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Cardiac output measurement : evaluation of methods in ICU patients

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Chapter 1

General introduction

General introduction

As for all mammals, we have to breathe for oxygen uptake and for the release of carbon dioxide. Most of the oxygen is consumed in the mitochondria. Thus, oxygen has to be transported from the lungs to the mitochondria and carbon dioxide has to be transported back to the lungs. It is the purpose of this thesis to evaluate methods that measure this transport function i.e. circulation or cardiac output. Furthermore we study factors that determine cardiac output. In a normal individual who is breathing spontaneously, blood pressure decreases on inspiration and recovers on expiration. However, the change in systolic pressure does not exceed 5 mmHg. This change in pressure as well as in blood flow with respiration is reversed and increased during applied intermittent positive pressure ventilation (IPPV) in mechanically ventilated patients, figure 1.1.

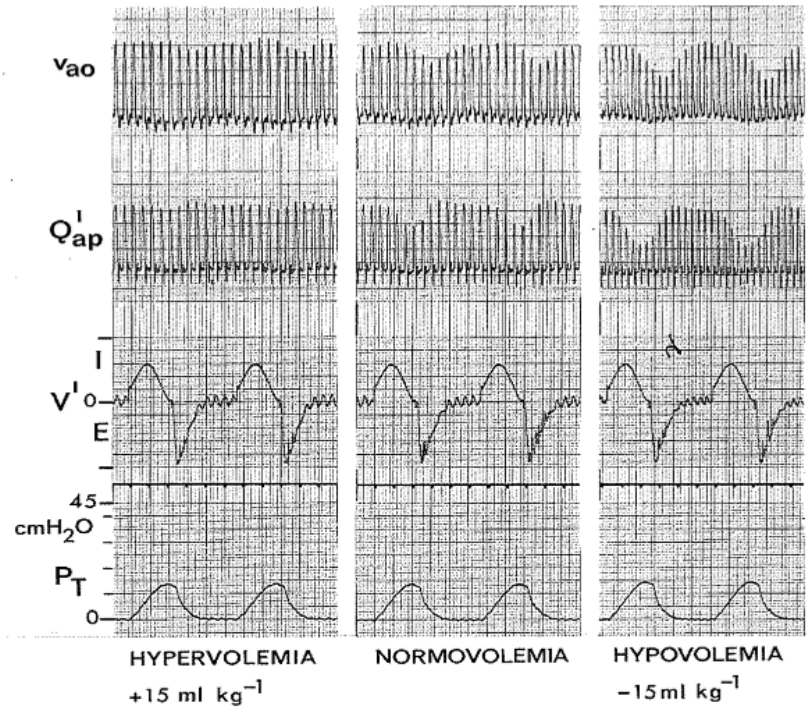

Figure 1.1 Fluctuations of blood flow dependent on blood volume. Recordings of flow velocity an the aorta (V_{ao}) and volume flow in the pulmonary artery (Q'_{ap}) during the ventilatory cycle (V' is air flow measured in tracheal cannula and P_T is airway pressure) at different blood volumes. From Versprille et al. 1982 [2].

For instance, Jansen [1] and Versprille [2] conducted in the early-1980s several studies describing the influence of mechanical ventilation on cardiac output (cardio-pulmonary interaction) in animals. From these results it became obvious that monitoring cardiac output and cardio-pulmonary interaction provides invaluable clinical information about an individual's hemodynamic status (such as amount of effective circulating blood, effects of volume loading on cardiac output and effects of different ventilator setting on cardiac output) and the abilities to transport oxygen.
Today, there are a number of companies that market devices for monitoring cardiac output and cardiac-pulmonary interaction. These devices all have a number of

characteristics that need to be understood before the devices can be used appropriately. Furthermore, these devices need to be extensively evaluated before they can be introduced safely and reliably in the Intensive Care Unit (ICU). The aim of the introduction is to give some historical, physiological and methodological background information.
This thesis aims to describe the evaluation of the cardiac output methods most often used in the ICU.

Historical and physiological aspects of cardiac output and respirator induced changes in blood flow and pressure

In early studies of continuous positive pressure ventilation (CPAP) and intermittent positive pressure ventilation (IPPV) in man and animals the measurement of blood flow was too time-consuming (Fick and indicator-dilution methods) for studying cyclic changes in blood flow. The presence of such fluctuations has been reported already in 1869 by Hering in a paper entitled: "Ūber den Einfluss der Athmung auf den Kreislauf" [3]. From the mid-1960s, after development of the electromagnetic flow meter, ventilator related changes in flow during IPPV and continuous positive airway pressure (CPAP) ventilation were published [2, 4-6]. Recordings made by Jansen [1] and Versprille [2], showed the characteristic phenomenon of flow modulation by IPPV, figure 1.1.

