Resuscitation 82 (2011) 423–426

Contents lists available at ScienceDirect

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

Clinical paper

Comparison of non-calibrated pulse-contour analysis with continuous thermodilution for cardiac output assessment in patients with induced hypothermia after cardiac arrest☆

Matthias Haenggi[a,*], Daniel Barthelmes[a], Hanno Ulmer[b], Jukka Takala[a], Stephan M. Jakob[a]

[a] Department of Intensive Care Medicine, Bern University Hospital and University of Bern, Inselspital, Freiburgstrasse, 3010 Bern, Switzerland
[b] Department of Medical Statistics, Informatics and Health Economics, Innsbruck Medical University, Schoepfstrasse 41/1, 6020 Innsbruck, Austria

ARTICLE INFO

Article history:
Received 24 August 2010
Received in revised form
26 November 2010
Accepted 7 December 2010

Keywords:
Cardiac arrest
Hypothermia
Pulse contour analysis
Cardiac output measurement
Resuscitation

ABSTRACT

Aim: Induced mild hypothermia after cardiac arrest interferes with clinical assessment of the cardiovascular status of patients. In this situation, non-invasive cardiac output measurement could be useful. Unfortunately, arterial pulse contour is altered by temperature, and the performance of devices using arterial blood pressure contour analysis to derive cardiac output may be insufficient.
Methods: Mild hypothermia (32–34 °C) was induced in eight patients after out-of-hospital cardiac arrest and successful resuscitation. Cardiac output (CO) was measured simultaneously by continuous thermodilution using a pulmonary artery catheter and a cardiac output monitor (Vigilance II, Edwards Lifesciences) and by pulse contour analysis using an arterial line and the Vigileo monitor (Edwards Lifesciences) during both normothermia (>36 °C) and hypothermia. Continuous CO from both monitors was compared (Bland–Altman) and concordance of changes measured in consecutive 8-min intervals was measured.
Results: Mean cardiac output was 3.9 ± 1.2 l/min during hypothermia and 6.1 ± 2.6 l/min during normothermia ($p < 0.001$). During hypothermia (normothermia), bias was 0.23 (0.77) l/min, precision (1 SD) was 0.6 (0.72) l/min, and the limits of agreement were −1.06 to 1.51 (−0.64 to 2.18) l/min, corresponding to a percentage error of ±34% (±24%). Concordance of directional CO changes >10% was 53.9% in hypothermia and 51.4% in normothermia.
Conclusion: Induced hypothermia was not associated with increased bias or limits of agreement for the comparison of Vigileo and continuous thermodilution, but percentage error was high during normothermia and increased further during hypothermia. Less than 50% of clinically relevant CO changes during hypothermia were concordant.

1. Introduction

Induced mild hypothermia is now regarded as standard therapy in patients resuscitated from out-of-hospital cardiac arrest, and is recommended in comatose patients suffering from in-hospital cardiac arrest [1]. In these patients, adequate tissue oxygen delivery is crucial. However, when hypothermia is applied, clinical signs of hypoperfusion such as cold, clammy skin and delayed capillary refill are not reliable.

Pulse contour analysis for cardiac output estimation is a rapidly evolving technology, mainly due to its ease of use and the relative non-invasiveness of the method [2]. The basic principle of cardiac output (CO) measurement by pulse contour analysis is the proportional relationship of stroke volume and arterial pulsatility [3]. The differences between the various devices available are mainly related to different calibration methods. The latest development is non-calibrating devices that use nomograms based on age, weight/height and gender [4].

During hypothermia, vasoconstriction alters pulse contour [5]. Measurements of cardiac output with pulse contour might be inaccurate in this situation, but studies are lacking. In a literature search, only a case report was retrieved, in which calibration failure in a PiCCO device was reported [6].

The aim of this study was to describe the performance of a device using pulse contour analysis without calibration during hypothermia and to compare it with conventional thermodilution. We hypothesized that differences between spontaneous changes in cardiac output measured by thermodilution and pulse contour analysis increase during hypothermia.

☆ A Spanish translated version of the abstract of this article appears as an Appendix in the final online version at doi:10.1016/j.resuscitation.2010.12.015.

* Corresponding author. Tel.: +41 31 632 3029; fax: +41 31 632 9644.
E-mail addresses: matthias.haenggi@insel.ch (M. Haenggi), daniel.barthelmes@gmx.ch (D. Barthelmes), hanno.ulmer@i-med.ac.at (H. Ulmer), jukka.takala@insel.ch (J. Takala), stephan.jakob@insel.ch (S.M. Jakob).

