

New Formulae for Calculating Left Heart Pressure in Pulmonary Artery Hypertension Patients at the Bedside

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Abstract: *Objective:* To compare new empirical formulae in HeartSmart, to calculate the mean pulmonary artery and mean pulmonary artery occlusion (wedge) pressures to that of the Pulmonary Artery Catheter Thermodilution Method.

Method: 20 adult patients with pulmonary artery hypertension admitted on to Bradford Royal Infirmary NHS Trust Hospital UK Intensive Care Unit, where haemodynamic monitoring is routinely performed as part of the treatment using the thermodilution method compared to the HeartSmart to guide interventional fluid resuscitation etc. Each subject has six paired values of each left heart pressure and cardiac indexes to test the robustness of HeartSmart against the perceived 'gold standard' thermodilution method. This was a double blind study the haemodynamic variables of each technology were close enough to each other.

Results: Bland-Altman plot comparing the measured mean pulmonary artery pressure (MPAP) mmHg to the HeartSmart calculated pulmonary artery pressures (CPAP) mmHg: *For mean of the differences between MPAP mmHg and CPAP mmHg = - 1.08 mmHg, Legend 1.*

Comparing the measured mean pulmonary artery occlusion (wedge) pressure (MPWP) mmHg to the HeartSmart calculated pulmonary artery occlusion (wedge) pressure (CPWP) mmHg: *For mean of the differences between MPWP mmHg and CPWP mmHg = - 0.56 mmHg, Legend 2.*

Comparing the measured mean cardiac index in litres/min/m² MCI to the HeartSmart calculated mean cardiac index in litres/min/m² CCI: *For mean of the differences between MCI litres/min/m² and CCI litres/min/m² = -0.03 litres/min/m²; Legend 5.*

Conclusion: The results demonstrate HeartSmart™ software compares favourably with the Pulmonary Artery Catheter thermodilution method at the bedside and could be used interchangeably or replace PACTD.

Background: The incidence of pulmonary artery hypertension is on the increase in the United Kingdom. Primary pulmonary arterial hypertension is a rare disease that is characterized by increased pulmonary-artery pressure in the absence of common secondary causes of pulmonary hypertension, such as viruses auto immune system, chronic heart, lung, or thromboembolic disease. Before the advent of new and some novel therapies, patients with idiopathic or familial pulmonary arterial hypertension average survival rates were less than 7 years. Despite the progress in diagnostic techniques and treatment, pulmonary arterial hypertension is becoming more common although remaining a progressive, debilitating fatal disease. The clinical signs and symptoms can be nonspecific, patients often receive a diagnosis too late as the condition advances, deteriorates and of course treatment is less effective.

The use of the (PAC) right heart floatation pulmonary artery catheter (Swan-Ganz) to measure the mean pulmonary artery and mean pulmonary artery occlusion (capillary wedge) pressures is one means of confirming the diagnosis of pulmonary artery hypertension, although its use is not appropriate in neonates or paediatric cases.

Keywords: Empirical physiological formulae, left heart pressures, haemodynamics, pulmonary artery hypertension.

1. INTRODUCTION

The new empirical physiological formulae embedded in the continuous cardiac dynamic monitoring software (CCDM), calculates the mean pulmonary artery and mean pulmonary artery occlusion (capillary wedge) pressures with cardiac indexes [1, 2]. HeartSmart, values were compared with the same haemodynamic values provided by the pulmonary artery catheter thermodilution method (PACTD), in 20 adult patients with a primary history of pulmonary artery hypertension (PAH).

PAH is a complex problem characterized by nonspecific signs and symptoms and having multiple potential causes [3]. It may be defined as a pulmonary artery systolic pressure greater than 30 mmHg or a pulmonary artery mean pressure greater than 20 mmHg, at rest.

The normal pulmonary artery systolic pressure at rest is 18 to 25 mmHg, with a mean pulmonary pressure (MPAP) ranging from 12 to 16 mmHg. This low pressure is due to the large cross-sectional area of the pulmonary circulation, which results in low resistance. An increase in pulmonary vascular resistance or pulmonary blood flow results in PAH.

This was one of the perspectives that the EPF's for calculating the left heart pressures, the mean

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pulmonary artery and pulmonary artery occlusion (wedge) pressures, MPAP and MPWP respectively, were formulated [3-7] and initially evaluated [8].