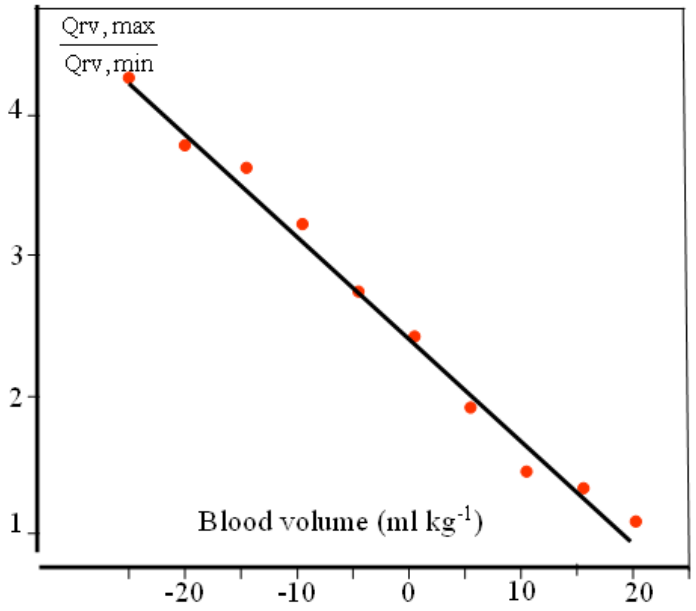

Figure 1.2 Fluctuation in right ventricular stroke volume dependent on blood volume. The ratio of maximum right ventricular stroke volume ($Q_{s,rv,max}$) and the minimum value ($Q_{s,rv,min}$) is plotted against changes of blood volume with respect to normovolemia, which is indicated on the abscissa. Note that at severe hypovolemia the ratio decreases; this is comparable to shock. A study in piglets. From Versprille et al. 1982 [2].

During inflation of the lungs, venous return is hindered by an increase in intra-thoracic pressure which results in a decrease in right ventricular output.

Right ventricular stroke volume is lowest at the end of lung inflation (and stays low during an end-inspiratory pause). When spontaneous expiration starts right ventricular output rapidly increases and stays at a constant level during the last part of expiration. Left ventricular output follows with a few heart beats behind right ventricular output due to the long (~ 2 seconds) transit time of blood through the pulmonary circulation. Left ventricular output is, however, slightly less modulated. In 1980 and 1982, Jansen [1] and Versprille [2] showed in their animal experiments that the amplitude of modulation was reversely related to mean blood flow and to the volemic status of the animals, figure 1.2. Here modulation of ventricular output is characterized by maximal blood flow divided by minimal blood flow (modulation =Q'max/Q'min).

According to the Frank-Starling mechanism [7] the decrease in transmural right ventricular pressure (Pra,tm) – i.e. the pressure difference over the wall of the right ventricle- with lung insufflation results in a decrease in right ventricular output [8, 9]. For a fixed change in transmural pressure the amount of decrease in ventricular output depends on the shape of and the work point on the Frank-Starling curve, figure 1.3.