0300-9572/$ – see front matter © 2011 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.resuscitation.2010.12.015

2. Methods

Patients were included after successful resuscitation from out-of-hospital cardiac arrest if they were assigned to induced therapeutic hypothermia by the attending intensivist, and if they had a pulmonary artery catheter in place, as judged necessary by the attending intensivist and cardiologist. Exclusion criteria were either (1) presence of an intraarterial balloon pump or (2) unstable hemodynamics despite fluid resuscitation and use of vasoactive drugs, with expected death within the next 24 h.

The institutional hypothermia protocol comprised start of hypothermia in the ambulance, and hypothermia was maintained at 33 °C for 12 h. Afterwards, controlled rewarming was started at a rate of 0.5 °C/h. All patients received continuous infusion of sedatives (propofol or midzolam) and opioids (fentanyl), targeted to a BIS Index of 40–60, and atracurium to prevent shivering during hypothermia and rewarming. After normothermia was reached, the sedation and atracurium were discontinued and a neurologic assessment was performed.

The need for informed consent was waived by the local ethics committee due to the observational character of the study: the pulse contour analysis device we used (Vigileo® /Flow-Trac®; software version 1.07; Edwards Lifesciences, Saint-Prex, Switzerland) does not require the placement of additional catheters, and the bedside team assigned to the patient was blinded to the variables measured by the device (cardiac output and stroke volume variability [SVV]). Continuous cardiac output (CCO) was measured by a pulmonary artery catheter and displayed by a Vigilance II® monitor (Edwards Lifesciences, Saint-Prex, Switzerland), as is routine practice in this intensive care unit (ICU). Vigileo® and Vigilance II® monitors were connected via the RS-232 interface to a laptop, where a custom-made data logger simultaneously stored cardiac output measurements from both devices as displayed on the monitor screens. Measurements were started after the patient arrived in the ICU and standard monitoring and resuscitation measures were successfully installed. For analysis, two sets of data from each patient were used: hypothermia period (recorded at a temperature between 33 °C and 34 °C) and normothermia period (after rewarming, at 36–38 °C). The two data sets had the same length of recording. The CCO obtained by the Vigilance II has a response time to changes in the cardiac output of 7–10 min [7,8]. Thus the recorded data were reduced offline to means of 8-min intervals and the Vigileo II data were shifted 8 min behind the ones recorded with the Vigileo device, using IGOR Pro 6.03 (WaveMetrics Inc., Lake Oswego, OR, USA). Data were analyzed and reported with the methods proposed by Bland and Altman (with correction for repeated measurements, as the original report compared only one dataset per person, and thus changes in the variance within the repeated measurements have to be accounted for) [9–11] and by Critchley and Critchley [12]. Accordingly, mean cardiac output was defined as the mean of simultaneously recorded cardiac output measurements by the two devices (corrected for the delay of the response time of 8 min), bias as the difference between the measurements obtained by the two devices, precision as one standard deviation (SD) of bias, limits of agreement as bias ±1.96 SD, and percentage error as ±2 SD divided by mean cardiac output. Standard parametric tests for comparisons of mean and proportions were used as appropriate with PASW Statistics 18 (SPSS Inc., Chicago, IL, USA). Significance was considered with a two-sided $p < 0.05$.

Magnitude and directions of blood flow changes between two consecutive intervals were compared between the devices. Because small changes will occur at random, with a high number of data the mean change of both CO measures will be zero. We therefore defined a clinically relevant difference between two consecutive measurements in blood flow arbitrarily as 10%.

3. Results

The eight patients included in the study had a median age of 68 years (range 54–85 years). Half of the patients survived to hospital discharge with intact neurological functions. Demographic data of the patients are presented in Table 1. Measurement recording lasted between 5.75 h and 12.5 h per patient per period, corresponding to 790 8-min intervals for comparison (see Fig. 1). Mean cardiac output was 3.9 ± 1.2 l/min during hypothermia and 6.1 ± 2.6 l/min during normothermia ($p < 0.001$). During hypothermia, bias was 0.23 l/min, precision 0.66 l/min, and the limits of agreement were −1.06 to 1.51 l/min. During normothermia, bias was 0.77 l/min, precision 0.72 l/min, and limits of agreement were −0.64 to 2.18 l/min (Fig. 1). The percentage error was 34% during hypothermia and 24% during normothermia.

