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Research Article

HEARTSMART® SOFTWARE COMPUTER PROGRAM FOR PERFORMING HAEMODYNAMIC STUDIES AT BEDSIDE DURING RESUSCITATIVE FLUID THERAPY: VASOPRESSORS AND INOTROPES

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ABSTRACT
The revolutionary HeartSmart® continuous cardiac dynamic monitoring (CCDM) by way of empirical physiological formulae (EPF) embedded into an EPROM chip or in any other device with a personal computing platform, permits for haemodynamic monitoring at bedside, see diagram 3. The physiological parameters required to provide the haemodynamic variables are: heart rate, blood pressure, core body temperature degrees Celcius, height (cm) weight (kg) and mean central venous pressure the only parameter that is not non invasive. Caring for shocked septic – sepsis adult patients is a real challenge. The outcome of any interventional procedure to a great extent relies upon quality, simple, robust haemodynamic monitoring to guide fluid resuscitation with the use of vasopressors and or inotropes. Using the Bland-Altman method for comparing two measurement techniques, there was good agreement between measured and calculated Cardiac Index (Ci), Mean Pulmonary Artery Pressure (MPAP) and the Mean Pulmonary Artery Occlusion or Capillary Wedge Pressures (MPAOP / MPWP) The measured (PACTD) and calculated (HS) values of CI are identical agreement mean of differences (CI-0.095 to 0.295) The 95 % limits of agreement -3.662 to 3.8611 / min / m^2), see Legend 1. The measured (PACTD) and calculated (HS) values of MPAP agreement the mean of differences PACTD 1.866 mmHg (CI 0.996 to 2.776) and for HS 1.383 mmHg (CI 0.557 to 2.210) The 95 % limits of agreement -15.266 to 19.037 mmHg for PACTD and -13.478 to 16.245 mmHg HS, see Legend 2. The measured (PACTD) and calculated (HS) values of MPWP agreement the mean of differences PACTD -1.056 mmHg (CI-1.552 to -0.561) and for HS -1.312 (CI -1.764 to -0.860) The 95 % limits of agreement -10.529 to 8.416 mmHg for PACTD and -9.867 to 7.243 mmHg HS, see Legend 3. This indicates that, when estimating CI and MPWP in critically ill septic patients, CCDM-HeartSmart® provides values close to those generated using PACTD.
Keywords: Computing software module, cardiac index / output, haemodynamic variables, errors of measurement, thermodilution, central venous pressure and sepsis septic - shock.

INTRODUCTION

Caring for shocked septic – sepsis adult patients is a real challenge. The outcome of any interventional procedure to a great extent relies upon quality, simple, robust haemodynamic monitoring to guide fluid resuscitation with the use of vasopressors and or inotropes. However, the choice of which vasopressor and or inotrope to use in clinical practice is something of guessing or 'Russian Roulett' as to the outcome of such interventional treatment in shocked septic – sepsis adult patients. This unique HeartSmart software permits the effects of pharmaceutical drugs that alter the physiological parameters affecting many haemodynamic variables especially cardiac output and left heart pressures in the heart and lungs. The aim of this study is to see if the methods agree well enough for CCDM to replace the industry gold standard method PACTD, or perhaps to be used interchangeably with it[1] in adult cases of sepsis or septic – shock, see Figure 5. The study meets the requirements of the Helsinki Declaration. A new bedside method of estimating continuous haemodynamic variables through a central venous pressure catheter using standard methods of ECG with blood pressure monitoring is described and validated[1]. This continuous cardiac dynamic monitor CCDM ($HeartSmart_{TM}$) is not based upon current mathematical platforms. CCDM uses a unique empirical set of physiological algorithms to derive haemodynamic variables[2,1], embedded into a computer software program that can run on any 'app' personal computer or monitor having computing functionality. The Pulmonary Artery Catheter employing the Thermodilution Method (PACTD) is considered as being the standard method of bedside haemodynamic monitoring since the 1970's. There is much controversy concerning the value of PACTD and the proclaimed values of the benefits PACTD can deliver. However, there is almost universal acceptance that PACTD carries a significant risk of complications, morbidity and mortality.[3-8]. In the healthcare environments the economical requirements to make large financial savings is also a key concern to healthcare providers throughout the world. PACTD is highly invasive and by comparison to alternative systems that can be described as being less invasive than PACTD. Invariably other technologies do require invasive procedures and come with large dedicated monitors that are expensive, unfriendly to use with the associated long learning skill curves. Clinicians are faced with the dilemma that if all these systems were applied to the patient and measurements recorded simultaneously, each technology would give differing haemodynamic values, so the question arises which of these haemodynamic values are reliable[9,10]. That question can only be answered by close scrutiny of the outliers against the clinical and pathophysiological background, the method employed here. Two teams of practiced physicians took part in analysing the results of this study as to what data should be removed based upon interrogating all the haemodynamic variables, treatments and diagnosis. Both teams agreed that cases 14, 50 and 60 were so obviously wrong due to suspected operator error using the above criteria and were discarded. The investigative team was at the Royal Hallamshire Hospital the analytical team was at the Leeds General Infirmary and University of York. The first team's removal of data is shown in the left side of the Figures 1 through 6 whilst the second team's observations are on the right hand side of Figure 1 through 6. The questionable results were shown to three independent anaesthetists outside of each team for assessment.

The Physical and Physiological Principles Underpinning CCDM

The Continuous Cardiac Dynamic Monitoring (CCDM) using Empirical Physiological Formulae (EPF's), are derived from haemodynamic observations during cardiac surgery and are analogous to established laws of physics (hydraulics) and cardiovascular physiological principles and laws, especially that described in the text books as the 'Elastic Band Law of the Heart' (EBLH)[11]. The application EBLH are the result of many medical scientist investigative work, Young[12], Starling[13], LaPlace[14], Bainbridge[15-17] Marey[18], Guyton[19] to name only but a few of many. The Laws of Flow appertaining to the heart and lungs are the work of Stephen Hales[20,21], Darcy and Poiseuille[22,23] again just some of a great number of physiologist and physicists of the past since 1733, who have contributed to our knowledge today. The HeartSmart cardiac index formula, see below, with some 30 subsets are built upon and analogous to the laws of Young, Darcy and Poiseuille, taking those physical expressions and surrogating the component parts within with physiological parameters to produce biophysical expressions. In addition the understanding of the principle of the EBLH the work of Starling, Marey, Bainbridge and Guyton, provides the links to the cardiovascular functions applicable to the 'K' grid that are used to estimate cardiac index from core body temperature in degrees Celscius, CVP and heart rate beats per minute.

HeartSmart Ci expression

$$Q = CVP.\ K\ .T/HR^2$$
or
$$Q = P.K.T/R$$
or
$$Q = P/R$$

Where Q = flow (cardiac index), CVP = pressure, T = temperature at the time of estimating flow, HR^2 = an empirical number for resistance (every heart beat changes the resistance) K = an empirical physiological drive or power constant accounting for viscosity of the blood, compliance and capacitance and elastic stretch of heart fibres etc.

