Blood Flow Assessment by Arterial Pressure Wave without External Calibration

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Abstract

Beat by beat evaluation of cardiac index (CI) can be determined by the Pulse Contour Method (PCM), which however is limited by the need for external calibration. In our study we have evaluated the CI by the Pressure Recording Analytical Method (PRAM) based only on the changes of the pressure wave morphology. PRAM does not require external calibration and/or pre-estimated parameters. Aim of this study was to evaluate in 50 cardiac patients measurements of CI from the signal pres-sure obtained invasively (ascending aorta) and non-invasively (Finapres), by PRAM as compared to the routine clinical method (i.e. thermodilution).

1. Introduction

Such traditional methods to measure cardiac index (CI) as Thermodilution (ThD) are affected by several drawbacks which greatly limit their application: they are invasive and do not allow continuous monitoring of cardiac function. Pulse Contour Method (PCM) has been developed to obtain continuous invasive or non invasive measurements of CI, working with pre-calculated parameters and/or by calibration [1-3]. In fact in order to obtain absolute values of CI, it is necessary to determine, at least once for each patient, a calibrating factor of the model parameters by comparison of the PCM result with an absolute CI estimate. Without such calibration, PCM may undergo a number of problems and hence may be not related in a significant way to the referral method [3,4]. The need for a comparison with a reference method greatly limits the utility of PCM, since the calibrating technique is either invasive (e.g. ThD) or cumbersome (e.g. inert gas rebreathing) and must be repeatedly applied when changes in the experimental procedure, that may alter the physical properties of the arteries, are induced [3]. It appears, therefore, that methods at the same time practical and reliable have not as yet become available to measure CI continuously invasively [2-4] and non-invasively. The problem with methodologies based on the calibration or on pre-estimated data may lead to, besides an erroneous flow evaluation in the absence of calibration, the masking of the real variations occurring in the course of instable physiological phases (critical patient) or in the course of a pharmacological or mechanical device support. This is because the external intervention (calibration or pre-estimated data) imposes values which can be higher than the real variations of compliance, ventricular contractility or peripheral resistances. These compensatory mechanisms contribute in maintaining within defined oscillations flow variations. For this reason, in order to evidence these adjustments (before than relevant variations due to a definitive break of the equilibrium occur), it is necessary to be able to follow without any interference and in a continuous pattern its behavior. In effect, when a significant flow variation occurs, this is the result of variations already implemented during the phases of compensation. Therefore from now both the calibration obtained with a referral method [3,4] and the parameters pre-estimated by other subjects [1,2]and then applied to the study subject, will be considered as an external intervention.

To this aim, we used a Pressure Recording Analytical Method (PRAM) for beat-by-beat evaluation of CI. PRAM is based on the analysis of the arterial wave-form, does not require calibration or pre-calculated parameters, and can be used either invasively in ascending aorta (PRAMa), or non-invasively at the finger (PRAMf). We observed the PRAM replay during simultaneous evaluation by ThD in 50 consecutive patients.

2. Materials and methods

We studied 50 cardiac patients by simultaneous recording of aorta and finger arterial pressure wave-forms at 1kHz. The pressure signal in ascending aorta was recorded by a filled catheter. A 7 French pulmonary artery thermistor-tipped catheter (Baxter, Edwards CriticalCare) was inserted through a femoral vein. The catheter was connected to the CO computer (Baxter, Edwards CriticalCare). A 10 ml sample of 4-7° C glucose solution (5%) was drawn from a cooling unit and injected over about 3 sec. Four injections of the thermal indicator were performed in each patient. A 6 French catheter (Cordis Corporation) was advanced into the ascending aorta. In all pressure determinations, resonance frequency and attenuation factors were within accepted limits. Non invasive arterial pressure was monitored with Finapres probe (Ohmeda, BP monitor 2300), on the third finger of the left hand. Four estimates of CI by both PRAMa and PRAMf were derived from the heartbeats corresponding in time to the four ThD injections. Comparisons between different methods were carried out for each patient of CI obtained by ThD.