In PAH the twelve lead electrocardiogram (ECG) may demonstrate signs of right ventricular hypertrophy, such as tall right pre-cordial R waves, right axis deviation and right ventricular strain. The higher the PAH value, the more sensitive are the ECG waveforms. The chest x-ray is inferior to the ECG in detecting pulmonary hypertension, but it may show evidence of underlying lung disease. Not infrequently, recognition of PAH begins with the discovery of right ventricular hypertrophy on the ECG or prominent pulmonary arteries on the chest x-ray.

Patients with signs, symptoms or electrocardiographic or x-ray findings is suggestive of PAH requires two-dimensional echocardiography with Doppler flow studies [10]. Echocardiography is the most useful imaging modality for detecting PAH and excluding underlying cardiac disease. Confirmation of PAH is based on identification of tricuspid regurgitation. The addition of mean right atrial pressure or central venous pressure to the peak tricuspid jet velocity gives an accurate noninvasive estimate of peak pulmonary artery pressure.

The left heart pressures MPAP and MPWP are useful indicators to establish PAH. Right ventricular dilatation and hypertrophy develops with the progression of the PAH pathology. Cardiac MRI is useful in assessing the severity of PAH but not necessarily the diagnosis.

Although RHC was considered to be the definitive measurement of pulmonary hemodynamics, it too must be interpreted with some caution. Even during short-term continuous monitoring, catheter-measured pulmonary arterial pressure can vary significantly in the absence of any interventions. Thus, brief follow-up measurements at intervals of months to years risk superimposing the "noise" of spontaneous variation (as well as the temporary effects of such characteristics as hydration status and anxiety) on changes in the patient caused by progression of disease or response to therapy.

Measurement inaccuracy can be further compounded by errors in technique, such as failing to confirm position with a wedged blood saturation (leading to imprecise MPWP, relying on thermodilution cardiac output measurement in the setting of tricuspid regurgitation or intracardiac shunt, and studying the patient during volume expansion or dehydration.

The problems caused by inaccuracies [14-16] of measurement and random sampling during follow-up have led to the concept that continuous ambulatory hemodynamic monitoring (HeartSmart) of patients may provide more reliable data about trends and responses of pulmonary hemodynamics over time, allowing for more precise predictors of outcome.

PAH refers to the presence of a MPAP of greater than 25 mmHg regardless of mechanism, pulmonary hypertensive disorders are classified into groups on the basis of underlying mechanism, presentation, clinical context, histopathology, and response to treatment. The term PAH pertains to the hemodynamic profile in which high pulmonary pressure is produced by elevation of pre-capillary pulmonary resistance. Thus, a diagnosis of PAH implies that pulmonary venous pressure, as measured by the pulmonary capillary wedge pressure (PCWP), is normal (≤ 15 mmHg) and that the transpulmonary gradient (i.e., the difference between the MPAP and the PCWP) is 10 mmHg or less. The goal of the diagnostic strategy for detection and assessment of PAH is to characterize the hemodynamic profile of PAH and correctly identify the clinical context in which it occurs to appropriately tailor an optimal therapeutic regimen [10].

The new empirical formulae in HeartSmart for calculating the MPAP, MPWP with the Cardiac Index (Ci) in liters/min/m², potentially over comes many of the difficulties in respect to RHC using the invasive pulmonary artery catheter with all the attendant risks associated with the procedure, when HeartSmart is performed using the external jugular venous pressure [12, 13] as a surrogate for the invasive CVP, non invasively.

2. BENEFITS

HeartSmart technology using physiological parameters heart rate, systolic and diastolic blood pressure, core body temperature with central venous pressure or non invasive external jugular venous pressure to activate the EPF,s in the HeartSmart module, deskills the necessity of the intrusive invasive nature of central venous catheterisation of the right atria or large vessels superior vena cava, a short triple lumen CVP using the jugular veins will suffice if an invasive measurement or route is required.

HeartSmart permits a method of quickly and simply assessinh left heart pressures without all of the attendant costs and skills required to operate intrusive,



Figure 1: The pulmonary artery catheter *in situ*.

unfriendly and costly haemodynamic monitoring technologies with ongoing consumable costs. The result is that not only are instrumentation cost very significantly reduced, the patients progress or response to treatment can be tracked haemodynamically in the physicians surgery or clinic, quickly and conveniently, providing a far higher standard of care and reduced costs of drugs that are not working efficiently to individual patient.

