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Comparisons of predictors of fluid responsiveness in major surgery

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Abstract— **The majority of studies on fluid responsiveness is focused on volume expansion maneuvers in intensive care unit (ICU), while fewer studies have analyzed the same problem during major surgery. Among them, the results are contrasting. The aim of this work was to compare the performance of different hemodynamic indices in the prediction of cardiac output variations following fast fluid infusion. The study was limited to a particular type of major surgery, i.e. liver transplantation and hepatectomy. Our results showed that pulse pressure variation (PPV) estimated according to the definition, i.e. within single respiratory cycles, and PPV estimated by PiCCO monitor system are coherent and very similar. Moreover, PPV and stroke volume variation (SVV) produced good values of sensitivity and specificity in separating the subjects into responsive and non responsive to maneuvers.**

I. INTRODUCTION

Hemodynamic monitoring plays an important role in the management of patients in intensive care and during major surgery. Functional hemodynamic monitoring can be defined as the assessment of the dynamic interactions of hemodynamic variables in response to a defined perturbation [1]. Clinical trials have shown the clinical usefulness of functional hemodynamic monitoring for predicting volume responsiveness and identifying hidden cardiovascular insufficiency. Fluids are primarily administered to revers hypovolemia. Hypovolemia may be due to external fluid losses caused by bleeding or losses from the gastrointestinal or urinary tracts, or internal losses due to extravasation of blood or exudation of body fluids. Optimal fluid resuscitation remains a matter of lively debate, particularly in recent years with controversy about choice of fluids. The end point of fluid resuscitation also remains unclear. However, fluid challenge must be clearly separated from an increase in fluids which are routinely administered to ensure patient hydration: it refers to the initial volume expansion period in which the response of the patient to fluid infusion is carefully evaluated [2]. In this work, rapid infusion is used as general term to describe large amounts of fluids administered over a short period of time.

Recently, the use of dynamic preload indices, such as pulse pressure variation (PPV) and stroke volume variation (SVV), has been increasingly advocated for fluid management in mechanically ventilated patients with various clinical conditions [3]. However, a systematic comparison between the performance of different indices has not been performed yet. The aim of this study was to compare the ability of several hemodynamic indices to predict fluid responsiveness (FR) in liver surgery.

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II. METHODS

A. Data and Protocol

Ten patients who underwent orthotopic liver transplantation (OLT) or hepatectomy were enrolled in this study. The exclusion criteria were: persistent arrhythmias, arteriosclerosis as it affects arterial compliance, tidal volume less than 8ml/(kg of ideal weight) [4]. Sedation was induced by propofol and/ or syfentanil (2mg/kg) and maintained by total intravenous anesthesia (TIVA, 6-8 mg /(kg hr)). In this study rapid infusions only were analyzed, and they consisted in boluses of 100ml or 500ml administered within 30 sec or 1 minute respectively. For each maneuver, arterial blood pressure (ABP), air flow (AF), air pressure (AP), pulse contour cardiac output (PCCO) and stroke volume (SV) estimated by Pulsion PiCCO were recorded and analyzed.

A custom software was developed (termed “Global Collect”, Labview 2009© environment) in order to simultaneously acquire, interpret and visualize data. All devices, i.e. Pulsion PiCCO© and GE S/5 Avance Carestation©, perform internal A/D conversion and transmit data (RS232 interfaces) sampled at heterogeneous frequencies and packaged through proprietary protocols. Invasive ABP was measured via an arterial catheter inserted in the brachial artery and placed in the aortic arch. ABP was recorded at a sample frequency of 100 Hz. Cardiac Output (CO) and all indices estimated by PiCCO were recorded as well. Surgeries were performed in the University Hospital Tor Vergata in Rome, Italy. The study was approved by the local Ethics Committee, and the patients gave their written, informed consent to participate.

B. Parameter extraction and Analysis

For each maneuver time intervals were selected beginning 20 sec before the start of infusion and including the following 3 minutes. Beat-to-beat series of pulse pressure (PP) were estimated from the continuos ABP waveform. Heart rate (HR) was derived by R peak detection on ECG waveform. Furthermore, two algorithms were implemented to analyze the continuos ABP signal in order to extract beat-to-beat values of CO and SV: the Lijestrand and Zander method (CO_{LM}, SV_{LM}) and the systolic area method (CO_{SA}, SV_{SA}), which are fully described in [5].

