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Fluid loading responsiveness

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Chapter 12

Pulse contour cardiac output and passive leg raising to assess fluid loading responsiveness in cardiac-surgery patients

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The selection of patients that will benefit from fluid loading is important since unnecessary fluid loading in a non-responsive subject may potentially cause pulmonary and general oedema. Passive leg raising (PLR) is a routinely-applied bedside method that accurately predicts volume responsiveness [1-6]. However, its clinical application requires dynamic assessment of cardiac output (CO). Transient increases in transthoracic and oesophageal Doppler CO and left ventricular stroke area by ultrasound during PLR predict preload responsiveness. However, ultrasound measurements are neither routinely performed, consistent among operators nor easy to perform continuously [7]. Furthermore, the HemoSonic ultrasound device most frequently used in PLR research [1-6] is currently withdrawn from the market. Recently, DeBacker and Pinsky hypothesized that other CO measurement techniques such as pulse power or pulse contour analysis could provide similar results and supplant Doppler ultrasound monitoring [8]. This approach is attractive, as it would provide the clinician with a simple, readily available and robust measure that can be obtained at the bedside.

The aim of our study is to evaluate the applicability of two different radial artery pulse contour CO devices, one using pulse power (COLi, LiDCO, London, UK) and the other using Modelflow arterial pulse contour analysis (COM, FMS, Amsterdam, the Netherlands) in prediction fluid loading responsiveness by tracking CO changes due to a PLR manoeuvre. The changes in cardiac output by these two methods are compared to changes in CO by thermodilution (COtd).

Methods

Twenty patients undergoing elective coronary artery bypass (CABG) and, or valvular reconstruction surgery were included into the study after approval of the University Medical Ethics Committee of the University of Leiden. All patients signed informed consent to be part of this study. Subjects were included in the study during their initial post-operative period once hemodynamically stable with a mean arterial pressure (MAP) > 70 mmHg, central venous pressure (CVP) between 5-10 mmHg and a cardiac index > 2.5 L · min⁻¹. Exclusion criteria included severe arrhythmias, advanced congestive heart failure (ejection fraction < 20%), intra-cardiac shunts, symptomatic peripheral vascular disease, symptomatic pulmonary disease, aortic aneurysm and significant valvular regurgitation after surgery.

Anaesthesia during surgery was with propofol and sufentanil infusions according to institutional standards. Upon arrival in the ICU sedation was continued. The lungs were mechanically ventilated in a volume-control mode with settings aimed to achieve normocapnia with a tidal volume of 8-12 ml · kg⁻¹ and a respiratory frequency of 12-14 breaths · min⁻¹. Fraction of inspired oxygen was 0.4 and PEEP 5 cmH₂O. During the

observation period, ventilator settings, sedation and vasoactive medication, when used, were continued unchanged.

All subjects had a pulmonary artery catheter (Intellith; Edwards Lifesciences; Irvine, CA, USA) inserted into the right jugular vein and a radial arterial catheter (20 G) inserted prior to ICU admission. COtd measurement was performed with an automated system under computer control. COtd was measured in triplicate (with 10 ml saline solution at room temperature) in two minutes, with the measurements equally spread over the ventilatory cycle. The three individual COtd measurements were averaged [9]. Blood pressure transducers were referenced to the level of the tricuspid valve and zeroed to atmospheric pressure. Arterial pressure, heart rate (HR) and CVP data were continuously recorded with a sample frequency of 100 Hertz and stored on a personal computer for documentation and offline analysis. MAP, systolic arterial pressure (SP), pulse pressure (PP) and pulse pressure variation (PPV) were calculated from arterial pressure. Stroke volume variation (SVV) and CO was averaged over 30 second intervals using pulse power (SVVli and COLi) and Modelflow (COM). The LiDCO system was calibrated. The Modelflow was used uncalibrated. A detailed description of the two methods can be found elsewhere [10-12].

Measurements were carried out within two hours after arrival in the ICU following MAP stabilization (85.0 ± 12.0 mmHg) and restoration of central body temperature (36.6 ± 0.7 °C). Characteristics and treatment data of each patient were collected. Passive leg raising was performed from the supine position by lifting both legs at a 30° angle and holding them there for 5 minutes. Measurements of HR, MAP, PP, SP, CVP, COtd, COM, COLi, PPV and SVV were performed 5 minutes before, 2 minutes after initial elevation of the legs with legs still elevated, and 5 minutes after return from passive leg raising.