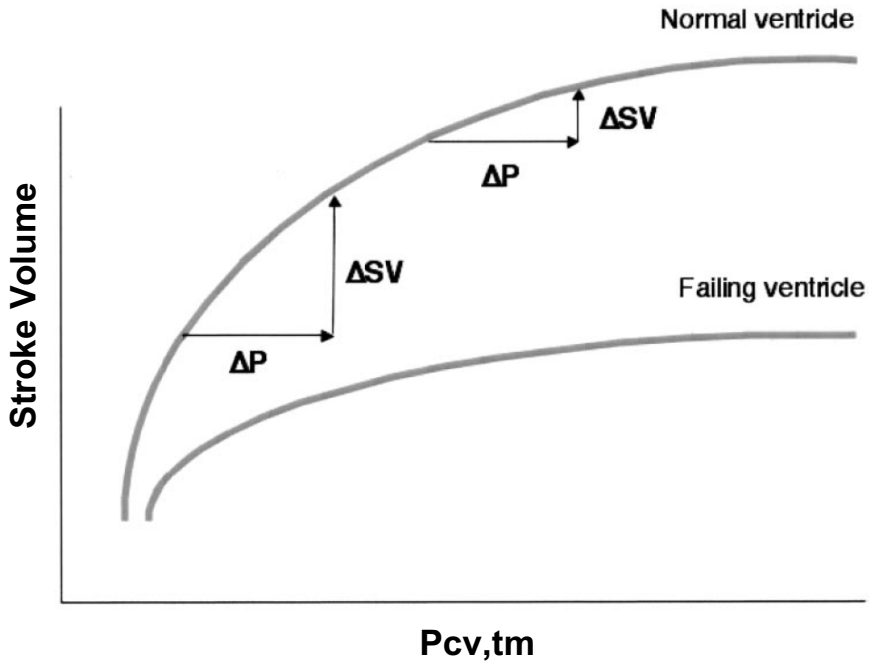

Figure 1.3 Schematic representation of the Frank-Starling relation between filling status and transmural pressure (X-axis) and stroke volume (Y-axis). During low filling status of the ventricle – with a low transmural pressure, the more likely the ventricle is operating on the steep portion of the curve and hence a given change in filling status (Δ Pcv,tm) will induce a significant change in stroke volume (ΔSV). From Michard 2005 [29].

During a low filling status of the ventricle -with a low transmural pressure- stroke volume diminishes markedly during insufflation whereas it diminishes less strikingly during a high filling status –with a high transmural pressure. Therefore, variation in

stroke volume during mechanical ventilation with a fixed tidal volume and respirator frequency is low in hypervolemia and high in hypovolemic filling status of the heart.

Perel et al. [10] used systolic arterial pressure as a surrogate for ventricular stroke volume and defined systolic pressure variation (SPV) during mechanical ventilation as the sum of Δup and Δdown, figure 1.4. For this determination a single prolonged end expiratory pause is needed.

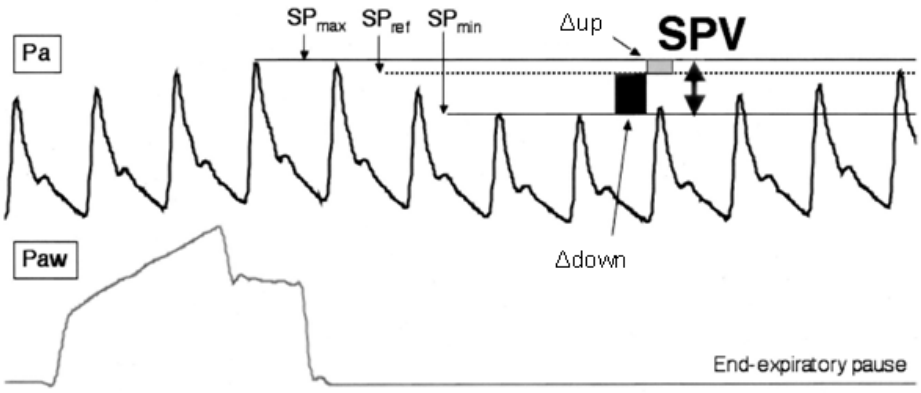

Figure 1.4 Description of respiratory changes in arterial pressure during mechanical ventilation. The systolic pressure variation (SPV) is the difference between SPmax and SPmin a few heart beats later, during expiration. Pa is arterial pressure; Paw is airway pressure. From Michard 2005 [29].

Michard et al. [11] proposed to quantify respirator induced variation in arterial pulse pressure (PP), as surrogate for stroke volume. Pulse pressure variation (PPV) is found by calculation the difference between maximum (PPmax) and minimum pulse pressure (PPmin) over a single mechanical breath divided by the mean of both values i.e. PPV(%) = 100*(PPmax-PPmin)/[(PPmax+PPmin)/2], figure 1.5.

Berkenstadt et al. [12] and Reuter et al. [13, 14] used a similar formula to determine pulse contour stroke volume variation. Stroke volume variation (SVV) is calculated as: SVV(%) = 100*(SVmax-SVmin)/[(SVmax+SVmin)/2]
Stroke volume variation (SVV) and pulse pressure variation (PPV) are an integral part of today's beat-to-beat pulse contour cardiac output monitoring systems (such as Pulsion's PiCCO system, LiDCO's PulseCO system and Edwards FloTrac-Vigileo system, which are evaluated in this thesis).