The 'K' grid shows the affects of the range values of CVP and HR to the product of the K values to provide an estimate of cardiac index. At certain values of CVP or HR they may cover two or three values of K, in such circumstances the two or three values are average, giving an average K value that will generate an approximate Ci value. See diagrams 1 and 2

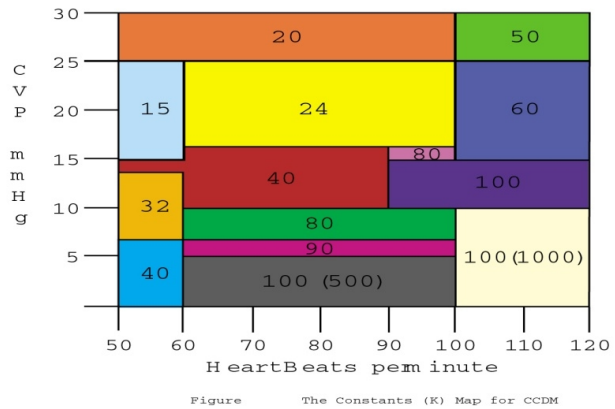


Diagram 1: The K Grid over ranges of CVP and HR

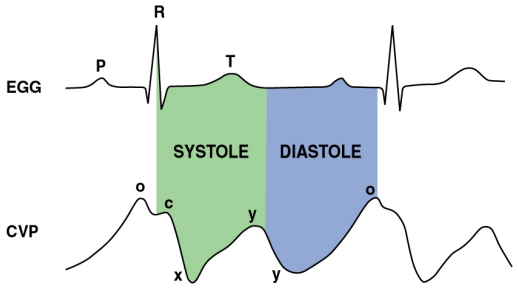


Diagram 2: The CVP Waveform Over Laid on ECG Waveform

Diagram 3: The Comparable Haemodynamic Values Displayed on the PACTD monitor against the haemodyanmic values calculated by HeartSmart on a laptop computer

Method

Having received institutional ethical committee approval for this prospective data study, the data came from three general intensive care units, who were taking part in the Department of Health pulmonary artery catheter management study PAC-Man, administered through the Intensive Care National Audit Research Centre ICNARC at the BMA House in London. Two teams of investigators were involved in this study, those recording the PACTD measurements and those computing the haemodynamic values using HR, BP, T^0C and CVP. Both teams were blind to each team's results. Every patient or their relatives gave written consent to take part in this double blind study. All subjects in this study would have had a right heart catheterisation using the floatation pulmonary artery catheter as part of their routine observations and or treatment. This study complies with the Helsinki declaration. A full clinical profile of each patient with the diagnosis were admitted into the general intensive care unit (GICU) especially those patients with sepsis or septic shock the criteria for being in this study, the patient data was available to all the investigators. The design of the study was by author being the same as that in other proactive and retrospective clinical studies that had or were taking place simultaneously with this study. The design of the study was based upon the fact that when performing PACTD cardiac output determinations three bolus injections of saline are made. If the results are

within 10 % of each other then you can take the average value to be the cardiac output. Usually haemodynamic trends are of most clinical use rather than single measurements, preferably over 24 h period, thus, every 4 h or as and when the patient's circumstances require haemodynamic evaluation. From a statistical analysis perspective repeatability of test methods 95 % agreement the more plots of data the better and more reliable the results. Thus, the design of these heamodynamic studies covers the necessary end points. Those performing the PACTD were experience clinicians used to performing PACTD, were unaware of this study taking place, except one who led the hospital studies. At no time did the author know which hospitals were involved, had no involvement in the selection of recruits into the study or with those investigators of the PAC – Man study. We analysed the data of 60 consenting adult patients admitted and clinically assessed as to the primary and secondary reasons for admission into in the general intensive care units (GICU), the study took place between the years 2002 – 2006. All patients were catheterised with PACTD as part of their normal treatment, recording 6 sets of measurements of the PACTD haemodynamic variables giving a total of 360 points of data. The measured physiological parameters of core body temperature in degrees Celsius, systolic and diastolic blood pressure mmHg, heart rate in beats per minute and CVP in mmHg were given to the author. The measured values of Ci, MPAP and MPWP were hidden until the author calculated 360 of each of the variables for Ci, MPAP and MPWP from the raw data, making this a double blind study. Fluid input and output was also recorded.

Demographics

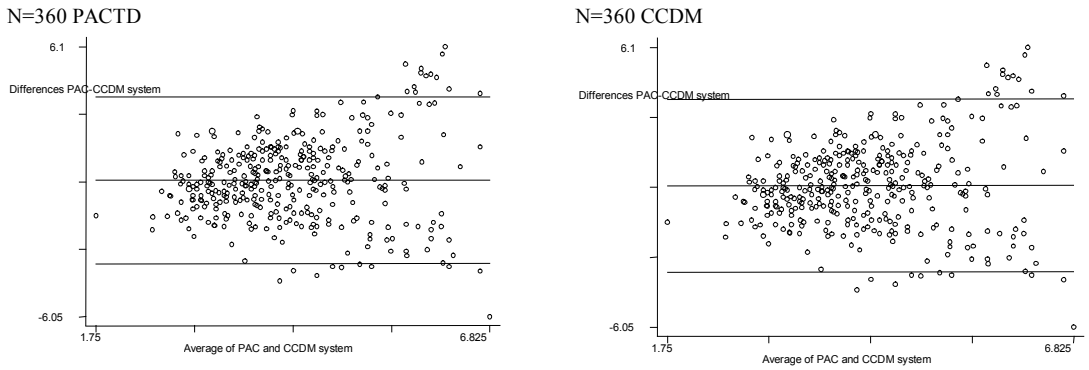
28 Females 46.66 %, age range 20 – 80 years old the average age being 63.93 years old. Of the 28 patients only 3 10.71 % were not suffering from sepsis or systemic inflammatory response syndrome (SIRS). 32 Males 53.33 %, age range 21 – 88 years old having an average age 61.4 years, 12 recruits 37.5 % were not suffering from shock conditions. Of the 60 patients admitted into the study 15 patients 25 % had an uncomplicated haemodynamic assessment.

RESULTS

The plots in Figures 1 through 6 inclusive below show a comparison of heamodynamic variables measured by the Pulmonary Artery Catheter Thermodilution Method (PACTD) against those haemodynamic variables calculated by the Continuous Cardiac Dynamic Monitoring (CCDM-HeartSmart) system – a new less invasive technique using empirical physiological formulae. The differences between the two methods have been plotted against the average of the two measurements to see easily the size of the differences and their distributions around zero. It is also possible to check that the differences are not related to the size of the measurements. The mean difference and limits of agreements are superimposed as three horizontal lines. (Provided differences within the limits of agreements would not be clinically important, the two methods can be used interchangeably.) Three independent consultants in intensive care checked the patient's forms to identify possible measurement recorded errors. Also the author reviewed the data with another two independent consultants. A sensitivity analysis was performed to see how the results changed once observations that were so obviously "wrong" were excluded see legends 1 through 3 inclusive.