We used a Kolmogorov-Smirnov test, paired t-test and linear regression analysis. The reliability to track changes in CO was analyzed by computing the area under the receiver operating characteristics (ROC) curve, with responders related to 7% COtd increase during PLR [13]. Usually, responders are characterized by an increase of 10-15% in CO after rapid fluid loading with 500 ml [14]. Lafanechere *et al.* [3] showed that the effect of PLR on CO of patients in supine position was equal to 250 ml fluid loading. We reasoned that in the same group of responders a PLR-induced auto-transfusion of 250 ml should result in an increase of CO of 5 to 7.5%. Our thermodilution technique with automated triplicate measurements equally spread over the respiratory cycle has shown a precision of 3.5% [9,11]. Therefore, this technique should detect changes in CO induced by PLR larger than 7% (2SD precision) accurately and identifying responders by a >7% increase in CO by PLR reliable. All values are given as mean \pm SD. Differences corresponding to a p value < 0.05 were considered significant.

Results

Twenty patients met the inclusion criteria and were enrolled in the study. All finished the study. Clinical patient data is shown in Table 1. An example of the effects of PLR on haemodynamics in one patient is given in Figure 1. Beat-to-beat systolic, mean and diastolic blood pressures increase and modulation of the variables by mechanical ventilation decrease during PLR, associated with no change in HR, an increase in SV and decrease in SVV.

Table 1 Demographic data of the patients.

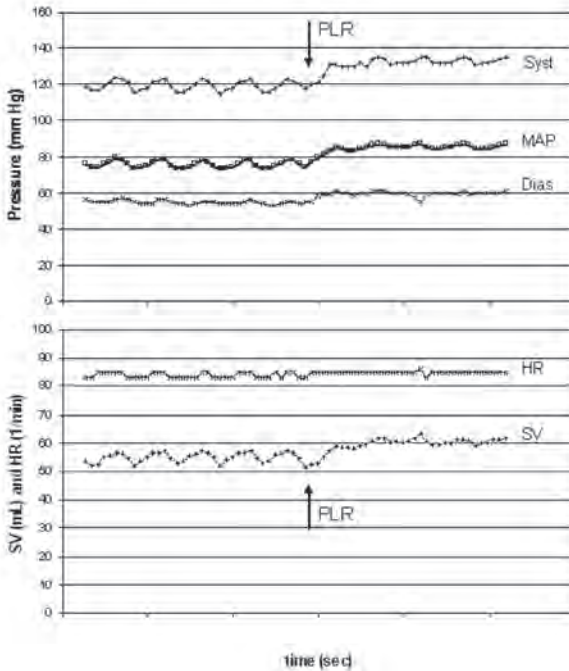
Patient	Gender	Type of surgery	Age years	Weight kg	Length cm	Propofol mg·h ⁻¹	Inotropic support µg·kg ⁻¹ ·min ⁻¹
1	m	AVR	52	80	160	250	0.25 nitroprusside
2	m	AVR	79	82	178	140	
3	m	AVR	61	73	186	150	4.0 dobutamin, 0.02 norepinephrine
4	m	CABG	72	97	178	200	
5	f	AVR	35	86	169	350	
6	m	CABG	65	69	170	220	
7	m	CABG	78	103	182	200	
8	m	CABG	56	118	178	250	
9	m	AVR	58	88	178	150	
10	f	CABG	69	73	158	200	3 dopamine
11	m	CABG	53	95	178	300	
12	m	CABG	67	83	175	200	2 dobutamine
13	m	CABG	75	88	178	250	
14	m	CABG, MVP, TVP	54	100	187	200	0.75 nitroprusside
15	f	CABG, AVR	59	59	158	150	
16	m	CABG	80	74	172	200	0.3 norepinephrine
17	m	CABG	66	72	183	200	
18	m	CABG	63	66	160	220	
19	m	AVR	62	106	176	250	0.25 nitroprusside
20	m	CABG, MVP, TVP	73	71	175	200	0.5 enoximone

Mean ±
SD

64 ± 11 84 ± 15 174 ± 9 214 ± 52

Abbreviations: CABG is coronary artery by-pass grafting; AVR is aortic valve replacement, TVP is tricuspid valve replacement; MVP; mitral valve replacement.