Pulse pressure variation and stroke volume variation were estimated according to the definitions (1) and (2):

$$PPV = 2 * \frac{PP_{max} - PP_{min}}{PP_{max} + PP_{min}} * 100 \qquad (1)$$

where PP_{max} and PP_{min} refer to the maximum and minimum values respectively obtained in a single respiratory cycle, previously identified by AF signal;

$$SVV = 2 * \frac{SV_{max} - SV_{min}}{SV_{max} + SV_{min}} * 100 \qquad (2)$$

where SV_{max} and SV_{min} refer to the maximum and minimum values respectively obtained in a single respiratory cycle. PPV and SVV provided by PiCCO monitor were used as well, for comparison purpose.

III. RESULTS

A. Patients and maneuvers classification

10 different surgical interventions were analyzed (8 hepatectomy and 2 OLT), for a total amount of 25 maneuvers. The principal motivation of the surgery was neoplasia (7 out of 10). All maneuvers were retrospectively classified according to CO variations measured by PiCCO monitor ($\Delta PCCO$ values). A maneuver was considered responsive if $\Delta PCCO$ resulted larger than zero in the successive three minutes after the beginning of infusion, and the maximum variation reached the threshold of 10%. 8 out 25 maneuvers satisfied this condition.

B. Indices of Fluid Responsiveness

The Bland-Altman analysis (figure 1) showed that the PPV values extracted from the monitor are consistent with the indices computed according to the definition. The average values of the difference is close to zero and the standard deviation of the difference is less than 5% (see figure 1). A different result was obtained with SVV indices: SVV_{SA} values were very similar to SVV_{PiCCO} for lower values, while for higher values SVV_{SA} overestimated the values of the monitor. SVV_{LM} showed higher differences with respect to SVV_{PiCCO}, and overestimated for low values as well, the average difference was 6.15%.

The performances of these indices are summarized in table I. PPV and SVV indices both provided by PiCCO monitor and calculated by the proposed algorithms resulted significantly different between the maneuvers classified as responsive (R) and non responsive (NR). As expected lower values corresponded to lower or no increase of CO. The relationship between fluid responsiveness indexes and the following CO variations was investigated by correlation analysis: PPV_{PiCCO} and PPV resulted significantly correlated to $\Delta PCCO$ (p-value$<$0.05), and the correlation coefficients were $\rho = 0.54$ and $\rho = 0.44$, respectively.

Sensitivity and specificity were analyzed to find threshold values that best separated the R maneuvers from NR ones. In particular, we obtained a threshold of 14.4% and 13.9% for PPV_{PiCCO} and PPV indexes respectively, which corresponded to Se=0.88 and Sp=0.86. Results related to SVV_{PiCCO} are reported in figure 2. The threshold of 19.7% produced a Se=0.88 and Sp=0.75.

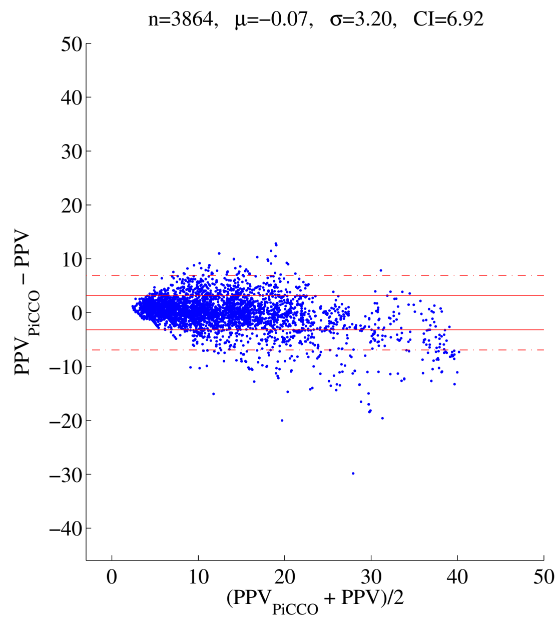

Fig. 1. Bland-Altman analysis with PPV values provided by the monitor PiCCO and PPV values computed by using the information of breathing cycle. The solid lines mark the interval $\pm\sigma$ (standard deviation of the difference between PPV_{PiCCO} and PPV), the dashed line marks the 95th confidence interval (CI). μ= mean of the differences