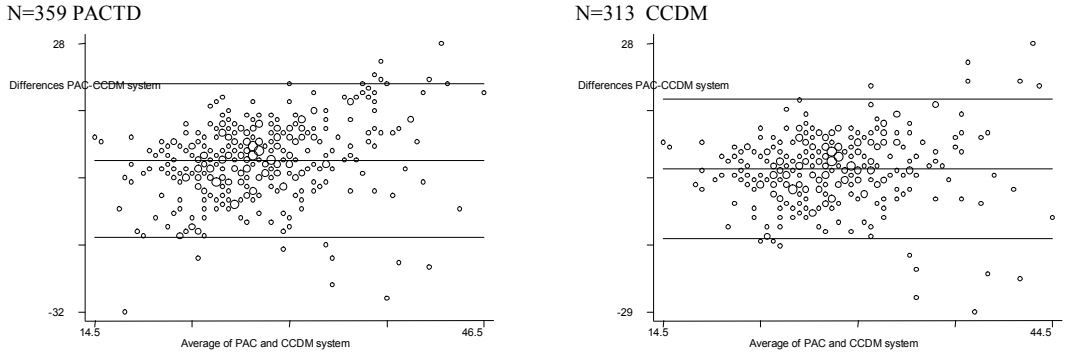
Legend 1: Cardiac Index (L / mins / m^2)

There seemed to be no errors so the two analyses are exactly the same.



	All data	Excl. wrong meas.
Limits of Agreements	-3.662 to 3.861	-3662 to 3.861
Mean Difference	0.100 (CI-0.095 to 0.295)	0.100 (CI-0.095 to 0.295)
Range	1.750 to 6.825	1.750 to 6.825
Pitman's Test of diff in var (p value)	0.011	0.011

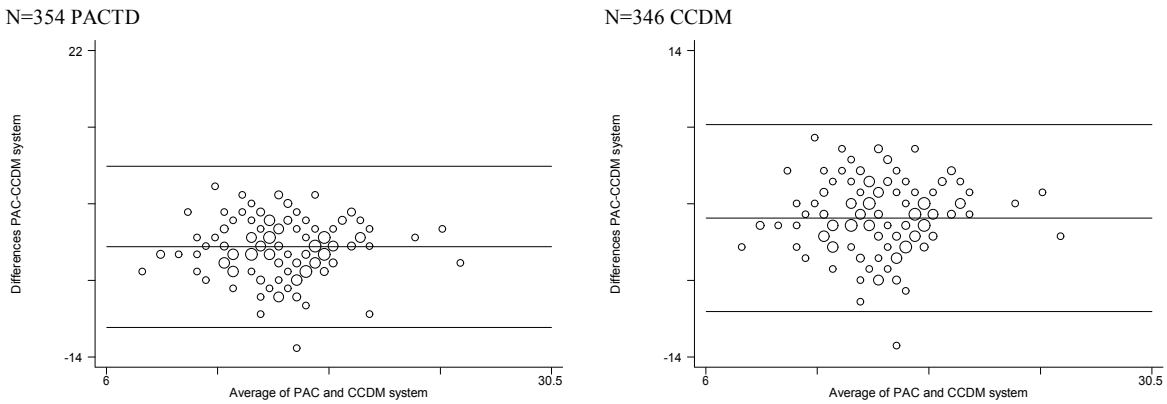
Legend 2: Mean Pulmonary Artery Pressure (mm Hg)
14 observations were identified as mistakes from the three independent consultants. Furthermore 32 observations were excluded on suggestion of KWD and two other independent consultants.



	All data	Excl. wrong meas.
Limits of Agreements	-15.266 to 19.037	-13.478 to 16.245
Mean Difference	1.866 (CI0.996 to 2.776)	1.383 (CI 0.557 to 2.210)
Range	14.500 to 46.500	14.500 to 44.500
Pitman's Test of diff in var (p value)	0.000	0.036

Figure 3: Mean Pulmonary Artery Wedge Pressure (mm Hg)

One subject (6 observations) was excluded from the beginning, 8 further observations were considered wrongly recorded and thus removed from the dataset.



	All data	Excl. wrong meas.
Limits of Agreements	-10.529 to 8.416	-9.867 to 7.243
Mean Difference	-1.056 (CI-1.552 to -0.561)	-1.312 (CI -1.764 to -0.860)
Range	6.000 to 30.500	6.000 to 30.500
Pitman's Test of diff in var (p value)	0.001	0.168

Figure 1: Scatter diagrams of the data

Figure 4(1): CI (360)

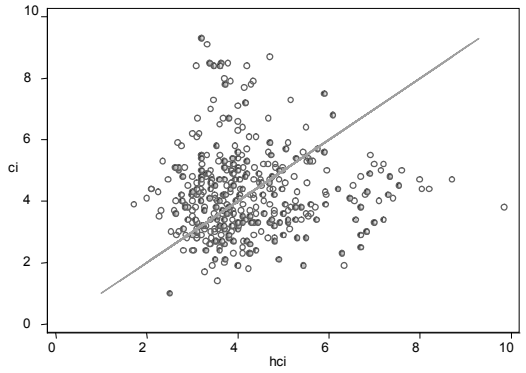


Figure 4 (2): CI (360)

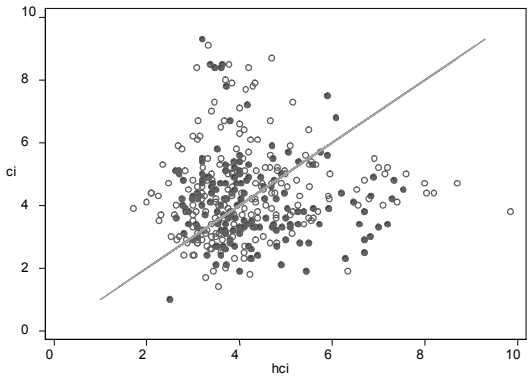


Figure 2 (3): MPAP (359)

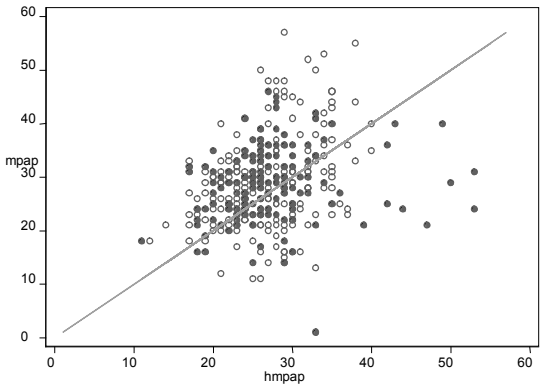


Figure 4 (4): MPAP (313)

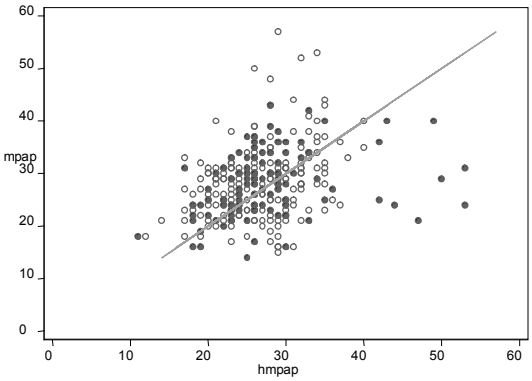


Figure 3 (5): MPAWP (354)