Figure 1 Beat-to-beat changes in hemodynamic variables by passive leg raising (PLR). Syst, MAP and Dias are systolic, mean and diastolic arterial blood pressure respectively; HR, heart rate; SV stroke volume



(187)

A Kolmogorov-Smirnov test indicated normal distributions of all hemodynamic data. Compared to baseline (Table 2), PLR increased COtd, COm, COli, MAP, PP, SP and CVP, decreased SVV and PPV, and had no effect on HR. All 20 subjects behaved in a qualitatively similar fashion to the one subject's example, Figure 1. Although COtd increased in all patients, COm increased in 19 of 20, COli increased in 15 of 20. Furthermore, MAP increased in 19 of 20, SP in 19 of 20, PP in 18 of 20, CVP in 18 of 20, HR increased in 5 and decreased in 7 out of 20 subjects. SVVm and SVVli decreased in 16 and 17 out of 20, respectively whereas PPV decreased in 18 out of 20.

Table 2 Haemodynamic variables at baseline and after 30° passive leg raising (PLR) in all 20 patients.

Parameters	Baseline	PLR	P-value
COtd (L·min ⁻¹)	5.62 ± 1.66	5.91 ± 1.67	< 0.001
COM (L·min ⁻¹)	6.17 ± 1.75	6.28 ± 1.76	0.002
COLi (L·min ⁻¹)	5.61 ± 1.39	5.85 ± 1.38	< 0.001
HR (min ⁻¹) [*]	79.1 ± 12.4	78.4 ± 13.2	0.256
CVP (mmHg)	9.2 ± 3.6	11.5 ± 4.0	< 0.001
PAP (mmHg)	19.9 ± 5.7	22.4 ± 5.8	< 0.001
MAP (mmHg)	84.7 ± 11.5	90.7 ± 13.4	< 0.001
PP (mmHg)	59.0 ± 10.3	65.2 ± 10.3	< 0.001
SP (mmHg)	124.8 ± 13.6	135.1 ± 17.2	< 0.001
SVVm (%)	5.8 ± 3.5	3.9 ± 2.7	< 0.001
SVVli (%)	7.3 ± 3.5	7.0 ± 2.1	< 0.001
PPV (%)	6.0 ± 4.2	4.3 ± 3.8	0.001
Rsys (dyne·sec·cm ⁻⁵)	1115 ± 341	1140 ± 325	0.296

Abbreviations: Thermodilution cardiac output (COtd), radial artery pulse contour cardiac output (uncalibrated Modelflow, COM and LiDCO, COLi), heart rate (HR), central venous pressure (CVP), pulmonary artery pressure (PAP), mean arterial pressure (MAP), systolic pressure (SP), pulse pressure (PP), stroke volume variation (SVVm and SVVli), pulse pressure variation (PPV) and systemic vascular resistance (Rsys).

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Results of linear regression for all 20 patients are summarized in Table 3. A significant relationship between the change in COtd and the change in MAP, PP, SP, COM and COLi was found. Noticeably, also baseline SVV and PPV related relatively well with the change in cardiac output due to passive leg raising.

Table 3 Slope of linear regression hemodynamic variables versus changes in thermodilution cardiac output due to PLR.

	Slope	95% Confidence Interval		P-value
		Lower	Upper	
ΔCOM	0.875	0.547	1.203	<0.001
ΔCOLi	0.810	0.488	1.131	<0.001
ΔHR	-0.585	-1.318	0.147	0.109
ΔMAP	0.428	0.074	0.782	0.020
ΔSP	0.276	0.047	0.506	0.021
ΔPP	0.190	0.028	0.352	0.024
ΔCVP	0.060	-0.036	0.157	0.207
SVVm baseline	0.738	0.249	1.228	0.005
SVVli baseline	0.660	0.138	1.181	0.016
PPV baseline	0.656	0.238	1.074	0.004

Abbreviations: Uncalibrated Modelflow cardiac output (COM), LiDCO cardiac output (COLi), heart rate (HR), mean arterial pressure (MAP), systolic pressure (SP), pulse pressure (PP), central venous pressure (CVP), stroke volume variation (SVV) and pulse pressure variation (PPV)