Changes between two consecutive means of 8-min recordings went in opposite directions in 49.5% of epochs during hypothermia and in 50% of normothermia epochs (n.s.). Changes with a magnitude of >10% occurred 76 times during hypothermia (19.5%) and 72 times during normothermia (18.5%, n.s.). Discordant direction of changes >10% occurred in 41 of 76 episodes (53.9%, 10.5% of all episodes) during hypothermia and in 37 of 72 episodes (51.4%, 9.5% of all episodes) during normothermia (n.s.) (Fig. 2).

4. Discussion

Induced hypothermia after cardiac arrest increased neither bias nor precision for the comparison between continuous thermodilution and pulse contour analysis without calibration. Nevertheless, because of the higher mean cardiac output in patients in the normothermia period, the percentage error increased during hypothermia, and exceeded the proposed acceptable limit of ±30% [12]. As expected, opposite short-term trends of CO were evenly distributed, but clinically relevant large changes of CO occurred rarely. Unfortunately, if large alterations occurred, the Vigileo device often could not track that change.

The bias and precision obtained in our study are in line with published comparisons between the same methods in normothermic patients [13–17]. Despite different characteristics of pulse pressure contour during normothermia and hypothermia, the algorithm in the tested device performed equally well under the two conditions. The basic principle of CO measurement by pulse contour analysis is the proportionality of stroke volume and arterial pulsatility. Thus, with alterations of the pulse contour, induced, for example, by changes in the vascular tone, intravascular volume, aortic valve alteration, or introduction of an intra-aortic balloon pump, the proportionality factor has to be recalibrated, or in the case of the Vigileo, recalculated. The proportionality constant of the Vigileo device is calculated on the basis of patient weight, height, age, mean arterial pressure, skewness, and kurtosis, but the exact calculation method is proprietary information.[3] CO data obtained with the Vigileo device are less reliable in situations with altered pulse contour waveforms—for example, as induced by vasoconstriction [18–22]. High flow/low resistance states as in septic shock [18] or liver failure [19] seem to be particularly difficult for the Vigileo system to handle. CO is regularly underestimated in these situations, and the sloping relationship between increasing bias at higher CO demonstrated by Biancofiore et al. [19] can also be seen here, especially in the normothermia group (Fig. 1). The systemic inflammatory response syndrome (SIRS) following global ischemia-reperfusion, as in out-of-hospital cardiac arrest (OHCA), seems to be well counterbalanced by the increase of systemic vascular resistance through hypothermia, as

Table 1
Demographic and basic data of the patients.

Pat #	Sex	Age (y)	Outcome	SAPS	LOS ICU (h)	LOS hosp (h)	Time to target (h)	Treatment in cath lab prior to ICU	Dobutamine	Niprusside
1	m	57	Survived	55	70.5	1092	14	PTCA/stent	h	n
2	m	53	Died	39	73.5	80	7.25	–	h	h/n
3	m	68	Died	68	90	95	2.5	PTCA /stent	h/n	–
4	f	78	Survived	68	60.25	924	8.75	–	–	h/n
5	m	65	Survived	66	34.5	152	7.75	PTCA /stent	–	h/n
6	f	84	Died	83	50	52	4.25	PTCA /stent	h/n	–
7	m	82	Survived	68	138.5	354	10.5	PTCA /stent	h	h/n
8	m	57	Died	79	100.5	102	2.5	–	–	h/n

h = hypothermia; n = normothermia; SAPS = Simplified Acute Physiology Score; LOS = length of stay; ICU = intensive care unit; PTCA = percutaneous transluminal coronary angioplasty.