If there is a downside to HeartSmart that will be because operators either do not calibrate or use the correct setting prior to making calculations, don't take time to become fully knowledgeable of the HeartSmart technology, or the medical practitioner does not have the required cardiovascular knowledge to interpret the haemodynamic variables delivered, this has often been the cause of controversy previously.

Although this study describes the application of HeartSmart in respect to calculating left heart pressures and cardiac index/output, HeartSmart can be used on any patient whether or not the pathophysiology is of a cardiac or respiratory nature, HeartSmart can be used to assess patients prior to surgery, guide fluid administration perioperative early goal directed therapy aggressive fluid resuscitation therapy with vaso pressors etc.

3. METHOD

Twenty adult patients all of who had a long standing primary diagnosis of PAH were admitted on to the

general intensive care unit of the Bradford Royal Infirmary, due to secondary pathological complications that caused haemodynamic instability etc. As part of their routine treatment each patient underwent RHC to insert the pulmonary artery catheter (PAC) utilising the thermodilution method to guide intravenous fluid treatment, see Figure 1.

Institutional ethical approval was granted for the study to take place, each patient or their next of kin gave written informed consent, this study which is a subset of the main study, conforms to the Helsinki Declaration.

The Mennen Medical Horizion 2000 bedside haemodynamic monitor with the Arrow or Edwards Life Sciences pulmonary artery catheters were used in this study.

The anaesthetist/intensivist who performed the haemodynamic measurements are highly experienced in the use of the pulmonary artery catheter thermodilution method (PACTD). Radial artery was catheterised to obtain and monitor the systolic and diastolic blood pressure of the patient, all the patients were mechanically ventilated.

4. DEMOGRAPHICS

The main study consisted of 226 adult patients of which this sub study consisting of 20 adults 8.8%. 12 of the 20 were females 60% and 8 males 40%, the age range of the female population was 16 – 41 years old

the average age was 27.75 years, the age range of the male population was 19–34 years old the average age 26.75 years.

Of the 20 patients 14 were medical and 6 were surgical cases, 8 cases pneumonia, 5 cases coronary, 1 case septicaemia, 3 peritonitis, 2 neurosurgery, 1 amputee, 2 patients 10% did not survive.

5. DESIGN

HeartSmart requires the input of the following physiological measurements: heart rate beats per minute, core body temperature in degrees Celsius, mean central venous pressure, systolic and diastolic blood pressure in mmHg. HeartSmart will calculate the majority of the haemodynamic variables associated with PACTD, see Figure 2.

Each patient had 6 paired sets of each haemodynamic variable, providing a pool of data of 120 paired sets of the mean pulmonary artery and pulmonary artery occlusion/wedge pressures in mmHg, the cardiac index in liters per minute per meter squared, the systemic and pulmonary vascular resistance indexes in dynes per cm^{-5} sec.

6. RESULTS

The study used a well validated method [1], to compare these two measurement techniques of the PACTD to the empirical physiological formulae HeartSmart; the 95% limits of agreement analysis assesses how closely two methods of measurement of a variable agree and the means of the differences are an estimate of the average bias of the PACTD method relative to that of the continuous cardiac dynamic monitoring method CCDM–HeartSmart™. The results



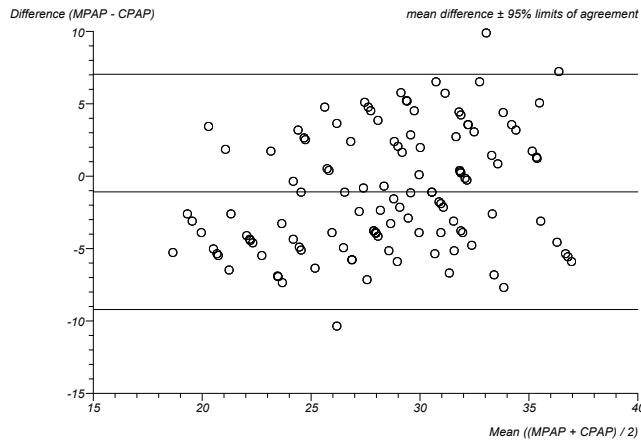
Figure 2: The HeartSmart® computer screen.