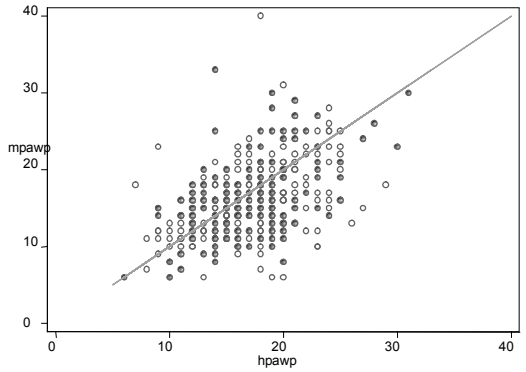
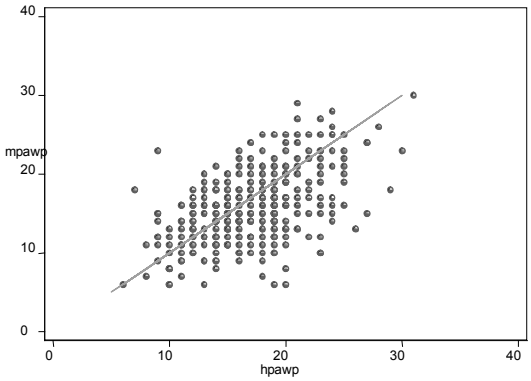
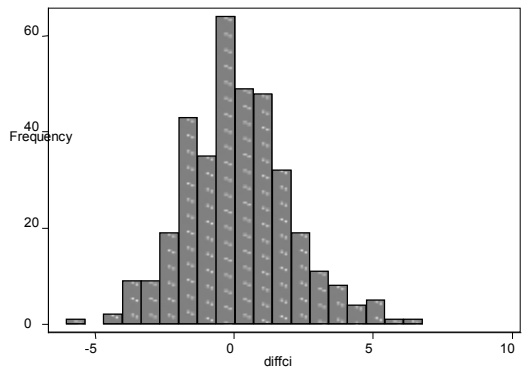


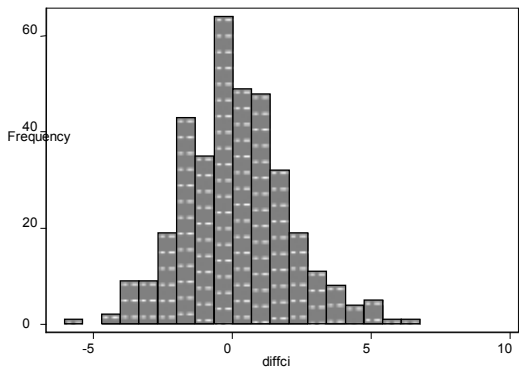
Figure 4 (6): MPAWP (346)

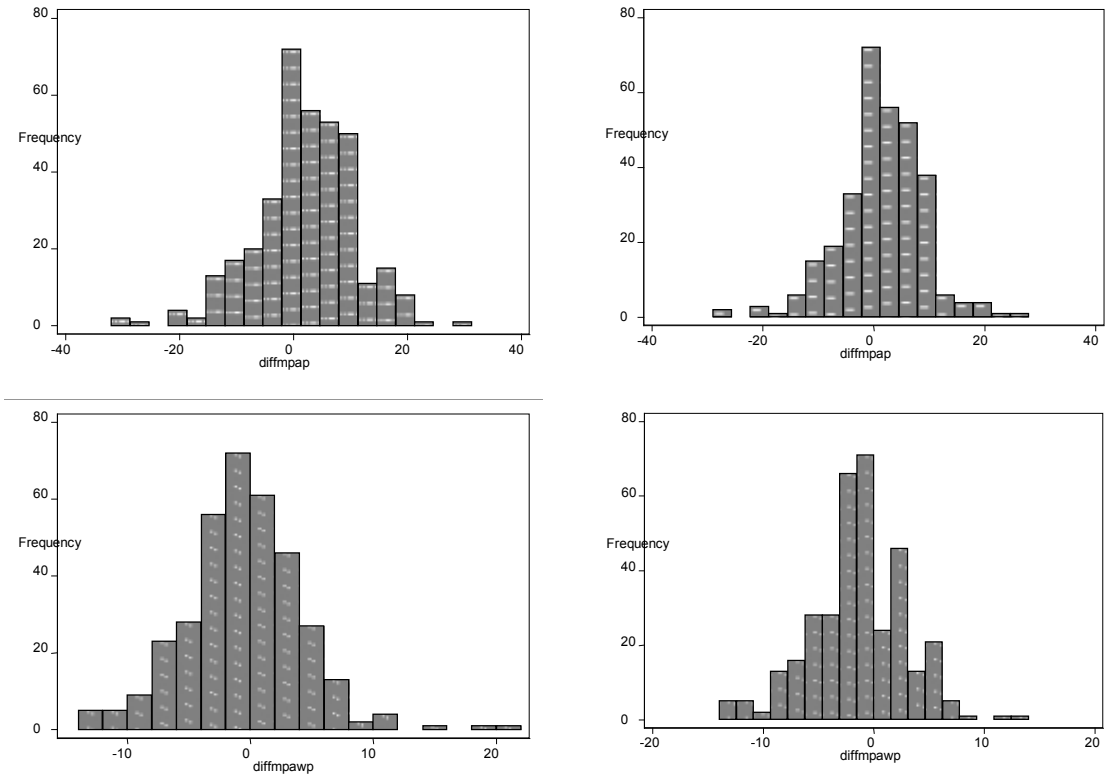


If the methods agree exactly the points would all lie on the line of equality

Figure 5: Histograms of differences (measures-calculations)







For CI the two methods appear to agree quite well on average, for MPAP the CCDM underestimate the values while for MPWP it seems to overestimate them. Both MPAP and MPWP are dependant upon the measured values of MAP and CVP and that the operator has zeroed the blood pressure and central venous pressure circuits. Mistakes in these values will affect the final MPAP and MPWP values.

Figure 6: Descriptive Statistics

Variable	Obs	Mean	Std. Dev.	Min	Max
diffci	360	.0995789	1.88065	-6.05	6.1
diffmpap	359	1.885794	8.575709	-32	28
diffmpawp	354	-1.056497	4.736355	-14	22
Variable	Obs	Mean	Std. Dev.	Min	Max
diffci	360	.0995789	1.88065	-6.05	6.1
diffmpap	313	1.383387	7.430877	-29	28
diffmpawp	346	-1.312139	4.27744	-14	14

Investigation of Outlying values

Invariably in clinical trials questionable data will present itself arising out of technical or operator errors severally or jointly. Such erroneous data can affect the outcome of the study leading to unsatisfactory conclusions being drawn by the investigators and others. The investigators with experienced anaesthetist outside and independent of the investigative teams, agreed on the erroneous recordings operator error of haemodynamic left heart pressures namely the mean pulmonary artery and mean pulmonary artery capillary wedge pressures, that were physiologically wrong. When scrutinising clinical trial data it is necessary that a robust method for discarding erroneous or misleading data is acceptable through a sound scientific process, in order that the reader(s) may readily concur why that outlying data should be omitted, from the results being statistically analysed. We first challenged some of the cardiac index results, whereas in a number of study subjects a set of spurious CI values were recorded that did not follow the trend of the measured values recorded and or estimated by HeartSmart, see Table 1. Initially the first team removed one pair of PACTD mean pulmonary artery pressures and the HeartSmart team removed 47, as there was a conflict between the MPAP and MPWP values, that is, the MPWP value being equal or higher than the measured MPAP or conversely the MPAP value being lower than the MPWP, see legend 1. The first team of investigators had missed these irregularities when assessing the quality of the study data. The same methodology of examination of spurious data was applied to the mean pulmonary artery occlusion/capillary wedge pressure against the mean pulmonary artery pressures. The team of investigators removed 6 MPWP measurements and the HS investigator(s) removed 14 sets of data. The reasons for this were slightly different to or first basis of those measurements in legend 2, here the test was the number of MPWP measurements that were lower than the mean central venous pressure measurements, there being no lung pathology to support that data etc. See Tables 1–3. There are only two bedside haemodynamic monitoring systems that are able to deliver all the haemodynamic variables, the pulmonary artery catheter thermodilution method (PACTD) and the continuous cardiac dynamic monitoring software (CCDM) trademark HeartSmart®. The estimated haemodynamic values of cardiac index (Ci), mean pulmonary artery (MPAP) and mean pulmonary artery occlusion (MPAOP) (wedge) pressures (MPWP) between two methods