To construct Receiver Operating Characteristics (ROC) curves the population was divided into responders ($n=10$) and non-responders ($n=10$) based on an increase of at least 7% in COTd during PLR in responders. When COM increased by $\geq 2.5\%$, a concomitant increase of $\geq 5\%$ COTd was predicted with 89% sensitivity and 100% specificity. The optimal cut-off for a change in MAP is 5.5% increase. The (area under the) ROC curves for ΔCOM , ΔCOLi , ΔMAP , ΔPP , ΔSP and baseline SVV and PPV are given in Table 4 and Figure 2.

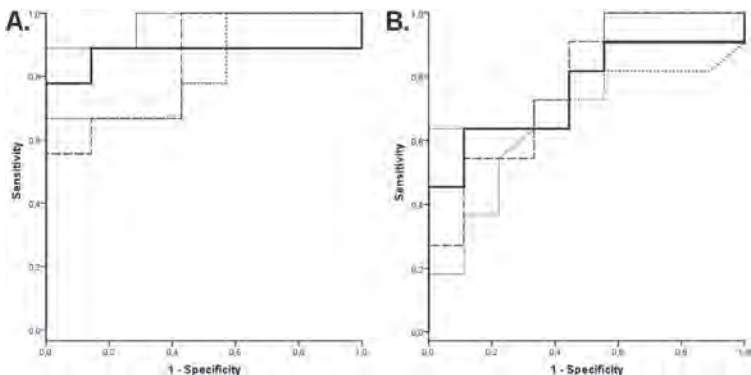
Table 4 Area under the ROC curves.

	Area	95% Confidence Interval	
		Lower	Upper
ΔCOM	0.968	0.890	1.000
ΔCOLi	0.841	0.643	1.000
ΔMAP	0.873	0.694	1.000
ΔPP	0.714	0.434	0.995
ΔSP	0.778	0.535	1.000
PPV baseline	0.808	0.615	1.000
SVV _m baseline	0.825	0.617	1.000
SVV _{li} baseline	0.873	0.665	1.000

Responders are defined by an increase in thermodilution cardiac output of at least 7% as a result of PLR. Abbreviations: Change in radial artery pulse contour cardiac output (uncalibrated Modelflow, ΔCOM and LiDCO, ΔCOLi), change in mean arterial pressure (ΔMAP), pulse pressure (ΔPP), change in systolic pressure (ΔSP), pulse pressure variation (PPV) and stroke volume variation (SVV_m and SVV_{li})

(189)

Figure 2 Receiver operating characteristics curves comparing the ability of passive leg raising induced changes. In A: ΔCOM (thin line), ΔCOLi (dashed line), baseline SVV_m (dotted line), baseline SVV_{li} (bold line). In B: ΔMAP (thin line), ΔPP (dotted line), ΔSP (bold line) and baseline PPV (dashed line) to predict $\geq 7\%$ change in ΔCOTd .



Discussion

We showed that PLR with 30° of both legs produced a rapid increase of COtd associated with a proportional increase in COm, COLi, MAP, PP and SP (Table 2). Furthermore, we found significant relationships between the change in COtd and the change in COm, COLi, MAP, PP and SP. Our PP results confirm and extend the results of Boulain *et al.* and support their conclusion that PLR induced changes in PP predict the response to fluid loading [1]. Our results also support the hypothesis of DeBacker and Pinsky that changes in pulse contour derived cardiac output due to PLR can be used to assess preload in cardiothoracic surgery patients [8]. Changes in COm tend to a slightly better predictive value than changes in MAP and COLi, or baseline SVV and PPV, these differences are not statistically significant.

Our findings concur with data previously reported by de Wilde *et al.* [10], who showed that Modelflow pulse contour has lower limits of agreement and a better correlation coefficient for the regression of changes in CO with changes in thermodilution CO compared to the LiDCO's technique. Furthermore, in another report de Wilde *et al.* [15] showed superior results of uncalibrated Modelflow compared to auto-calibrated FloTrac-Vigileo and HemoSonic in tracking changes in cardiac output.

190) Continuous measurements of COm are more feasible than oesophageal Doppler CO and left ventricular stroke area since these methods are not routinely performed and the quality of measurement is dependant on the expertise of the observer. Also passive raising of the legs may interfere with the echocardiographic image.