This is a double blind study the author was provided with the above physiological measurements but not able to see the patient haemodynamic monitor, the anaesthetist was unable to see the HeartSmart results (see Figure 1) until each investigator had made a written record of the patient's haemodynamic results.

Three sets of the PACTD cardiac output/index were made, if each measurement was not within 10% of each other two more measurement were made, of which three measurements had to be within 10% of each other, the total was divided by 3 to give an average value of the cardiac index in $\text{l}/\text{min}/\text{m}^2$, if of the whole 5 measurements 3 were not within 10% of each other the measurements were discarded.

showed good correlation between the groups of haemodynamic variables; data collected shows that the 95% limits of agreement and the mean bias were statistically sufficiently close across the full range of the mean pulmonary artery and mean pulmonary artery occlusion (wedge) pressures with the cardiac indexes observed, thus suggesting that the empirical physiological formulae in HeartSmart would be equally comparable to the PACTD method for estimating left heart pressures, cardiac indexes with the systemic and pulmonary vascular resistances.

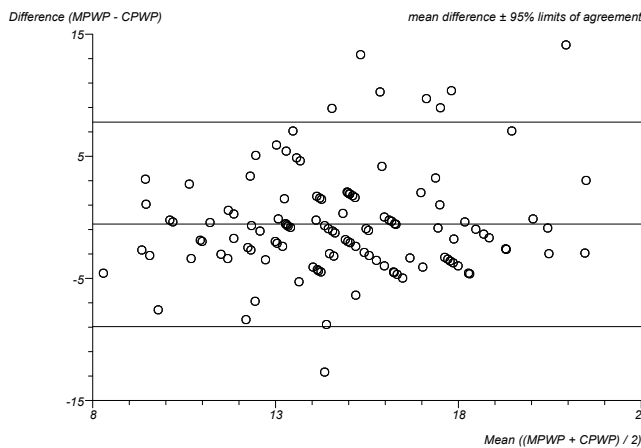
Bland-Altman [1] plot comparing the measured mean pulmonary artery pressure (MPAP) mmHg to the Heartsmart calculated pulmonary artery pressures



Legend 1: Differences PACTD MPAP and HS CPAP: n = 120 mean pulmonary artery pressure
 Mean of differences, -1.08 mmHg;
 Standard deviation, 4.15 mmHg;
 Standard error, 0.38 mmHg;
 95% limits of agreement, -9.22 to 7.05 mmHg.

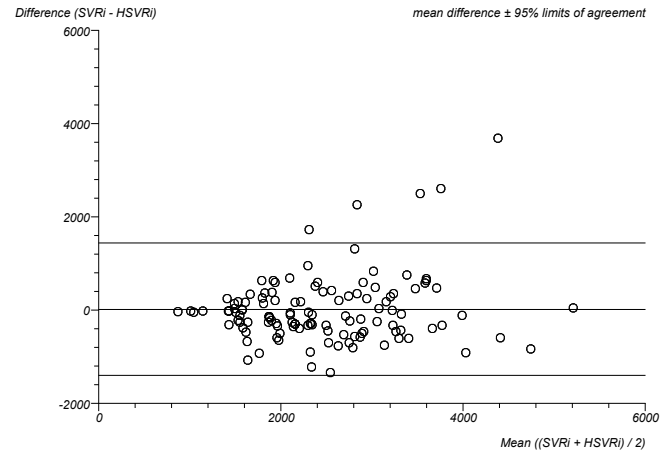
(CPAP) mmHg: Paired t test. For mean of the differences between MPAP mmHg and CPAP mmHg = -1.08 mmHg; two sample analysis of agreement. 95% limits of agreement = -9.28 mmHg to 7.05 mmHg, see Legend 1.

Bland-Altman plot comparing the measured mean pulmonary artery occlusion (wedge) pressure (MPWP) mmHg to the Heartsmart calculated pulmonary artery occlusion (wedge) pressure (CPWP) mmHg: Paired t test. For mean of the differences between MPWP mmHg and CPWP mmHg = -0.56 mmHg; two sample analysis of agreement. 95% limits of agreement = -8.94 mmHg to 7.82 mmHg, see Legend 2.