can be interrogated by a cardiovascular physiological challenge or analysis as to their clinical reliability or accuracy. For example, if the pulmonary artery catheter thermodilution method gave a hyperdynamic value for cardiac index/output, whilst the remaining haemodynamic values were in the normal range and there are no signs or symptoms indicating that the patient was in shock sepsis or SIRS, then, the conclusion would be in the absence of any other pathophysiological abnormality, that the value of cardiac index / output was wrong and should be ignored or discarded. It is known that the mean pulmonary arterial pressure MPAP is higher than the mean pulmonary artery occlusion (wedge) pressure MPWP, that the MPWP is generally higher than the mean right atrial RAP or central venous pressure CVP. See Diagram 3.

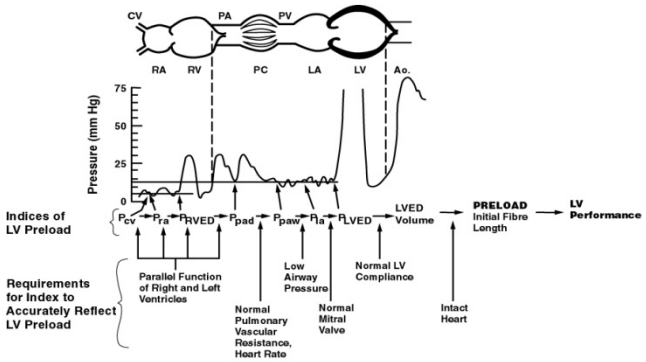


Diagram 4: The PACTD Pressure Waveforms in the Heart

However, it is not uncommon to encounter recordings of these left heart pressures that contradict the haemodynamic physiological possibilities, as demonstrated in this study. There are a number of other important haemodynamic variables that are calculated from the mean arterial pressure MAP, CVP, MPAP, MPWP, Ci and cardiac output (CO) as shown below. Two of the most important values are the systemic vascular resistance (SVR) and the pulmonary vascular resistance (PVR) from two expressions:

$$SVR = MAP - CVP \times 80 / (Ci \text{ or } Co) \text{ dynes per cm}^{-5} \text{ per second}$$

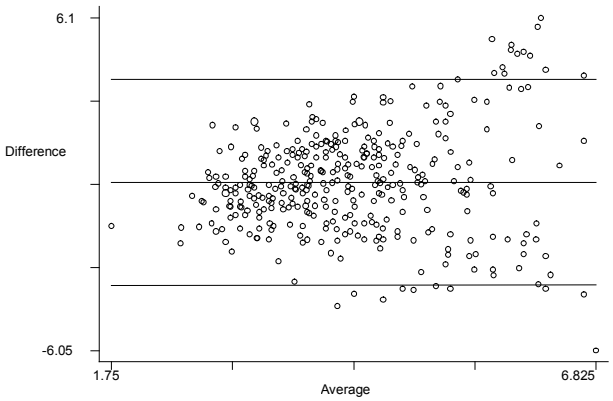
$$PVR = MPAP - MPWP \times 80 / (Ci \text{ or } Co) \text{ dynes per cm}^{-5} \text{ per second}$$

The HeartSmart expressions for MPAP and MPWP are derived from the measured MAP and CVP, if there are errors in the measured values those errors will be reflected in the empirical calculated values of MPAP and MPWP respectively, as shown by the expressions below:

$$MPAP = MAP \times 0.2 + CVP \text{ mmHg}$$
$$MPWP = MPAP \times 0.2 + CVP \text{ mmHg}$$

Clinicians take into account the two values of resistance, SVR and PVR when considering options of fluid management, in critically ill patients or for patients undergoing major general surgical or medical procedures, where haemodynamic peri-operative optimisation by way of goal directed therapy is desired. However, SVR, PVR with the left heart pressures MPAP and MPAOP (MPWP) are useful parameters when interrogating spurious and or questionable haemodynamic data. Hence, the outlying measurements between the PACTD and CCDM in this study have been scrutinised and challenged using cardiovascular physiological principles and laws combined with clinical expertise. For example, it is known that the pulse rate varies inversely with the blood pressure; i.e., the pulse is slow when the pressure is high; an expression of baroreceptor reflex influences on heart rate, Marey's law. Bainbridge's reflex when fluids are administered a corresponding increase in heart rate occurs. These two physiological reflexes will affect cardiac output or index as well as having an affect on vasoconstriction and dilatation of the blood vessels etc. The outlying value tables between the two methods are contained in the boxes below with the required physiological parameters necessary to perform the challenge to those two sets of results to the right and outside the inner box, see Legends 1 through 3. The Bland – Altman Scattergram Repeatability of test methods for each set of outlying estimations Ci, MPAP and MPWP respectively in each analytical box. The investigators came to the conclusion that the data in study numbers 14, 50, 60 being discarded entirely accounting for 12 sets of paired values or 5 % of the entire study population of 60 paired sets of measurements, see Tables 1 and 2. Looking at the 15 outliers of 360 (4.17 %) for the MPAWP in the measured 2 males and 4 female patients, values 12 are lower than the measured CVP values, none of these patients are suffering from a pulmonary embolus although two had aspiration pneumonia and all 6 patients were diagnosed as suffering from sepsis . Study numbers 3 and 5 accounts for 11 out of the 15 records 73.33 % of this suspicious questionable haemodynamic results. For the MPAP 15 outliers representing 4.17 % of 360 data points 10 patients 16.66 % 6 males and 4 females again study number 5 had 5 outliers 33.33 % of 15 outliers. 95 % limits of agreement would permit of 360 data plots 18 outliers for each heamodynamic variable, so 15 outliers for the MPAOP and MPAP is acceptable.