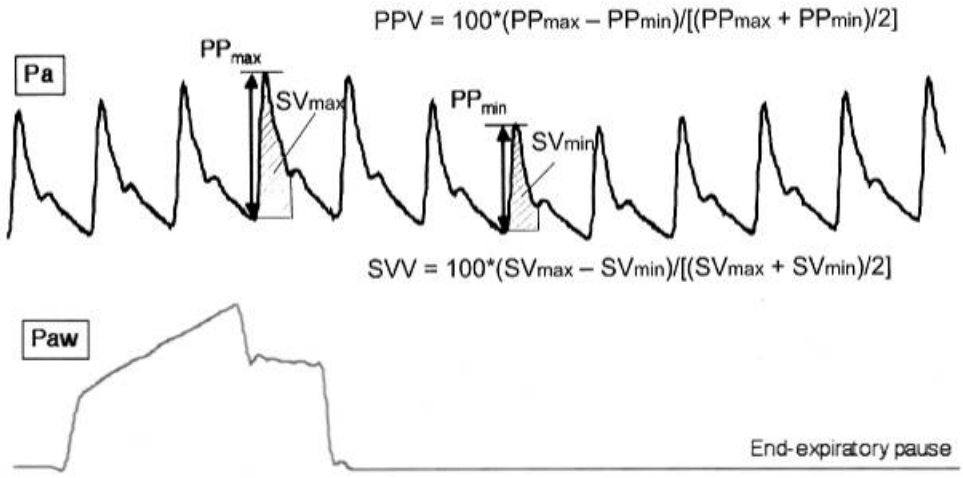

Figure 1.5 Description of resiratory changes in arterial pressure during mechanical ventilation. Pa is arterial pressure; Paw is airway pressure; PPV is pulse pressure variation; SVV is stroke volume variation. From Michard 2005 [29].

Also, Doppler recordings of aortic blood flow at the level of the aortic annulus or in the descending aorta have been used to quantify the respiratory variation in aortic peak velocity (APVV) or in aortic blood flow (ABFV) [15-17].

However, despite evidence generated in literature, the use of SPV, PPV or SVV (APVV and ABFV) for characterizing the volemic condition is limited to patients who are fully dependent on mechanical ventilation (with no spontaneous breathing activity), who are ventilated with tidal volumes larger than 8 mL/kg and who have a regular heart rate. These conditions are often not fulfilled in ICU patients.

Thermodilution as reference method for cardiac output

"In assessing any method of measurement it is clearly necessary to know the probable error of the standard against which it is compared" [18]. In this thesis pulmonary thermodilution is used as reference method for all methods evaluated. However, for a reliable application several conditions have to be fulfilled. First, complete mixing of cold injectate with blood; Second, no loss or gain of cold between the site of injection (entrance right atria) and site detection (pulmonary artery); Third, constant blood flow. The condition of constant blood flow is, as explained in the above paragraph, violated during mechanical ventilation. As shown in theoretical and physical models as well as in animal and patient studies [19-23], the errors in the estimation of mean flow –cardiac output- by the bolus injection technique may be very large, especially if the frequency content of the dilution curve is similar to that of the flow modulation as occurs during mechanical ventilation.

Among different solutions for this problem Jansen et al. [23] demonstrated a very practical one. By averaging the results of 4 estimates initiated at moments equally distributed over the ventilatory cycle highly reproducible results were found in animals and humans [23, 24] figure 1.6.