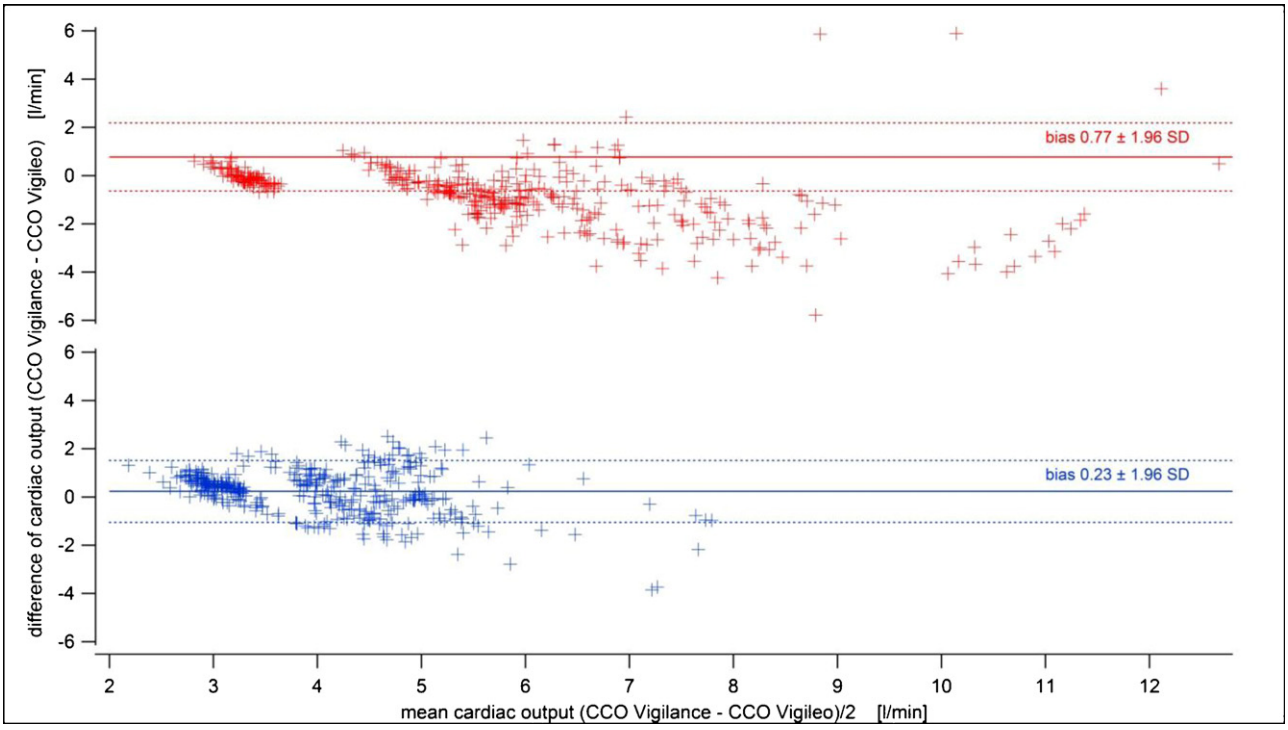

Fig. 1. Bland–Altman plot of cardiac output. The upper part represents data during normothermia, the lower part during hypothermia. All 790 data pairs are shown (43–97 per patient). Bias and limits of agreement (±1.96 SD) do not differ between normothermic and hypothermic conditions.

none of our patients needed a vasopressive drug; on the contrary, some patients received the vasodilator niprusside (Table 1). We hypothesized that differences between spontaneous changes in cardiac output measured by thermodilution and pulse contour analysis increase during hypothermia. With our results, we could not confirm this hypothesis; rather, we demonstrated that the calculated proportionality factor integrates the different waveforms of the pulse curve seen in hypothermic and normothermic patients.

Using continuous instead of intermittent thermodilution cardiac output measurement as a gold standard could be criticized. Continuous thermodilution was chosen since this is the routine method in our unit and because it enables comparison of cardiac output trends over time between the two methods. This would not have been possible with intermittent thermodilution. The bias and precision in this comparison are in the same range as those found in the comparisons of CO derived by intermittent and continuous thermodilution [23,24], and are even better than in comparisons of CO using esophageal Doppler vs. intermittent thermodilution [25] or PiCCO [18,26]. Also, it should be acknowledged that the correlation between intermittent and continuous thermodilution is strong over a broad temperature range [23,27].

In our opinion, more problematic is the interpretation of the values, especially which limits are considered as clinically acceptable. According to the literature, the percentage error of a new comparator should be below ±30% [12], so our data demonstrate that the performance of the new device in patients with induced hypothermia is worse than in normothermic patients. Another issue is whether it is important to know the absolute value of cardiac output or whether the trends are more informative. Here our data show that CO trends measured with uncalibrated pulse contour analysis often reflect values obtained with the thermodilution method, but, far more importantly, the device failed to track clinically important changes in CO in hypothermic patients in 50% of the cases. This is not significantly worse than in normothermic patients, as long as the low incidence of large changes of CO and the resulting insufficient power to detect a difference are taken in account. We cannot recommend the use of the Vigileo with the tested software in the specific clinical circumstance of patients successfully resuscitated from cardiac arrest and treated with therapeutic hypothermia. Our findings should not be extrapolated to other clinical situations in which non-calibrating pulse-contour analysis is considered useful, as in patients undergoing coronary artery bypass surgery [17], trauma surgery [4] or liver transplantation [14].