Table 1: Cardiac Index



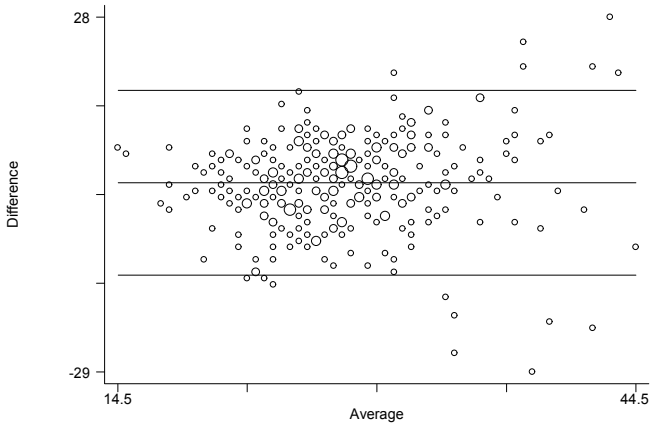
list studynum obs ci hci diffci if diffci>3.861

studynum	obs	ci	hci	diffci	temp.	cvp.	hr.	map.	pwp
23.	4	5	**8.5**	3.78	4.72	37.9	14.0	95	97.7	13.0
79.	14	1	**8.4**	3.08	5.32	34.5	10.0	82	56.0	15.0
80.	14	2	**8.4**	4.2	4.2	34.9	11.0	87	53.7	19.0
81.	14	3	**8**	3.7	4.3	35.4	10.0	85	**45.7**	18.0
82.	14	4	**7.9**	3.84	4.06	35.9	9.0	82	**46.3**	16.0
149.	25	5	**8.7**	4.7	4	37.4	21.0	93	60.0	24.0
180.	30	6	**9.1**	3.33	5.77	34.6	16.0	79	84.0	20.0
295.	50	1	**8.5**	3.63	4.87	37.8	**36.0**	137	68.3	**11.0**
296.	50	2	**8.5**	3.38	5.12	37.9	**36.0**	142	91.3	**11.0**
297.	50	3	**9.3**	3.2	6.1	36.3	**27.0**	126	95.0	**5.0**
298.	50	4	**8.4**	3.47	4.93	36.4	27.0	119	70.7	**5.0**
299.	50	5	**7.8**	3.72	4.08	36.4	27.0	115	95.7	**6.0**
300.	50	6	**8.4**	3.61	4.79	36.6	27.0	117	70.0	**7.0**

list studynum obs ci hci diffci if diffci<-3.662

studynum	obs	ci	hci	diffci	temp.	cvp.	Hr.	map	pwp
41.	7	5	3.8	9.85	-6.05	37.8	16.0	96	78.6	20.0
66.	11	6	1.9	6.34	-4.44	38.4	11.0	100	69.3	17.0
130.	22	4	4.7	8.7	-4	37.6	17.0	121	81.7	22.0
131.	22	5	4.4	8.2	-3.8	37.4	14.0	113	56.7	19.0
205.	35	1	3	6.83	-3.83	37.8	11.0	78	74.3	16.0
226.	38	4	2.5	6.7	-4.2	37.8	15.0	113	71.3	16.0
351.	59	3	2.9	6.7	-3.8	40.2	9.0	103	62.7	14.0
352.	59	4	2.3	6.29	-3.99	40.3	15.0	124	54.3	19.0
355.	60	1	3.3	7	-3.7	37.1	8.0	79	84.3	11.0
356.	60	2	3.4	7.2	-3.8	37.1	8.0	65	78.3	12.0

Table 2: MPAP



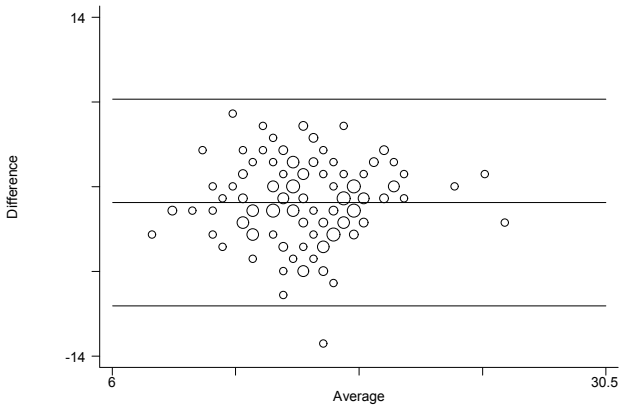
. list studynum obs mpap hpap diffmpap if diffmpap>16.245 and diffmpap!=.

ci	studynum	obs	mpap	hpap	diffmpap	cvp.	Sys.	Dys.	map
13.	3.69	3	1	**53**	24	29	12.0	94.0	49.0 64.0
14.	4.87	3	2	**50**	21	29	10.0	61.0	38.0 45.7
15.	3.98	3	3	**48**	38	10	21.0	136.0	60.0 85.3
16.	4.3	3	4	**57**	29	28	11.0	119.0	59.0 79.0
18.	3.82	3	6	**52**	32	20	14.0	123.0	66.0 85.0
52.	3.1	9	4	40	21	19	19.0	97.0	65.0 75.7

list studynum obs mpap hpap diffmpap if diffmpap<-13.478

ci	studynum	obs	mpap	hpap	diffmpap	cvp.	Sys.	Dys.	map
7.	3.25	2	1	**16**	21	-5	7.0	96.0	55.0 68.7
166.	4.4	28	4	15	**31**	-16	12.0	**169.0**	60.0 96.3
295.		50	1	24	53	-29	**36.0**	89.0	58.0 68.0
296.		50	2	29	50	-21	**36.0**	99.0	65.0 76.0
297.		50	3	21	47	-26	**27.0**	133.0	76.0 95.0
298.		50	4	24	44	-20	**27.0**	94.0	59.0 70.7
299.		50	5	31	53	-22	**27.0**	131.0	78.0 95.7
300.		50	6	25	42	-17	**27.0**	94.0	58.0 70.0
348.	5.45	58	6	16	30	-14			

Table 3: MPAOP



. list studynum obs mpawp hpawp diffmpawp if diffmpawp>7.243 and diffmpawp!=.

studynum	obs	mpawp	hpawp	diffm~wp	cvp	map
44.	8	2	**18**	7	11	**4** 73
52.	9	4	23	9(25.6)	14	19 70
328.	55	4	29	21	8	14 70

. list studynum obs mpawp hpawp diffmpawp if diffmpawp<-9.867

studynum	obs	mpawp	hpawp	diffm~wp	cvp	map
8.	2	2	**6**	19	-13	14 80
9.	2	3	**7**	18	-11	13 84
25.	5	1	**6**	20	-14	15 70
26.	5	2	**10**	23	-13	18 58
27.	5	3	**12**	22	-10	18 63
28.	5	4	**12**	23	-11	19 90
29.	5	5	**10**	23	-13	18 81
55.	10	1	**15**	27	-12	23 64
88.	15	4	**13**	26	-13	21 94
150.	25	6	**18**	29	-11	24 75
233.	39	5	**14**	24	-10	19 57
314.	53	2	**8**	20	-12	14 93

