

Summary

In this thesis, we explored confounders of measurements by the transpulmonary thermodilution technique, in patients with intrathoracic pathology (**chapter 3**) or valvular insufficiencies (**chapter 5**). The possible role of mathematical coupling explaining the superiority of volumes over pressures as indicator of preload and the influence of cardiac function on preload parameters is described in **chapter 4** and **6**, respectively. Furthermore, we evaluated whether two non-calibrated pulse contour cardiac output techniques track thermodilution cardiac output changes during altering preload and afterload, in patients after cardiac surgery (**chapter 8** and **9**).

Chapter 1

In the critically ill, hemodynamic monitoring is usually performed with a pulmonary artery catheter (PAC), allowing assessment of central venous pressure (CVP) and pulmonary artery occlusion pressure (PAOP), both which are assumed to be reliable guides for fluid therapy. Moreover, cardiac output can be measured via thermodilution. However, CVP and PAOP measurements are influenced by lung compliance and intrathoracic pressures. Moreover, the PAC is invasive with inherent risks. To bypass these flaws, a less invasive technique was developed which is able to measure volumes instead of pressures, not influenced by positive pressure ventilation. However, there are some drawbacks of the transpulmonary thermodilution method, inherent to technique. Indeed, in patients with valvular insufficiencies or intrathoracic pathology, measurements can be confounded. Moreover, the contribution of mathematical coupling to the superiority of volumes over pressures as indicators of preload is unclear, when both cardiac output and cardiac volumes are derived from the same thermodilution curve. These doubts form the basis of the first aim of this thesis: to clarify some issues associated with the transpulmonary thermodilution technique in assessing cardiac output, preload and fluid responsiveness. In the critically ill both preload and afterload conditions of the heart change over time, due to altered cardiac compliance, volume status, change of inotropic or vasodilator doses and ventilator settings, which will result in CO changes. In the second part of this thesis we evaluate whether two minimally invasive, non-calibrated arterial waveform based techniques, the modified ModelFlow and FloTrac/Vigileo, track these CO changes.

Chapter 2

We give a summary of the literature of the role intrathoracic blood volumes determined by transpulmonary thermodilution, in the monitoring of critically ill patients, with respect to assessing volume status, heart function and response to fluids in the treatment of hypovolemia and shock. We concluded that functional hemodynamic monitoring of intrathoracic volumes with double or single indicator dilution is a useful tool to assess preload and fluid responsiveness in critically ill patients. However, the effect of volumetric (rather than pressure) monitoring on morbidity and mortality of critically ill patients is lacking, although the method is less invasive compared to the PAC.

Chapter 3

We describe two patients, one with severe haemorrhage and one with a partial anomalous pulmonary vein in which cardiac output measurements were performed simultaneously by means of the single-indicator transpulmonary thermodilution technique and continuous pulmonary artery thermodilution method. In both cases, the methods revealed clinically significant different cardiac output values based upon the site of measurement and the underlying pathology. In the first patient with excessive blood loss, cold indicator could be lost due to the accumulation of blood in the thorax. Vliers et al.¹ demonstrated the leave and re-entrance of indicator from the vascular bed into the lungs by recording the intrabronchial air temperature changes during the passage of the cold indicator through the pulmonary vascular bed. This will lead to a reduction and distorted thermodilution curve, resulting in overestimation of the cardiac output. However, in the second patient a persistent anomaly

was present. In this patient, both techniques, for cardiac output measurement, seem to measure the real-time cardiac output of, respectively, the left and right ventricle, since the amount of blood passing the thermistor of the pulmonary artery catheter is the sum of the shunt flow and of the vena cava inferior and superior flow.

Chapter 4

This study investigated the role of mathematical coupling of shared measurement error when cardiac volumes and cardiac output are obtained from the same thermodilution curve. Eleven consecutive and mechanically ventilated patients with hypovolemia after coronary artery surgery and a pulmonary artery catheter in place, allowing continuous cardiac index (CCI_p) measurements, received a femoral artery catheter for transpulmonary thermodilution measurements (PiCCOTM, CI_{tp}). A total 48 fluid loading steps of 250 mL were done. We found that central venous pressure and volumes equally related to CI_{tp} and CCI_p and that fluid responses were predicted and monitored similarly by CI_{tp} and CCI_p. However, during fluid loading, changes in volumes related better to changes in CI_{tp} when derived from the same curve than to changes in CI_{tp} of an unrelated curve or changes in CCI_p. These data suggest that the superiority of volumes as indicator of fluid responsiveness over filling pressures can be caused, at least in part, by mathematical coupling of shared measurement error when cardiac volumes and output are derived from the same thermodilution curve.