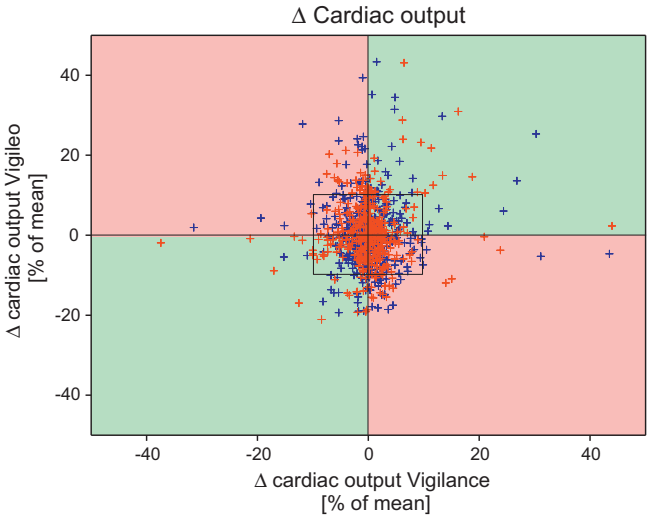

Fig. 2. Percentage changes in cardiac output between consecutive 8-min epochs. The *x*-axis represents data derived from continuous thermodilution, the *y*-axis data derived from pulse-contour analysis during the same period. Data points in green rectangles represent trends in the same direction (concordant trends), data points in red rectangles those in the opposite direction (discordant trends). The small rectangle in the center of the figure separates changes >10% from trends <10%. Blue data points: values obtained during hypothermia. Red data points: values obtained during normothermia.

5. Conclusion

Induced hypothermia after cardiac arrest does not affect bias or precision, but it does affect percentage error at a magnitude which is clinically relevant for the comparison between uncalibrated pulse contour analysis using Flowtrac/Vigileo and continuous thermodilution cardiac output measurement. Under both hypothermia and normothermia, small discordant changes in cardiac output measured by the two methods were frequent, and in the occurrences of clinically important changes of cardiac output, Vigileo/Flowtrac could not track the change in more than 50% of the cases. Based on our findings in a small study population, we cannot recommend the use of this device in patients with induced hypothermia. Whether this remains true for other pulse-contour-based CO monitors has to be shown.

Conflicts of interest

MH, DB, JT and SJ: The Department of Intensive Care Medicine has received research funding from Edwards Lifesciences to carry out research projects related to cardiovascular monitoring. This study was not influenced by Edwards Lifesciences. Edwards Lifesciences was not involved in any way in collection, analysis or interpretation of data, in writing of the manuscript, or in the decision to submit this manuscript. HU declares that he has no competing interests.

Acknowledgements

The authors would like to thank the nurses in the ICU for their patience and invaluable help. We also thank Jeannie Wurz (Department of Intensive Care Medicine, Bern University Hospital) for editorial assistance.