DISCUSSION

We live in a turbulent world where disasters can occur at any given moment and where urgent medical aid is required, combined with the problems of the astronomical rise in costs of health care provision, the political climate of cost cutting, the need for robust, simple portable haemodynamic monitoring is key to survival of patients. The use of pharmacuetical drugs in all types of pathologies lies at the very centre of the medical and surgical treatment of patients. However, it is relatively unknown how those drugs maybe interacting on the cardio-dynamics of patients as they carry out daily activities, especially those patients who have long term conditions such as respiratory pathologies, for example, the treatment of pulmonary artery hypertension and the incidence of such is on the increase. There's no method of being able to evaluate the efficacy of a particular drug treatment as to which drug is the most appropriate for that patient or patient group(s). The requirement for each cell in the body to be able to meet an adequate metabolic requirement oxygen supply and demand cannot be overstated, of which many drugs may interfere with especially if those drugs are causing side effects etc. The potential of HeartSmart computer software for use by the Pharmacuetical industry in the development of new drugs, monitoring efficacy and in research as or as educational tool for the medical profession are almost unlimited. HeartSmart computer software is in the final phase of writing a non invasive version(s) paediatric and adult modules, clinically trialled and to regulatory requirements etc. HeartSmart is a system that is easy to use, cheap, reliable with a short learning curve, providing consistent results, that does not require the hospital to spend money on new expensive monitors or get involved with long term contracts for excessively priced consumables, which unfortunately is the position in many NHS Trust Hospitals UK, this situation of mixed opinions and choice of method is likely to continue. HeartSmart CCDM is a computer software program that's not based upon mathematical platforms, whereas other alternative technologies are. Hence, this is a real time disruptive or destructive technology to existing technologies. However, the cardiovascular physiology and physics underpinning the empirical physiological formulae need to be vigorously tested not only against established haemodynamic technologies but its performance in the most serious of clinical situations. Amongst all the controversy of the benefits of haemodynamic monitoring and its usefulness, there is little doubt that haemodynamic monitoring plays a useful role in the fluid management either for the critically ill or those patients undergoing major surgical or medical procedures[23-28]. In the face of such a controversial subject of any haemodynamic monitoring to assist in assessing cardio-dynamics in the management of fluids, or by optimising blood flow using goal directed therapy, with the all the differential outcomes, the necessity for a system such as HeartSmart-CCDM is a key technology to simply resolve many of the issues of the value of haemodynamic monitoring. The basis of this study had one aim to rigorously evaluate HeartSmart CCDM against the industry 'standard' pulmonary artery catheter thermodilution method PACTD. This aim also raised the question to see if the methods agree well enough for CCDM HeartSmart to replace PAC, or perhaps to be used interchangeably. That question from scrutiny and analysis of the results of these paired set of measurements indicates the answer is in the affirmative. From the data analysed the answer for CI the two methods appear to agree quite well on average, for MPAP the CCDM underestimate the values while for MPWP it seems to overestimate them. The clinical study data also determines from the outliers for the MPAP and MPAOP these are caused by technical and or operator error, because those results are not consistent physiologically or with the clinical diagnosis of the patient see Figure 5. Therefore, if the general trend is that CCDM truly underestimates the MPAP whilst overestimating the MPWP, such vagaries are unlikely to be of major clinical significance providing that difference is no more than 15 % away from the measured value. Even more so if the results stay within the

normal or abnormal bandwidths. Similar results in other prospective and retrospective clinical trials since 1995 where CCDM – HeartSmart has been compared with PACTD would indicate that HeartSmart's performance is comparable with PACTD[28-39], HeartSmart-CCDM appears to be an important technological advance in bedside haemodynamic monitoring. However, the issue of the nurses and physcians knowledge and skill in performing haemodynamic measurements using PACTD remains a major issue some high a century later[40,41]. Hence the need for a simple haemodynamic system that is not so operator dependant, simple and easy to use, and far less costly that can be used on any group of patients routinely, would be of great benefit. But of special importance and usefulness haemodynamic monitoring is the ability to be able to reasonably assess the haemodynamic status of those patients who are suffering from shock by way of sepsis based on SIRS, where aggressive interventional therapy is being administered to the patient by the medical staff[28-30]. CCDM HeartSmart has to be validated against existing technologies and in particular against the perceived 'standard' the pulmonary artery catheter thermodilution method PACTD. More often than not comparative haemodynamic studies are performed on patients who require ICU support after major surgery, though not necessarily suffering from sepsis or SIRS. In this study 75 % of those admitted into the study were assessed by experienced investigators using clinical judgment with the pathology to confirm that these patients were suffering from sepsis or SIRS. All those recruited into the study had a chest X-Ray to confirm the PACTD was correctly placed in the West Zone of the heart. Because of all the difficulties encountered with PACTD there is a long standing requirement by the profession for a simpler reliable method in order that the nursing and medical staff can get haemodynamic data easily, that will follow trends of treatment against baseline values, and can be understood[28]. This is especially relevant in ICU's where patients are compromised by multiple organ dysfunctions and in many cases this status maybe irreversible. Nevertheless, fluid management it still necessary requirement for the treatment of the critically ill[30,31,38-42]. This study is evidenced based upon the results indicates that the CCDM – HeartSmart could either be a reliable replacement for or interchangeable with PACTD in the general intensive care units etc.

CONCLUSIONS

The CCDM-HeartSmart® computer software module could prove invaluable for optimizing response to fluid replacement and for guiding cardiovascular support in shock septic - sepsis patients. This new, simple technology may help to facilitate routine adoption of perioperative optimization of blood flow using early goal-directed therapy.

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Dr. Kenneth J. Warring-Davies is the inventor of CCDM HeartSmart® and has personally financed this invention. No financial contributions were made to any institution or person. He is the CEO of Medics and HeartSmart Limited.