Chapter 5

This study investigated whether residual left-sided valvular insufficiencies after valvular surgery confound transpulmonary thermodilution cardiac output (CO_{tp}) technique. We compared the technique with the continuous right-sided thermodilution technique (CCO) after valvular and coronary artery surgery. After valvular surgery, there was minimal aortic insufficiency in 4 patients and minimal to moderate mitral valve insufficiency in 6. 5 Fluid loading steps (250 mL) were done in each patient. We found a lower cardiac output after valvular than coronary artery surgery but responses to fluid loading steps were similar among surgery types and techniques. We also found that after valvular and coronary artery surgery, cardiac output was lower prior to responses than in nonresponses to fluids, by either technique. After valvular surgery, CO_{tp} and CCO correlated but fluid-induced changes did not. After coronary artery surgery, CO_{tp} and CCO correlated and changes also did. At fluid-induced CCO increases <20%, the *r* for changes in cardiac output measured by both techniques was similar after valvular and coronary artery surgery. These data imply that CO_{tp} and CCO are of similar value in predicting and monitoring fluid responses after both surgery types, therefore arguing against left-sided valvular insufficiencies, severely confounding CO_{tp}.

Chapter 6

In this chapter we compared the value of cardiac filling pressures and volumes in patients after valvular (VS) and coronary artery surgery (CAS) patients, since cardiac function may differ after both types of surgery and therefore may affect assessment of fluid responsiveness. Eight patients after VS and 8 after CAS were included. In each patient, five sequential fluid loading steps of 250 mL of colloid were done. Fluid responsiveness was defined by a cardiac index (CI) increase >5% or ≥10% per step. We found a lower global ejection fraction and a higher pulmonary artery pressure (PAOP) after VS compared to CAS. In responding steps after VS, PAOP and volumes increased, while central venous pressure (CVP) and volumes increased in responding steps after CAS. After VS, baseline PAOP as well as changes in PAOP and volumes were of predictive value and PAOP and volume changes equally correlated to CI changes. After CAS, CVP and volumes were of predictive value and changes in CVP and volumes correlated to those in CI. These data suggest an effect of systolic cardiac function on optimal parameters of fluid responsiveness and superiority of the pulmonary artery catheter over transpulmonary dilution for hemodynamic monitoring of VS patients.

Chapter 7

In this chapter we summarize the physiology of static indicators used to predict and monitor preload responsiveness in critically ill patients on mechanical ventilation. First, we explain the definitions preload and fluid responsiveness used in the literature. Secondly, we discuss filling pressures and volumes of the heart and the influence of positive pressure mechanical ventilation on both measurements. In the last part, we describe the influence of contractility and afterload of the heart on the cardiac function curve relating cardiac output to end-diastolic filling pressure. We also explain the relative predictive value of volumes versus pressures for changes in cardiac output, depending on the position on the compliance curve and the position and shape of this curve. Furthermore, we illustrate the clinical implications of these physiological considerations. We concluded that the relative predictive value of static filling pressures and volumes for the cardiac output response to preload changes depends on biventricular systolic and diastolic function. Overall, this implies that both pressures and volumes may be needed to predict and monitor fluid responses. However, the ultimate guide to fluid therapy may be frequently intermittent or continuous cardiac output monitoring to prevent fluid overloading by discontinuing fluid infusion when cardiac output does not further increase.

Chapter 8

This chapter reports on our prospective study to investigate whether changes in less invasive, non-calibrated pulse-contour cardiac output (by modified ModelFlow, COMf) and derived stroke volume variation (SVV), as well as systolic and pulse pressure variations predict changes in bolus thermodilution cardiac output (COtd), induced by continuous and cyclic increases in intrathoracic pressures by increases in positive end-expiratory pressure (PEEP) and tidal volume (Vt), respectively. We found that SVV increased at PEEP 10cmH₂O and 15 cmH₂O, concomitantly with a decrease in COMf and COtd. In contrast, systolic and pulse pressure variation did not increase. We also found that changes in COMf correlated with those in COtd, whereas changes in SVV did not. Remarkably, variables did not change when Vt was increased up to 50%. Thus, in mechanically ventilated patients after cardiac surgery, during continuous increases in intrathoracic pressure, tracking a fall in COtd by COMf is more sensitive than a rise in SVV, which is more sensitive than systolic pressure variation and pulse pressure variation. These results suggest that PEEP causes a reduction in biventricular preload and is the main factor in decreasing cardiac output and increasing SVV.

Chapter 9

In this prospective study we investigated whether cardiac output and its postoperative course by a new non-invasive pulse-contour technique of radial artery pressure waves, without need for calibration (FloTrac™/Vigileo™ [FV], Edwards Lifesciences) conforms with the standard bolus thermodilution method via a pulmonary artery catheter. Fifty-six simultaneous measurement sets were obtained, in 20 patients up to 24 h after cardiac surgery. We found that cardiac output measured by the non-invasive pulse-contour FV method reasonably well compares to that measured by bolus thermodilution via pulmonary artery catheter, in cardiac surgery patients, over a relatively wide range of cardiac output. Moreover, for clinical purposes the concordance of detected changes in cardiac output over time was satisfactory. Thus, the FV pulse-contour method is a clinically applicable non-invasive pulse-contour method for cardiac output assessment without the need for calibration, after cardiac surgery.