TABLE I

VALUES OF FLUID RESPONSIVENESS INDICES

	R	NR	p-value
PPV_{PiCCO}	20.1 (17.7-21.1)	9.2 (7.5-11.7)	$<$0.001
PPV	17.1 (15.1-22.5)	9.3 (7.0-12.8)	$<$0.05
SVV_{PiCCO}	24.1 (19.3-25.5)	13.4 (10.9-18.7	$<$0.005)
SVV_{SA}	23.2 (19.3-24.5)	14.1 (9.6-18.0)	$<$0.05
SVV_{LM}	10.7 (8.2-14.6)	6.8 (4.8-9.8)	n.s.

The maneuvers were classified as responsive (R) and non responsive (NR). Values are expressed as median (25^{th} and 75^{th} percentile range). The p-values refer to Wilcoxon rank sum test.

IV. DISCUSSION AND CONCLUSIONS

The majority of studies on volume expansion maneuvers takes into account intensive care unite (ICU) patients, while fewer studies have been published relating to major surgery. Among them, the results are contrasting [6][7]. The aim of this work was to compare the ability of hemodynamic indices to predict cardiac output increase in response to rapid fluid infusions. The study was limited to a particular type of major surgery, i.e. OLT and hepatectomy. This

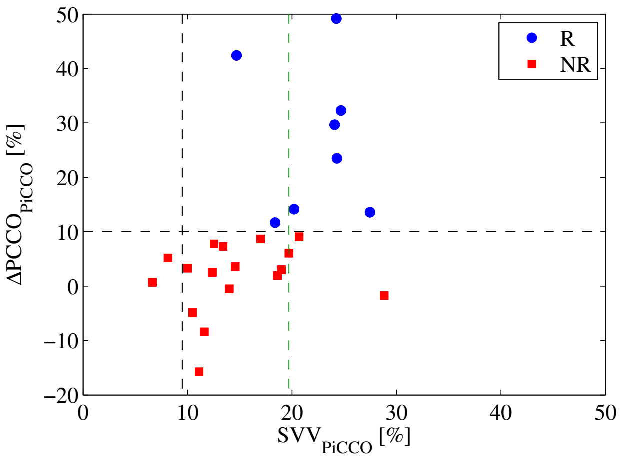

Fig. 2. Values of SVV estimated by PiCCO before the rapid infusion and values of maximum variation of cardiac output (ΔPCCO) obtained during the third minute after the maneuver. The dashed horizontal line marks the threshold which separates the responsive (R) from non responsive (NR) maneuvers. The dashed black vertical line marks the threshold commonly used in literature (9.5%) for SVV index in order to predict the outcome. The green line marks the threshold obtained in the present work.

choice to analyze this interventions was motivated by the fact that the liver is a highly perfused organ and the amount of volume involved in its surgery is high. Our results showed that PPV estimated according to the definition, i.e. by considering the ventilatory signals, and PPV estimated by PiCCO are coherent and very similar. Moreover, PPV and SVV produced good values of sensitivity and specificity in separating the maneuvers. The thresholds obtained in the present study resulted higher with respect to those reported in literature. However, PPV threshold (14%) resulted slightly higher than values reported in [8][9] (13%). A larger difference was instead obtained for SVV index, whose threshold resulted double with respect to ones reported in literarature [10]. These differences can be explained by this type of intervention and by the fact that PPV is an index assessed on a direct measure, i.e. ABP, while SVV is derived by SV, whose values are estimated from ABP waveform.

Future studies are needed in order to standardize and validate the criteria used to evaluate the maneuvers, for instance the length of time window before and after the infusion, in a larger population. The development and improvement of new methods able to assess the hemodynamic condition of the patient from available signals like ABP, will enable to optimize fluid infusion maneuvers. Moreover, current research is devoted at developing closed-loop control of fluid administration, as dynamic predictors of fluid responsiveness proved to be robust parameter to guide fluid administration [11].

Finally, future advances in noninvasive monitoring of cardiac output and other hemodynamic variables make goal-directed therapy applicable to very diverse patients in a variety of clinical care settings.

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