REFERENCES

1. Berridge JC, Warring Davies KJ, Bland JM, Quinn AC. A new, minimally invasive technique for measuring cardiac index: clinical comparison of continuous cardiac dynamic monitoring and pulmonary artery catheter methods. Anaesthesia 2009; 64: 961–967 http://dx.doi.org/10.1111/j.1365-2044.2009.05943.x
2. Gareth SG, Kantor JR. Svirbely MG Automated Medical Algorithms: Issues for anaesthesiology. Risk indices: What is their value to the clinician and patient. Anesthesiol 2001; 94: 191-3. http://dx.doi.org/10.1097/00000542-200102000-00005
3. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986; i: 307-310. http://dx.doi.org/10.1016/S0140-6736(86)90837-8
4. Soni N. Swan song for the Swan-Ganz catheter? Brit Med J 1996; 313: 763-764. http://dx.doi.org/10.1136/bmj.313.7060.763 PMid:8842058 PMCid:PMC2352214
5. Simini B. Pulmonary Artery Catheters in Intensive Care. Lancet 2006; 66: 435-436.
6. Harvey S, Young D. et al. Pulmonary artery catheters for adult patients in intensive care. Cochrane Database of Systematic Reviews: 2013:2:CD003408; 2006.
7. Harvey S, Harrison DA, Singer M. Assessment of the clinical effectiveness of pulmonary catheter in management of patients in intensive care (PAC-MAN): a randomized controlled study. Lancet 2005; 366: 472–477. http://dx.doi.org/10.1016/S0140-6736(05)67061-4
8. Hadian M, Pinsky MR. Evidence-based review of the use of the pulmonary artery catheter: impact data and complications. Critical Care 2006; 10(Suppl 3): S8. http://dx.doi.org/10.1186/cc4834
9. Jansen JRC. Novel methods of invasive/non-invasive cardiac output monitoring. European Society for Intravenous Anaesthesia. http://www.eurosiva.org/Archive/Lisbon/SpeakerAbstracts/Novel%20methods%20of%20invasive.htmH (accessed 02/10/2007).
10. Williams JE, Pfau SE, Deckelbaum LI. Effect of Injectate Temperature and Thermistor Position on Reproducibility of Thermodilution Cardiac Output Determinations Chest 1994; 106: 895-898.
11. Hainsworth R. Vascular capacitance: Its control and importance. Reviews of Physiology, Biochemistry and Pharmacology 1986; 105: 101-173. Springer Berlin Heidelberg ISBN 973-3-540-16874-4
12. E Rosenberg. The elasticity of mammalian lungs. An historic perspective Chest 1988; 93: 632-637. http://dx.doi.org/10.1378/chest.93.3.632 PMid:3277807
13. Braunwald E, Frahm CJ, Ross J. Jr. Studies on Starling's Law of the Heart verses Left Ventricular function in man J Clin Invest 1961; 40(10):1882–1890.http://dx.doi.org/10.1172/JCI104412 PMid:13872650 PMCid:PMC290886
14. Prange DP. Misconceptions Laplace's Law and the Alveolus: A misconception of the anatomy and misapplication of physics Adv Physiol Educ 2003; 27: 34-40. http://dx.doi.org/10.1152/advan.00024.2002 PMid:12594072
15. Jones JJ. The Bainbridge reflex. J. Physiol February 1962; 160(2): 298–305. PMid:14452295 PMCid:PMC1359533
16. Hakumäki MO. Seventy years of the Bainbridge reflex Acta Physiol Scand 1987; 130(2): 177-85. http://dx.doi.org/10.1111/j.1748-1716.1987.tb08126.x PMid:3300168
17. Vatner S, Zimpfer M. Bainbridge reflex in conscious, unrestrained and tranquilized baboons AJP - Heart and Circulatory Physiology 240(2): 164-H167.
18. Gangong WF. Review of Medical Physiology 21st Edition McGraw-Hill ISBN 007-1402365 2003 Chp3. p. 78-84
19. Guyton AC, Jones CE, Coleman TG, Granger HG. Circulatory Overall Regulation Ann Rev Physiol 1972; 34: 13–46. http://dx.doi.org/10.1146/annurev.ph.34.030172.000305 PMid:4334846
20. Hales S. An account of some hydraulic and hydrostatical experiments made on blood and blood vessels of animals. Statistical Essays Haemasticks Pfizer 1st Edition; 1965. p. 1-25
21. Levick JR. Introduction to cardiovascular physiology. 2nd edition, Butterworth Heinmann ISBN 0 7506 2167 2; 1995.
22. Parker K, McDonald DA. Blood flow in arteries. Med Biol Eng Comput 2009; 47(2): 111–118. http://dx.doi.org/10.1007/s11517-009-0440-5
23. Connors A, Speroff T, Dawson N et al. The effectiveness of right heart catheterization in the initial care of critically ill patient. JAMA 1996; 276: 889-97. http://dx.doi.org/10.1001/jama.1996.03540110043030
24. Boyd O, Grounds RM, Bennet ED. A Randomised clinical trial of the effect of deliberate perioperative increase of oxygen delivery on

mortality in high risk surgical patients. JAMA 1993; 270: 2699-707. http://dx.doi.org/10.1001/jama.1993.03510220055034 PMid:7907668
25. Wilson J, Woods I, Fawcett J et al. Reducing the risk of major elective surgery: randomised controlled trial of preoperative optimization of oxygen delivery BMJ 1999; 318: 1099-103. http://dx.doi.org/10.1136/bmj.318.7191.1099 PMid:10213716 PMCid:PMC27840
26. Rivers E, Nguyen B, Havstad S et al. Early goal directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med 2001; 345(19): 1368-1377. http://dx.doi.org/10.1056/NEJMoa010307 PMid:11794169
27. Modernizing care for patients undergoing major surgery. Improving patient outcomes and increasing clinical efficiency. A report by the improving surgical outcomes group. http://www.reducingleng thofstay.org.uk/isog.htmlH
28. Tibby SM, Murdoch IA. Monitoring cardiac function in intensive care Archives of Disease in Childhood. BMJ Publishing Group and Royal College of Paediatrics and Child Health 2003; 88: 46-52
29. Gordon AC, Russell JA. Goal directed therapy: how long can we wait? Critical Care 2005; 9: 647-648. http://dx.doi.org/10.1186/cc3951 PMid:16356258 PMCid:PMC1414039
30. Pearse R, Dawson D, Fawcett J, Rhodes A, Grounds RM, Bennett ED. Early goal-directed therapy after major surgery reduces complications and duration of hospital stay. A randomised, controlled trial [ISRCTN38797445] Critical Care 2005; 9: R687-R693. http://dx.doi.org/10.1186/cc3887PMid:16356219 PMCid:PMC1414018
31. Donati A, Loggi S, Preiser J C, et al. Goal-Directed Intraoperative Therapy Reduces Morbidity and Length of Hospital Stay in High-Risk Surgical Patients Chest 2007; 132: 1817-1824.
32. Warring Davies KJ. PhD Thesis: An Empirical Formula for Determining Cardiac Index in Adults Hartford University; 2006. www.heartsmartcardiac.com
33. Warring Davies KJ. The benefits of pre- and perioperative optimisation using goal directed therapy Technic 2009; 5(7): 12–16.
34. HeartSmart for cardiac dynamic monitoring. The National Institute for Health Research National Horizon Scanning Centre Research The National Horizon Scanning Centre, Department of Public Health and Epidemiology University of Birmingham; 2007.
35. Warring Davies KJ, Bland JM. Validating HeartSmart® against the cardiopulmonary bypass machine. Surgical Science 2012; 3(1): 21–27. http://dx.doi.org/10.4236/ss.2012.31004
36. Pandit JJ. Graphical presentation of data in non-invasive algorithms for cardiac output estimation. Anaesthesia 2010; 65(3): 310–311. http://dx.doi.org/10.1111/j.1365-2044.2010.06256_1.x PMid:20236273
37. Fabbroni D, Quinn A. A retrospective evaluation of the Heartsmart(TM) continuous cardiac dynamic monitor in neurosurgical patients. J Neurosurg Anesthesiol 2005; 17(3): 156 (abstract).
38. Warring Davies K, Bland M. HeartSmart® for routine optimization of blood flow and facilitation of early goal-directed therapy. Open Access Journal of Clinical Trials 2010; 2: 115–123. http://dx.doi.org/10.2147/OAJCT.S9843
39. Warring Davies KJ, Bland JM. HeartSmart™: A new method of assessing hydration in neurosurgical patients. Surgical Science 2012; 3(11): 546–553. http://dx.doi.org/10.4236/ss.2012.311108
40. Iberti TJ, Fischer EP, Leibowitz AB, Panacek EA, Silverstein JH, Albertson TE. A multicenter study of physicians' knowledge of the pulmonary artery catheter. Pulmonary Artery Catheter Study Group. JAMA 1990; 264(22): 2928–2932. http://dx.doi.org/10.1001/jama.264.22.2928 PMid:2232089
41. Iberti TJ, Daily EK, Leibowitz AB, Schecter CB, Fischer EP, Silverstein JH. Assessment of critical care nurses' knowledge of the pulmonary artery catheter. The Pulmonary Artery Catheter Study Group. Crit Care Med 1994; 22(10): 1674–1678. http://dx.doi.org/10.1097/00003246-199422100-00025 PMid:7924381
42. Warring Davies KJ. Haemodynamic monitoring. British Patent Office. Publication No. WO/2003/041587 PCT/005128; 2003.

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