2.1 PRAM methodology

The PRAM represents the practical application of a theoretical model[5]. The concept behind PRAM is based on the physics theory of perturbations, by which each physical system under the effects of a perturbing term tends to react in order to reacquire its own condition of stability, i.e. the situation of minimal energy required. Such model allows the integrated evaluation of the different physical determinants of CI. In the PRAM method, the whole systolic area below the pressure curve (*A*) is measured at each cardiac cycle. Simultaneously, *Z(t)* is directly obtained based on the morphology of both the pulsatory and the continuous contributions to the CI, with no need for predicted data or calibrating factors [5].

$$SV = \frac{A}{Z(t)} = \frac{A}{\frac{P}{t} \times K} \qquad (1)$$

where A(mmHg×sec) is the whole area under the systolic portion of the pressure curve, K is a dimensional factor, inversely related to the instantaneous acceleration of the vessel cross-sectional area (cm/sec^2×cm^2), and P/t (mmHg/sec) is the analytical description of the pressure wave profile as changes in pressure (P) with time (t) along each cardiac cycle. The variables A, K, and P/t are strictly interdependent and simultaneously evaluated. The way A is computed allows to entail both pulsatile and non-pulsatile contributes of the physical forces underlying the relationship between pressure curve morphology and blood flow. The value of K is obtained from the ratio between expected (under physiologic conditions) and measured mean blood pressure[6]. Since the perturbations of the pressure wave are reflected in the instantaneous acceleration of the arterial vessel cross-sectional area, in eq.1 a value of K above or below unity permits to take into account the deviation from physiology of the transmitted pressure wave. The expression used to approximate Z(t)=P/t*K links together the morphologic changes with time of the pressure wave (P/t) during a cardiac cycle and a K. P/t is objectively obtained from the analytical description of the systolic and diastolic arterial pressure profile in the time domain. K is approximated from the ratio between the expected level of the mean arterial pressure (similar for everybody) and the value actually measured. To justify why K is defined as a ratio of pressures the theoretical treatment of an oscillating harmonic system undergoing the effects of a time dependent perturbing forcing term has to be considered. By applying a dynamic equation to any point P of a pressure tracing, we may consider that this point is under the effects of an elastic forces field (due to the physical properties of the cardiovascular system), a viscous resistance (due to the transmission of the pressure wave through blood), and a forcing term (due to the oscillating series of perturbations resulting from the effects of previous cardiac cycles on the cardiac cycle under evaluation). Z(t) for the cardiac cycle *i+1* can be estimated as follows:

$$Z_{i+1} = \frac{P}{t} * \left(\sum_{n=0}^{i-1} \frac{f(\bar{P}_{i-n})}{\bar{P}_{i+1}} \right) \qquad (2)$$

where *I* is a natural number and $\bar{P}$ is the mean pressure actually measured. Z_{I+1} must be a real number of positive value and, for this reason, the series within round brackets must be an oscillating series with alternating positive and negative values. Otherwise Z_{I+1} will tend to infinity. It is now to consider that each physical system under the effects of a perturbing term tends to react in order to reacquire its own state of stability, corresponding to the situation of minimal energy required. The condition of stability, in physiologic terms, is satisfied when both $\bar{P}_{i+1}$ and $\sum_{n=0} f(\bar{P}_{i+1})$ tend to the physiologic value of mean pressure and, consequently, their ratio will be close to unity. Also when the actually measured mean pressure differs from expected values, we may assume that the system will invariably operate to reach a condition of stability with a ratio between expected and measured blood pressure that would not greatly deviate from 1. In this respect, the value at the numerator of the series, which incorporates the effects of summation of previous cardiac cycles contributions, will tend to dump the perturbation induced in the system and to approach the value of expected mean pressure ($\bar{P}_e$).This can be expressed analytically as:

$$K_{i+1} = \frac{\sum_{n=0}^{i-1} f(\bar{P}_{i-n})}{\bar{P}_{i+1}} \approx \frac{\bar{P}_e}{\bar{P}_{i+1}} \qquad (3)$$

The numerator of the relationship to derive K is constant, the denominator, which is actually measured, may change, and, consequently, K too may change, not only from subject to subject, but also from cardiac cycle to cardiac cycle. Accordingly, K is neither a constant calibration factor nor a random expected value but, on the contrary, it is an inherent variable of the circulatory system under evaluation. The expected mean arterial pressure does not depend on anthropometric data; in fact, it should be similar for everybody irrespective of sex, age, height, and weight. Thus, the use of K in the expression to define Z is not based on models or look-up tables [5].

