a proportionally similar increase in PP. This is confirmed by examination of Eq. (10); where compliance is defined as the ratio of SV to PP.

3.5 Discrimination analysis

Further analysis of these data has demonstrated that both F and KE appear to have more discriminative power than either PV or MA. Inspection of Table 1 also shows that F and KE appear to have been more sensitive to physiologic and pharmacologic changes than either PV or MA. Additionally, the range and variance of both F and KE were always greater than either PV or MA. Although not statistically significant, KE consistently had the greatest values of both range and variance.

Figure 6 illustrates the statistical significance of these comparisons. Since there had been a total of twenty-four tests conducted, the Bonferroni method of correction was utilized to maintain the overall significance, or family-wise error rate, at a 0.05 level [32]. Thus, a more stringent P value $= 0.05/24 = 0.00208$ was necessary as the definition of statistical significance.

4 Discussion

The EDM provides safe and clinically reliable measurements of both cardiac output and volume status. As demonstrated in this paper, additional hemodynamic measurements are obtainable which reflect meaningful physiologic data and their associated changes. Specifically, EDM-based estimates of F and KE have been preliminarily assessed as potential contractility indices. After a straightforward normalization technique, inspection of these terms has revealed that they may be more sensitive to clinical contractile changes than either PV or MA.

Currently, ejection fraction (EF) remains the parameter most commonly used, to assess contractility, in the clinical setting [33]:

$$\text{Ejection Fraction}(\%) = \frac{SV}{EDV} \cdot 100 \tag{15}$$

where EDV represents LV end-diastolic volume (EDV). Typically, EF is determined through the use of either transthoracic or transesophageal echocardiography. EF, being a ratio, may be "deceiving" as simultaneous changes in both SV and EDV could lead to a "false normal" assessment of cardiac status. A direct, or indirect, measure of SV is needed to clarify this situation. Of note, SV and EDV are linearly related in clinical studies [34].

EF also does not take into account the amount of time associated with ejection. Thus, an LV which ejects faster may be functioning better than one with a slower rate of ejection. This is based on the assumption that both volume status and afterload remain constant while making this comparison [35]. Time-dependent indices of contractility that use FT (LVET) have also been examined clinically [36].

Therefore, the continuous measurement, of F and KE, may be useful, as adjuncts, in contractility assessment. This

Table 1 Range and (variance) of the normalized data

Patient	Normalized PV	Normalized MA	Normalized F	Normalized KE
1	0.39 (0.017)	0.67 (0.055)	0.92 (0.096)	1.28 (0.186)
2	0.46 (0.019)	0.68 (0.04)	1.37 (0.20)	1.95 (0.38)
3	0.40 (0.01)	0.28 (0.01)	0.73 (0.04)	1.17 (0.10)
4	0.14 (0.002)	0.17 (0.004)	0.44 (0.03)	0.66 (0.06)

Note that after normalization F and KE displayed a greater discriminative ability than either PV or MA

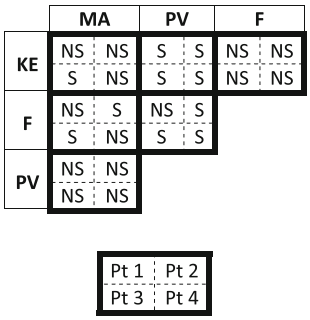

Fig. 6 The normalized values for KE, F, MA and PV have been assessed using statistical bootstrapping. This subsequently allowed for the comparison of their discriminative abilities. KE and F produced the most discrimination. S represents a statistical significance of $P < 0.00208$ whereas NS represents a non-significant difference

is in addition to the PV and MA of distal thoracic aortic blood flow, which are both currently measured by the EDM.

EF is, however, difficult to measure on a continuous basis. This is particularly significant with respect to patients who are either prone or in other non-supine positions; as commonly occurs during surgery. Conveniently, the small size of the EDM probe facilitates long-term continuous hemodynamic assessment; particularly with nasal placement in awake patients.

The acceleration of proximal aortic blood flow has been previously shown to correlate very well with EF; whereas velocity was shown to correlate moderately well [5]. The time-rate change of pressure, dP/dt, has also been used as a means of assessing LV contractility. Furthermore, dP/dt is also proportional to the acceleration of blood flow, dv/dt [37, 38]:

$$\frac{dP}{dt} = Vpw \cdot \frac{dv}{dt} \tag{16}$$

where V_{pw} represents pulse wave velocity. It should be appreciated that the above equation is the first derivative, with respect to time, of the water hammer effect. Excellent clinical correlation, of dP/dt with proximal aortic blood flow acceleration, has been previously documented; whereas velocity, and the square of velocity, correlated moderately well [7].