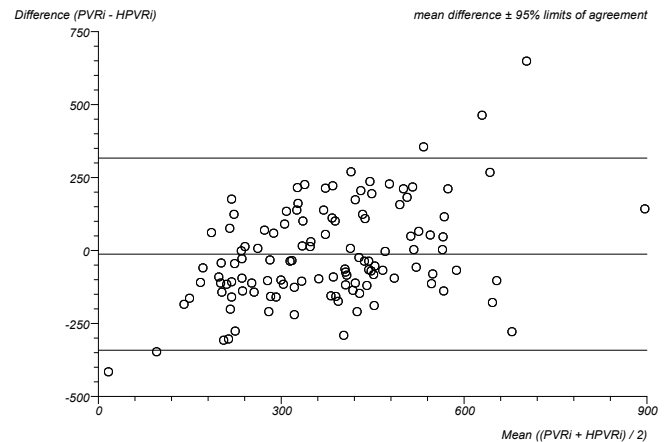


Legend 2: Differences PACTD MPWP and HS CPWP: n = 120 mean pulmonary artery occlusion (wedge) pressure:
 Mean of differences, -0.56 mmHg;
 Standard deviation 4.28 mmHg;
 Standard error, 0.39 mmHg;
 95% limits of agreement, -8.94 to 7.82 mmHg.

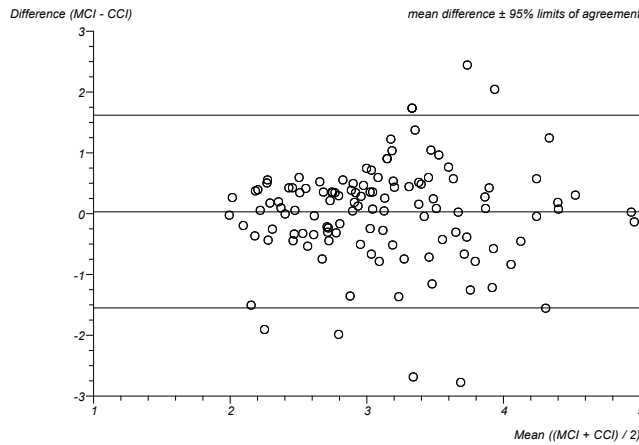
Bland-Altman plot comparing the measured mean cardiac index in litres/min/m² MCI to the Heartsmart calculated mean cardiac index in litres/min/m² CCI: Paired t test. For mean of the differences between MCI litres/min/m² and CCI litres/min/m² = -0.03 litres/min/m²; two sample analysis of agreement. 95% limits of agreement = -1.55 to 1.62 litres/min/m², see Legend 5.



Legend 3: Differences PACTD SVRi and HS CSVr: n = 120 mean syatemic vascular resistance index in dynes per cm⁻⁵ per sec,
 Mean of differences, 18.28 dynes per cm⁻⁵ per sec;
 Standard deviation 723.94 dynes per cm⁻⁵ per sec
 Standard error, 66.07 dynes per cm⁻⁵ per sec;
 95% limits of agreement, -1400.62 to 1437.17 dynes per cm⁻⁵ per sec.



Legend 4: Differences PACTD PVRi and HS CPVRi: n = 120 mean pulmonary vascular resistance index in dynes per cm⁻⁵ per sec,
 Mean of differences, -11.96 dynes per cm⁻⁵ per sec;
 Standard deviation 167.78 dynes per cm⁻⁵ per sec
 Standard error, 15.32 dynes per cm⁻⁵ per sec;
 95% limits of agreement, -340.81 to 316.89 dynes per cm⁻⁵ per sec.



Legend 5: Differences PACTD MCI and HS CCI: n = 120 mean cardiac index l/min/m².
 Mean of differences 0.03 l/min/m²;
 Standard deviation, 0.81 l/min/m²;
 Standard error, 0.07 l/min/m²;
 95% limits of agreement -1.55 to 1.62 l/min/m².

We now analyse and compare these results between the PACTD measurements and HeartSmart empirical physiological formulae in far greater detail [2]:

First we check whether the differences between the PACTD and HeartSmart empirical physiological formula appear to be independent of the magnitude of the measurement, by plotting difference against average of the two measurements for each haemodynamic variable, see Legends 1 through 5.

A measurement cannot have closer agreement with another measurement than it does with itself and it is useful to compare the limits of agreement with the repeatability coefficient, within which about 95% of differences between pairs of measurement by the same method will fall. In the present data, we have repeated measurements for both methods. The left heart pressures and cardiac indexes do not change greatly over the period of measurement, so we can estimate the repeatability.