3. Results

In all patients the monitored systemic variables (HR, mean aortic and peripheral arterial pressures) were stable during the ThD evaluations. Our patients (M/F=1.5) undergoing heart catheterization were 62±14 years old (mean±SD). Aortic mean pressure was 96±18 mmHg, and finger mean pressure 78±15 mmHg, HR 80±14, CI values by ThD 2.63±0.8 l/min/m^2 (range: 1.4-5.3). The mean coefficient of variation among the four random estimates of CI obtained in each patient by ThD was 8.3% (range: 2.1 to 28%). CI values by PRAMa and PRAMf were 2.7±0.6 l/min/m^2 (range: 1.6-4.2) and 2.5±0.8 l/min/m^2 (range: 1.5-4.3), the mean coefficient of variation of the four repeated measurements in each patient was 3.9% (range: 1.2 to 7.6%) and 4.8% (range: 0.7 to 14.3%), respectively. The CI estimates by PRAMa and PRAMf were then compared with those obtained simultaneously by the ThD (mean of four evaluations).

3.1. PRAM versus thermodilution

Figure 1 depicts the comparison between CI measured by ThD and CI derived from both PRAMa and PRAMf. The coefficient of variation (r^2) is derived, in the 50 consecutive patients, comparing the values of CI obtained from the four repeated ThD measurements with the simultaneous estimates by PRAMa and PRAMf. The results of the Bland-Altmann analysis (Figure 2) are quite similar to those obtained by averaging the four individual values yielding a mean difference (bias) of -0.03l/min/m^2 (SD=0.42l/min/m^2) for PRAMa and -0.05l/min/m^2 (SD=0.40l/min/m^2) for PRAMf. Only three individual differences are not comprised within the limits of agreement for PRAMa, and only two for PRAMf.

4. Discussion

The present study was aimed at assessing, in the clinical routine, the characteristics and reliability of a method, without calibration, for CI measurement based on the morphologic analysis of the pressure wave recorded invasively (PRAMa) and non-invasively (PRAMf). In the PCM methodologies, in order to establish a relationship between pressure and flow, the mechanical properties of the arteries are approximated either by several empirical formulae, by calibration [1-4] or by a model based on age-and sex-predicted (from other patients) values. As a consequence, absolute values of CI can be obtained only by calibrating the PCM results against a reference method. Therefore, CI estimates by PCM depend more on fixed predicted parameters than on measurements obtained from the evaluated subject. Indeed, parameters to measure CI derived directly from the pressure wave are limited to pulsatile systolic area, mean blood pressure, and HR. Parameters characterizing the elastic properties of the arteries which can be derived from the shape of the pressure curve, such as the time of obtained peak systolic pressure, the presence of sudden slope changes, and the length of the diastolic phase, are not taken into consideration for the computation of CI. As such, accurate computation of CI by PCM is strictly dependent on the measurement of a calibrating factor by comparison with a standard reference method, rather than depending on the actual pressure waveform morphology. Moreover the methods with calibration and/or predicted values may have problems both for absolute evaluations and for CI variations in unstable patients, because of the scarce sensitivity of PCM[3,4] in following variations due to the super-impositions of the calibration and/or pre-estimated data, and to problems related to the calibration itself [7-9].