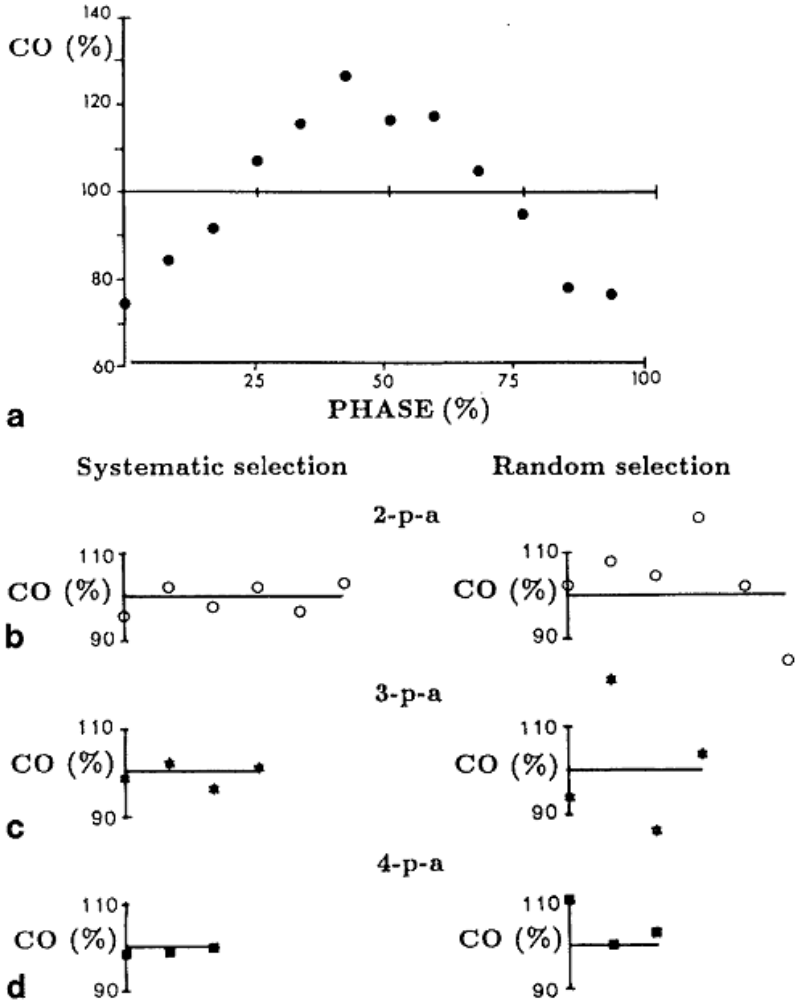

Figure 1.6 Calculation of cardiac output average based on a systematic selection and random selection of sinle estimates. Values are given in % of the mean of a series of all 12 estimates. a; 12 single estimates of a patient plotted against the moment of injection in the ventilatory cycle. Phase 100% is the same as 0% coincide with the start of insufflation. b; 6 two point averaged (2-p-a) values consecutively plotted on the horizontal axis, c; 4 three point averaged (3-p-a) values , and d a 3 four point averaged (4-p-a) value. From Jansen 1995 [25].

In a patient study [25], the standard deviation decreased from 13.0% for single thermodilution estimates to 3.2 % if the averaged value of 3 measurements equally distributed over the ventilatory cycle (for instance the first at 0% the second at 33% and the third at 66% of ventilatory cycle) was taken. This standard deviation was still 7.2% for the averaged value of three randomly applied measurements. In this thesis the averaged value of three measurements equally spread over the ventilatory cycle was taken, unless it was explicitly stated differently.

Analysis of agreement between methods of measurement
A correct evaluation of cardiac output devices from literature is often hampered by 1) incomplete description of the methods, patient characteristics and measurement conditions, 2) incomplete description of results, or 3) use of a non validated reference method or acceptance of an imprecise method. In this thesis different less invasive methods of cardiac output measurement and monitoring are evaluated against a well studied reference method with high precision, i.e. the bolus thermodilution method.

The evaluation of new methods to measure physiological variables is facilitated by standardization of reporting results. It has been proposed that assessing repeatability should be followed by assessing agreement with an established technique. Bland and Altman [26] advocated the use of a graphical method by plotting for each subject the difference between the method under study and the reference method against their mean and argued that if the new method agrees sufficiently with the old, the old may be replaced. Here the idea of agreement plays a crucial role. Limits of agreement are calculated as mean difference (bias) ± 1.96 * standard deviation (SD). SD is also called precision [26, 27]. Strict rules when a new method may replace an older reference method are given by Critchley and Critchley [28] and not by Bland-Altman. These rules as well as Bland-Altman plots are analysed throughout the thesis.

Outline of the thesis

In this thesis, different recently developed methods to monitor cardiac output and ventilator induced stroke volume and pulse pressure variation are evaluated in ICU patients. The thesis contains the following items:

- In the second chapter the interchange-ability of femoral artery pressure and radial artery pressure as input for the PiCCO pulse contour system is tested.
- In chapter 3 the quality and tracking ability of five different pulse contour methods are evaluated by simultaneous comparison of cardiac output values with that of the conventional thermodilution technique (COtd). The five different pulse contour methods enclosed in this study were: Wesseling's cZ method; the modified Modelflow method; the LiDCO system; the PiCCO system and a recently developed Hemac method.
- In chapter 4 a review of the PiCCO pulse contour cardiac output monitoring system is given addressing our clinical experiences with this device.
- In chapter 5 the FloTrac-Vigileo pulse contour cardiac output system is evaluated. Its results are compared with that of other pulse contour methods.
- In chapter 6 the tracking abilities of cardiac output changes by three less invasive cardiac output methods requiring no calibration were evaluated. The following methods were studied: 1. FloTrac-Vigileo, 2. uncalibrated modified Modelflow and 3. HemoSonic100 trans-esophageal ultrasound. In this study cardiac output changes were achieved by changing ventilator settings and by passive leg raising.
- In chapter 7 an alternative method for calibration of the modified Modelflow is tested. For this purpose aortic diameter is measured by the HemoSonic 100 transesophageal ultrasound system.

- In chapter 8 data of stroke volume variation (SVV) obtained with two different pulse contour systems were compared in different clinical conditions.
- The last chapter of this thesis the main results of previous chapters will be summarized in English and Dutch.

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