Each patient had six paired sets of PACTD measurements to that of the HeartSmart computer calculations of the following haemodynamic variables: mean pulmonary artery and pulmonary artery occlusion (wedge) pressures, the systemic and pulmonary vascular resistances with the cardiac indexes.

The HeartSmart[®] empirical physiological formulae[®] are:

1. Mean pulmonary artery pressure = MAP * 0.2 + CVP.

2. Mean pulmonary artery occlusion (wedge) pressure = MPAP * 0.2 + CVP.
3. Cardiac index = CVP * K * T / HR².

Where MAP is the mean arterial pressure, that is the systolic blood pressure + diastolic blood pressure * 2/3 in mmHg, CVP is the mean central venous or right atrial pressure, K is a constant from the HeartSmart look up table of CVP v HR, see Figure 3. HR² is heart beats per minute squared.

4. Systemic vascular resistance index = MAP - CVP * 79.9/Ci.
5. Pulmonary vascular resistance index = MPAP - MPWP * 79.9/Ci.

Where the MPAP is the mean pulmonary artery pressure and the MPWP is the mean pulmonary artery occlusion (wedge) pressure.

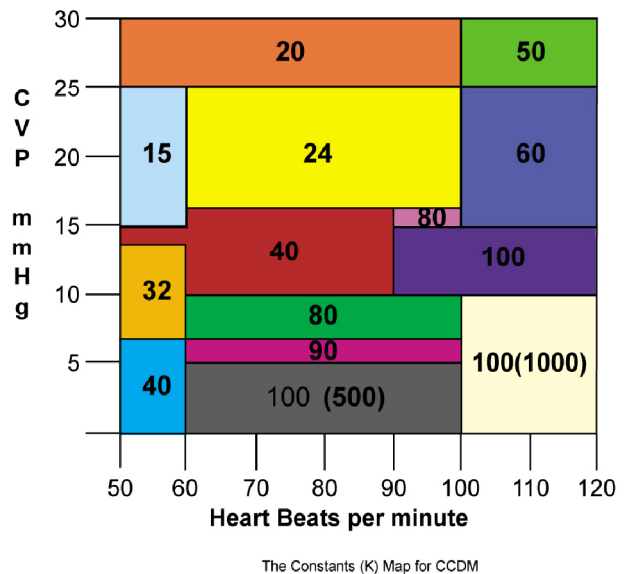


Figure 3: Bandwidths of CVP and HR producing the value of K.

7. INTER-RELATIONSHIPS

As can be shown there is a direct linear relationship between MAP and the MPAP as there is with MPAP and MPWP.

There is a direct relationship between CVP and MAP upon MPAP, there is an indirect relationship between CVP and MPWP, in practical terms usually the MPWP is approximately 25% greater than the CVP.

In the paired data set for the HeartSmart calculation of the MPAP and MPWP it was observed how the MAP

when 100mmHg or more with a high CVP increases the MPAP results, the relationship of the CVP upon the MPWP is hardly affected, and most interestingly how in those cases where there was not a difference of 40mmHg between the systolic and diastolic blood pressure, caused a lowering of the MPWP but increased Ci.

In the first group the range of CVP was 6mmHg–14mmHg, where the range of systolic arterial blood pressure was 110–174 mmHg resulted in MAP >100mmHg in 50% of the paired measurements producing high MPAP values but did not significantly raise the MPWP values, with a range of Ci values of 1.4 l/min/m² through to 4.2 l/min/m². In this group the SVR_i were abnormally high ranging from 1491–5233 dynes per cm⁻⁵ per sec, whilst the PVR_i ranged from 304 through to 1027 dynes per cm⁻⁵ per sec.

In the second group the range of CVP was 5 mmHg–14mmHg, where the range of systolic arterial blood pressure was 56–99 mmHg, resulting in MAP <100mmHg, in remaining 50% over the paired measurements still produced high MPAP values but did not significantly raise the MPWP values, with improved range of Ci values of 2.8 l/min/m² through to 4.96 l/min/m². In this group the SVR_i were abnormally high range 1491–2540 dynes per cm⁻⁵ per sec, whilst the PVR_i ranged from 154 through to 439 dynes per cm⁻⁵ per sec.

In the third group the range of CVP was 5 mmHg–14mmHg, where the difference between the systolic and diastolic blood pressures was less than 40 mmHg in the second group the Ci ranged from 2.42 through to 5.02 l/min/m².