Discriminative analysis was performed by normalizing the acquired PV, MA, F and KE data. This was accomplished by dividing each parameter by its own initial value. Inspection of these normalized parameters demonstrated a greater amount of sensitivity for both F and KE, as compared to either PV or MA. KE consistently exhibited the greatest discriminative ability. However, this increase was not statistically significant. Further research may possibly elucidate a statistical difference.

Additional research, evaluating the ability of the EDM to assess LV contractility, would seem rational based upon these initial observations. Thus, a clinical comparison of EF, as measured by transthoracic echocardiography, to parameters simultaneously obtained with an EDM, would be both reasonable and straightforward. Comparison of dP/dt to EDM-based measurements would require invasive aortic catheterization for verification.

The ability for F and KE to be more sensitive to physiologic and pharmacologic changes may stem from the fact that both of these parameters use M_{sv} whereas PV and MA do not. This may be explained using the Frank-Starling mechanism in which greater stroke volumes are associated with an increased LV contractile state. It should be noted that this situation applies to a non-failing heart [35]. Graphical inspection also shows that F and KE, as well as PV and MA, are sensitive to changes in afterload. Thus, afterload and contractility appear to be inversely related. This has been examined previously [35].

Clinically, continuous afterload assessment using $TSVR_i$, as well as continuous measurements of compliance, C, may be potentially useful in the acute management of specific operative and non-operative pathologic states such as hypertensive crisis and pheochromocytoma. Furthermore, these parameters may also be useful for critically ill patients being managed with vasoactive medications such as norepinephrine, vasopressin, and epinephrine. These medications are frequently necessary for patients in various shock states. Currently, there is no device which allows for continuous measurement of either C or $TSVR_i$ in real time. Thus, the combination of simultaneous pressure and flow measurements would allow for both comprehensive and "instantaneous" hemodynamic monitoring.

Further research would correlate the PV, MA, F and KE of proximal aortic blood flow with that measured in the distal thoracic aorta by the EDM. Additional prospective data, examining the utility and possible limitations of both $TSVR_i$ and C, would also be clinically beneficial.

This study was limited primarily by its small sample size. Furthermore, it was neither randomized nor prospective in nature.

5 Conclusions

This preliminary study has documented that additional hemodynamic measurements may be derived using an EDM in conjunction with simultaneously-obtained blood pressure and blood density information. Specifically, F, KE, C and $TSVR_i$ have been examined and appear to reflect both meaningful physiologic and pharmacologic changes. Furthermore, F and KE may be more sensitive than either PV or MA to changes in contractility. Measurement of afterload,

as assessed by $TSVR_i$ and C, may also useful for patients in shock or those requiring vasoactive medication.

Together, the overall utility and limitations of these "new" measurements should be further examined with respect to clinical patient management and outcome. Certainly, it is safe and economically feasible to measure and assess these parameters, utilizing the minimally-invasive EDM, *concomitantly* with both blood pressure and blood density information.

Conflicts of Interest Glen Atlas: Has neither financial disclosures nor conflicts of interests. David Brealey: Has neither financial disclosures nor conflicts of interests. Sunil Dhar: Has neither financial disclosures nor conflicts of interests. Gerhard Dikta: Has neither financial disclosures nor conflicts of interests. Mervyn Singer: Is on the advisory board of Deltex Medical and also has received an unrestricted donation into his research fund. University College London holds shares in Deltex Medical bestowed by the charitable trust of its late founder.

Appendix 1: Derivation, of the density of human blood, from either hemoglobin or hematocrit

Based upon the graphical data from Hinghofer-Szalkay, the slope of the blood density (ρ) versus hematocrit (Hct) line is [39]:

$$\begin{aligned}\text{Slope} &= \frac{(1060-1040)\left(\frac{g}{L}\right)}{(60-30)(volume\%)} \\ &= 0.667\text{g}/\{\text{L}\cdot(\text{volume }\%)\}\end{aligned} \tag{17}$$

Examination, at a single point, then yields the linear relationship:

$$\rho = \left(\frac{2}{3}\right)\cdot(Hct) + 1020 \tag{18}$$

where Hct is expressed as a volume percentage (e.g. 30 or 40 %). ρ has equivalent dimensions of either grams/liter or kg/m^3.