To compare the effects of PLR on MAP, PP, SP, COm, COLi and baseline SVVm, SVVli and PPV we separated responders from non-responders by setting the cut-off level for COtd change to 7%, considering the described effect of PLR from supine position [3] and the precision of our thermodilution method. Next, the reliability to predict preload dependency by changes in COm, COLi, MAP, PP, SP due to PLR and baseline SVV and PPV was evaluated by calculating the area under the ROC curves. No statistical differences between the the AUC of the ROC curves for COm, COLi, PPV and SVV were found. This uniformity might be explained by the fact that all predictors have the same radial arterial pressure source. However, the COm and COLi techniques use different algorithms, therefore, some of the agreement must reflect similar accuracy of the two techniques.

In a large two-center study Monnet and co-authors [2] included 71 general ICU patients of which 31 had spontaneous breathing activity and/or arrhythmias. In the group of ventilator dependent patients they showed, by using the HemoSonic ultrasound system, that a PLR induced increase of aortic blood flow $\geq 10\%$ predicted the effect of a 500 ml fluid load responsiveness with a 97% sensitivity and 94% specificity. Whereas a PLR induced increase in PP $\geq 12\%$ had a 60% sensitivity and 85% specificity. In the patients with spontaneous

breathing activity the sensitivity and specificity were 88% and 93% for the aortic blood flow and as poor as 75% and 46% for PP. Other studies [3,5,6] confirmed that PLR predicts fluid responsiveness. Essential to the use of the PLR procedure to assess preload responsiveness is the need of a fast responding cardiac output method during the manoeuvre (Figure 1). The studies mentioned above used Doppler ultrasound techniques, however, these techniques may not be routinely performed or widely available. In addition, the quality of measurement is dependant on the expertise of the observer. Our results with beat-to-beat pulse contour cardiac output in patients after cardiac surgery agree with the results of Monnet *et al.* obtained with HemoSonic Doppler aortic blood flow (ABF) [2]. Therefore, measurement of pulse contour CO seems interchangeable with ultrasound ABF and may supplant it as was hypothesized by DeBacker and Pinsky [8].

We showed that various hemodynamic changes in response to PLR, such as COLi, PP, MAP, COm can predict a positive CO response to PLR. The response to PLR can probably, in most circumstances, be used as a surrogate for response to fluid loading, because of its high sensitivity and specificity. We expected PLR to mimic a reversible fluid loading of approximately 250-300 ml. However, it is unsure whether the volemic status of a patient will change the volume of autotransfusion by PLR. We did not follow our initial measures with volume challenges because all the patients were deemed to be haemodynamically stable, and thus not needed further fluid resuscitation. (191

Our study confirms that baseline SVV and change in COm and COLi by PLR can be used to predict preload dependence in patients receiving mechanical ventilation. Since COm and COLi can also be measured in normal breathing patients, we expect that COm and COLi are more appropriate candidates to predict preload dependence during PLR in these patients. However, further study is needed into the reliability in spontaneous breathing patients. Differences exist in the implementation of the PLR procedure between studies [2,3,6]. These differences could interfere with a direct comparison of our results with beat-to-beat pulse contour and Doppler ultrasound cardiac output measurements. In our study, patients remain in a supine position throughout the protocol and only the legs are raised. The heart and baroreceptors are in-level and do not change, thus, blood pressure transducers do not have to be re-referenced resulting in a constant quality for pulse contour cardiac measurement. In half of the Doppler ultrasound studies [2,5,6], the patient moved from a semi-recumbent position (45°) to a position with the lower limbs raised to 45° while the patient's trunk was lowered to supine position. This approach was probably chosen to keep the ultrasound probe in position but it changes the position of the baroreceptors in relation to the heart. Since heart rate was unchanged, this change in position may be considered as unimportant. Although, these differences may influence the comparability between studies we did not observed large differences.

Conclusions

In stable CABG patients under mechanical ventilation after cardiac surgery a correlation was observed between changes in method of the arterial pulse contour and thermodilution techniques. Preload reserve or responsiveness could therefore be determined. Further studies are necessary to determine the usefulness of these techniques in situations of shock or hemodynamic instability.

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