In the fourth group where the MAP and CVP were normal the MPAP and MPWP values were in the normal range.

This study limitations are that the number of participants diagnosed with PAH is small. However other studies using PACTD compared to HeartSmart in populations of patients who do not suffer from PAH, concluded that the MPAP and MPWP values can be calculated by the EPF in the HeartSmart computer [17-24] software module, compared to the PACTD values.

8. DISCUSSION

Pulmonary artery hypertension is a difficult and complex pathology which is increasingly becoming more prevalent, whilst death from heart disease is also on the increase and major cause of death [23].

The aetiology and mechanisms of primary PAH are not completely understood. Secondary PAH can be a complication of many pulmonary, cardiac, respiratory or thoracic conditions. Cor pulmonale is enlargement of the right ventricle (hypertrophy) as a consequence of disorders of the respiratory system. PAH invariably precedes cor pulmonale. Unrelieved PAH regardless of the underlying cause, leads on to right ventricular failure and premature death.

Early diagnosis of PAH is of major importance as to the aetiology and classification of PAH in respect to the prognosis and treatment of the condition. Conventionally right heart pulmonary artery floatation catheterisation utilising the thermodilution method PACTD, to measure the mean pulmonary artery and pulmonary artery occlusion (wedge) pressures has been the diagnostic procedure to establish PAH etc.

PAH, is a disorder characterized by abnormally elevated blood pressure in the pulmonary circulation and increased pulmonary vascular resistance, is classified into five diagnostic categories: PAH idiopathic PAH with left-sided heart disease, PAH associated with lung disease and/or hypoxemia, PAH due to chronic thrombotic and/or embolic disease, and a miscellaneous group. Right-sided heart catheterization (RHC) is the current reference standard for the diagnosis and assessment of the severity of PAH, see Figure 1.

PACTD is in itself a highly invasive procedure and not without risk to the patient let alone the benefits of performing the procedure. PACTD technology used at the bedside is surrounded by controversy not all of it justified, and there is a long learning curve in respect to interpreting the haemodynamic variable results, as we have touched upon in the discourse above.

However, there is a greater consideration when treating a patient suffering from PAH, that is tracking the efficacy of the drugs used to treat the patients condition on a regular short term basis, every three months for example. One of the major benefits of such a regime is the potential of reducing the number of premature deaths or increasing the life span of those patients with PAH through more appropriate treatment. Of course there are other hidden benefits of such a regime such as costs etc. [25].

Presently there is no technology that is readily available for such a regime, however, the HeartSmart non invasive method of surrogating the measured

invasive CVP by using the external jugular venous pressure manually or by using a hand held ultrasound device, potentially makes that provision of non invasive haemodynamic monitoring using HeartSmart a routinely is a real possibility.

Additionally, the pulmonary artery pressures are not only used to confirm a diagnosis of pulmonary artery hypertension or any other respiratory pathology, left heart pressures are useful in the assessment of the suitability of donor organs for transplanting internal organs, for example, liver or heart/lung transplants etc.

Because HeartSmart is a computer program it can be downloaded to any PC or laptop, see Figure 4, via a dedicated website, or to a mobile phone 'app', especially where patients are in remote parts of the world, for example, the out backs of Australia or in countries where patients do not have access to medical facilities etc. Of course not only patients with PAH benefit from a technology that provides haemodynamic monitoring on demand [26].

9. CONCLUSION

HeartSmart has the potential to replace or be used interchangeably with the pulmonary artery catheter thermodilution method PACTD in adults or any other haemodynamic monitoring technology, thus, HeartSmart is a disruptive or destructive technology with tremendous cost savings to the healthcare provider or health care insurer. The main advantage of the HeartSmart software is that it provides the left heart pressures without the need of right heart catheterisation under general anaesthetic, with all of the potential risks, complications and costs associated with the PAC procedure etc.

HeartSmart overcomes the major technical hurdles which have obstructed medical practitioners from not being able to routinely monitor haemodynamics and intervene when a patients cardiovascular or respiratory status requires. Professional healthcare practitioners only need to become conversant with the HeartSmart technology that has a friendly short learning curve, indeed the most junior of medical or nursing staff will soon become confident in using HeartSmart routinely.

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The author is the inventor of HeartSmart®.

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