Using the formula that relates Hct, to hemoglobin (Hb), from Nijboer [40]:

$$Hct = 2.953\cdot(Hb). \tag{19}$$

Substituting:

$$\rho = (1.969)\cdot(Hb) + 1020. \tag{20}$$

Hb is expressed in units of grams/dl or grams/(0.1·L).

Appendix 2: Derivation of kinetic energy

Kinetic energy, KE, is defined as the work necessary to move the stroke mass, M_{sv}, which is initially stationary, to its peak velocity, PV. This is equal to the force generated by the LV which acts on the stroke mass as it is displaced:

$$KE = \int F\cdot dx. \tag{21}$$

Substituting $F = M_{sv}\cdot Acc$ where M_{sv} = stroke mass and Acc = acceleration then yields:

$$KE = \int (M_{sv}\cdot Acc)dx. \tag{22}$$

As acceleration is equal to the time-rate change of velocity or dv/dt:

$$KE = \int \left(M_{sv}\cdot\frac{dv}{dt}\right)dx. \tag{23}$$

By definition, velocity is defined as differential displacement, *dx*, divided by differential time, *dt*:

$$\frac{dx}{dt} = v. \tag{24}$$

Therefore:

$$dx = v\cdot dt. \tag{25}$$

Substituting (25) into (23) yields:

$$KE = \int \left(M_{sv}\cdot\frac{dv}{dt}\cdot v\right)dt. \tag{26}$$

Simplifying, and realizing that after the M_{sv} has been displaced, it eventually reaches a peak velocity, PV:

$$KE = \int_0^{PV} (M_{sv}\cdot v)dv. \tag{27}$$

Thus:

$$KE = \frac{1}{2}(M_{sv})\cdot(PV)^2 \tag{28}$$

Appendix 3: American Society of Anesthesiologists physical status classification system [41]

1. A normal healthy patient.
2. A patient with mild systemic disease.
3. A patient with severe systemic disease.
4. A patient with severe systemic disease that is a constant threat to life.
5. A moribund patient who is not expected to survive without the operation.
6. A declared brain-dead patient whose organs are being removed for donor purposes.

Note that the suffix E refers to an emergency situation.

Appendix 4

See Table 2.

Table 2 Terms, abbreviations, and units

Abbreviation	Term	Equation	Units
A	Aortic cross sectional area	2	m^2
Acc	Acceleration of aortic blood flow	16, 2B	m/s^2
C	Compliance	10	ml/mmHg
C_i	Cardiac index	12	$L/(min \cdot m^2)$
CO	Cardiac output		L/min
COa	Cardiac output within the distal thoracic aorta	3	L/min
DBP	Diastolic blood pressure	13	mmHg
DTABF	Distal thoracic aortic blood flow		L/min
dP/dt	Time rate change of pressure	16	mmHg/s
dv/dt	Time rate change of velocity = Acceleration	16	m/s^2
ECG	Electrocardiogram		
EDM	Esophageal Doppler monitor		
EDV	End-diastolic volume	15	ml
EF	Ejection fraction	15	%
F	Force	9, 1B	N
FT	Flow time	1	ms
FTc	Flow time corrected	5	$\sqrt{ms}$
FTp	Flow time to peak velocity	4	ms
Hb	Hemoglobin	2A, 3A	g/dl
Hct	Hematocrit	2A, 3A	%
HR	Heart rate	3	beats/min
KE	Kinetic energy	14, 1B	J
LV	Left ventricle		
LVET	Left ventricle ejection time		ms
MA	Mean acceleration of distal thoracic aortic blood flow	4	m/s^2
MAP	Mean arterial blood pressure	13	mmHg
M_{sv}	Stroke mass	8	kg
PP	Pulse pressure	11	mmHg
PV	Peak velocity	4	cm/s
ρ	Blood density	2A, 16	g/L or kg/m^3
RR	R to R interval	6	ms
SBP	Systolic blood pressure	13	mmHg
SVa	Stroke volume within the distal thoracic aorta	2	ml
SV	Stroke volume	**7**	ml
SVR	Systemic vascular resistance		dyne s cm^{-5}
SVR_i	Systemic vascular resistance index		dyne s cm^{-5} m^{-2}
TSVR	Total systemic vascular resistance		dyne s cm^{-5}
$TSVR_i$	Total systemic vascular resistance index	12	dyne s cm^{-5} m^{-2}
v, *v*(*t*)	Velocity of blood flow in the distal thoracic aorta	1	cm/s
V_{pw}	Pulse wave velocity	16	m/s

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