In our experience, PRAMa and PRAMf were considerably accurate when compared to ThD. The most evident differences are recordable both for extremely low and for extremely high values of CI; in effect a difference is present, and this could be attributed to an intrinsic limit of the routine reference method (ThD which can over- or under-estimate in the case of low or high blood flow) [7,8]. For this reason we have also conducted the statistical check of Bland-Altmann analysis in which in the abscissa axis the semi-sums of the two evaluations are reported. This statistical check has been much appreciated in medicine because of the fact that, in performing the

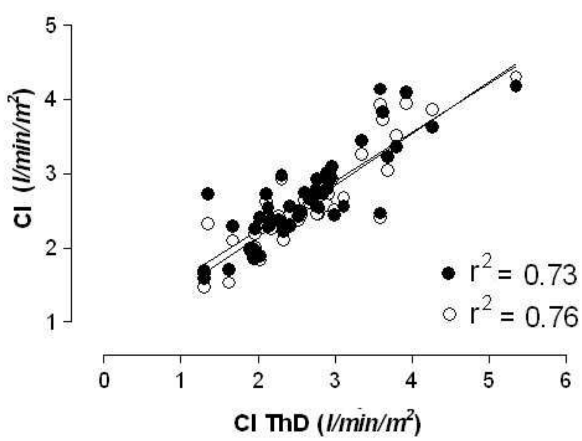

Figure 1. Coefficient of variation for the CI obtained by PRAMa (black circle) and PRAMf (open circle), vs ThD.

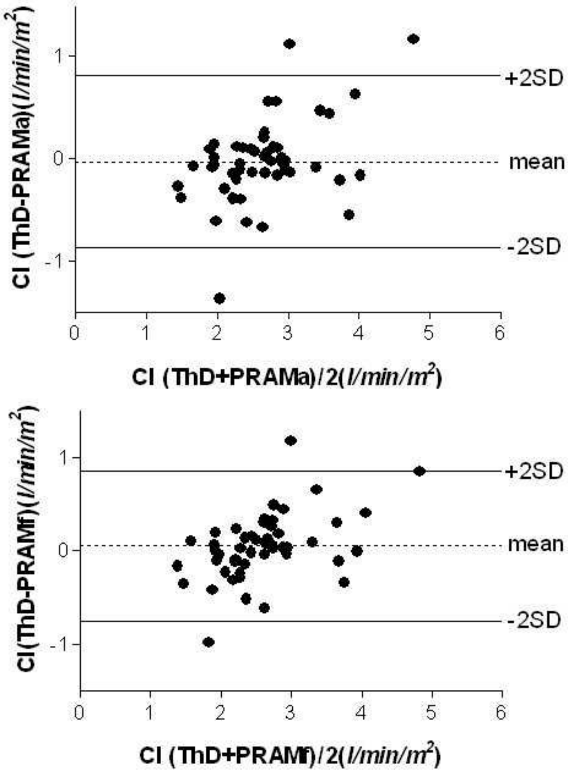

Figure 2. Bland-Altmann analysis between ThD and PRAMa (top panel) and PRAMf (bottom panel).

Comparison between the two methodologies, in the light of the fact that the reference technique includes an intrinsic not avoidable error, due to the philosophy and to the technology adopted, admits that the true value of the measurement may be more probably around the mean value of the two evaluations.

5. Conclusions

These work was aimed at describing the characteristics and assessing the reliability of a method to measure CI based on the morphologic analysis of the pressure wave. Our results indicate that estimates of CI derived by the new approach are in close agreement with those obtained by the clinical routine method, ThD. Even though a clinical (true) standard reference value of CI for comparison is not available, we have shown that, over a wide range of CI values, the mean difference and the limits of agreement between the ThD and the PRAM are acceptable for clinical purposes. The lack of considerable discrepancies between the values of CI computed by ThD and PRAM for low and high CI values could be linked to the instable blood flow[7-9]. In this connection, the good level of agreement observed between values of CI obtained by PRAM with respect to ThD is a further indication of the accuracy of PRAM. The estimates of CI by PCM depend more on fixed predicted parameters [1-3] than on measurements obtained from the subject under evaluation. Estimates of CI by PRAM do not depend on fixed parameters, but on the objective analytic description of shape changes in the domain of time of the pressure curve whole contour. This approach, as shown by the results obtained in the comparison with established techniques, reflects with good accuracy the relationship between pulse-stroke and volume-stroke [5,10,11]. In conclusion, PRAM proved to be a reliable, practical and accurate, invasive and non invasive continuous method for blood flow evaluation, comparing favorably with routine clinical methods (i.e. ThD).

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