References

[1]. ECC Committee SaTFotAHA. American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation 2005;112:1–203.
[2]. Morgan P, Al-Subaie N, Rhodes A. Minimally invasive cardiac output monitoring. Curr Opin Crit Care 2008;14:322–6.
[3]. Manecke Jr GR. Cardiac output from the arterial catheter: deceptively simple. J Cardiothorac Vasc Anesth 2007;21:629–31.
[4]. Manecke GR. Edwards FloTrac sensor and Vigileo monitor: easy, accurate, reliable cardiac output assessment using the arterial pulse wave. Expert Rev Med Dev 2005;2:523–7.
[5]. Edwards DG, Gauthier AL, Hayman MA, Lang JT, Kenefick RW. Acute effects of cold exposure on central aortic wave reflection. J Appl Physiol 2006;100:1210–4.
[6]. Ong T, Gillies MA, Bellomo R. Failure of continuous cardiac output measurement using the PiCCO Device during induced hypothermia: a case report. Crit Care Resus 2004;6:99–101.
[7]. Nakamura R, Izumi H, Shioyama K, Koga T, Shigeoka H, Akiyama R. In vitro response time of continuous cardiac output measurement in STAT mode of Vigilance after controlled flow change. Masui 2006;55:630–4.
[8]. Siegel LC, Hennessy MM, Pearl RG. Delayed time response of the continuous cardiac output pulmonary artery catheter. Anesth Analg 1996;83:1173–7.
[9]. Mantha S, Roizen MF, Fleisher LA, Thisted R, Foss J. Comparing methods of clinical measurement: reporting standards for Bland and Altman analysis. Anesth Analg 2000;90:593–602.
[10]. Myles PS, Cui J. Using the Bland–Altman method to measure agreement with repeated measures. Br J Anaesth 2007;99:309–11.
[11]. Bland JM, Altman DG. Measuring agreement in method comparison studies. Stat Methods Med Res 1999;8:135–60.
[12]. Critchley LA, Critchley JA. A meta-analysis of studies using bias and precision statistics to compare cardiac output measurement techniques. J Clin Monit Comput 1999;15:85–91.
[13]. Breukers RM, Sepehrkhouy S, Spiegelenberg SR, Groeneveld AB. Cardiac output measured by a new arterial pressure waveform analysis method without calibration compared with thermodilution after cardiac surgery. J Cardiothorac Vasc Anesth 2007;21:632–5.
[14]. Biais M, Nouette-Gaulain K, Cottenceau V, et al. Cardiac output measurement in patients undergoing liver transplantation: pulmonary artery catheter versus uncalibrated arterial pressure waveform analysis. Anesth Analg 2008;106, 1480-6, table.
[15]. Mayer J, Boldt J, Schollhorn T, Rohm KD, Mengistu AM, Suttner S. Semi-invasive monitoring of cardiac output by a new device using arterial pressure waveform analysis: a comparison with intermittent pulmonary artery thermodilution in patients undergoing cardiac surgery. Br J Anaesth 2007;98:176–82.
[16]. McGee WT, Horswell JL, Calderon J, et al. Validation of a continuous, arterial pressure-based cardiac output measurement: a multicenter, prospective clinical trial. Crit Care 2007;11:R105.
[17]. de Waal EE, Kalkman CJ, Rex S, Buhre WF. Validation of a new arterial pulse contour-based cardiac output device. Crit Care Med 2007;35:1904–9.
[18]. Sakka SG, Kozieras J, Thuemer O, van Hout N. Measurement of cardiac output: a comparison between transpulmonary thermodilution and uncalibrated pulse contour analysis. Br J Anaesth 2007;99:337–42.
[19]. Biancofiore G, Critchley LA, Lee A, et al. Evaluation of an uncalibrated arterial pulse contour cardiac output monitoring system in cirrhotic patients undergoing liver surgery. Br J Anaesth 2009;102:47–54.
[20]. Lorsomradee S, Lorsomradee S, Cromheecke S, De Hert SG. Uncalibrated arterial pulse contour analysis versus continuous thermodilution technique: effects of alterations in arterial waveform. J Cardiothorac Vasc Anesth 2007;21:636–43.
[21]. Bein B, Meybohm P, Cavus E, et al. The reliability of pulse contour-derived cardiac output during hemorrhage and after vasopressor administration. Anesth Analg 2007;105:107–13.
[22]. Johansson A, Chew M. Reliability of continuous pulse contour cardiac output measurement during hemodynamic instability. J Clin Monit Comput 2007;21:237–42.
[23]. Bottiger BW, Soder M, Rauch H, et al. Semi-continuous versus injectate cardiac output measurement in intensive care patients after cardiac surgery. Intensive Care Med 1996;22:312–8.
[24]. Boldt J, Menges T, Wollbruck M, Hammermann H, Hempelmann G. Is continuous cardiac output measurement using thermodilution reliable in the critically ill patient? Crit Care Med 1994;22:1913–8.
[25]. Dark PM, Singer M. The validity of trans-esophageal Doppler ultrasonography as a measure of cardiac output in critically ill adults. Intensive Care Med 2004;30:2060–6.
[26]. Compton FD, Zukunft B, Hoffmann C, Zidek W, Schaefer JH. Performance of a minimally invasive uncalibrated cardiac output monitoring system (Flotrac/Vigileo) in haemodynamically unstable patients. Br J Anaesth 2008;100:451–6.
[27]. Sun Q, Rogiers P, Pauwels D, Vincent JL. Comparison of continuous thermodilution and bolus cardiac output measurements in septic shock. Intensive Care Med 2002;28:1276–80.