CONSTANT CARDIAC OUTPUT MONITORING USING THE PiCCO AND LiDCO METHODS VERSUS PAK IN SEPTIC PATIENTS: WHEN TO DO CALIBRATION?

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SUMMARY – The accuracy of cardiac output measurement by two most widely used methods of less invasive hemodynamic monitoring and by the standard technique of thermodilution with pulmonary catheter was assessed. The measurements were carried out in septic surgical patients immediately after and between system calibrations. Study results showed satisfactory compatibility of measurements performed by the two methods and by pulmonary catheter in both phases, thus system calibration being recommendable in hemodynamically unstable septic patients.

Key words: *Cardiac output – physiology; Monitoring, physiologic – methods; Sepsis; Intensive care units*

Introduction

Comparative cardiac output measurements by the standard Pulmonary Artery Cardiac Output (PAK-CO) technique using pulmonary catheter for continuous cardiac output monitoring and two novel real-time methods, Pulse Contour Cardiac Output (PiCCO) and Lithium Diluted Cardiac Output (LiDCO), were performed to assess compatibility of measurements in septic patients. In addition, we compared the level of compatibility immediately after and between continuous method calibrations, and assessed the need of calibration. Target use of the novel methods, and in some cases substitution of hemodynamic monitoring by use of pulmonary catheter with less invasive continuous methods appear to be justified by the less invasiveness of these methods and thus the lower rate of complications. LiDCO and PiCCO are less invasive methods of hemodynamic monitoring based on cardiac output calculation according to the area under arterial curve, i.e. pulse contour methods. Both methods are calibrated with previous dilution (LiDCO) and thermodilution (PiCCO) technique[1-3]. Upon calibration, Pulse CO software calculates cardiac output *per* pulse[4].

Methods

A total of 269 comparative cardiac output measurements using PAK and PiCCO, 203 consecutive measurements with PAK and LiDCO with 18 comparative measurements in the phase of PiCCO system calibration, and 21 measurements in the phase of LiDCO system calibration were performed in 11 septic patients aged 43-59 without previous history of cardiovascular disease indicators. Continuous measurements were done in the patient hemodynamically stable stage, and at the time of PiCCO system and LiDCO system calibration. Patients belonged to the group of surgical patients with severe sepsis defined

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according to the Sepsis Surviving Campaign (SSC), showing signs of the septic inflammatory response syndrome (SIRS) with organ failure and microbiologically proved sepsis. Disease severity was estimated by the Sepsis Organ Failure Assessment (SOFA) and Acute Physiology And Chronic Health Evaluation II (APACHE II) scores. The mean SOFA score was 11 and the mean APACHE II score 24.

Cardiac output was determined by use of the PiCCO plus-Pulsion technology (Pulsion, Germany) with Pulsion catheter Ø 1.7 mm, length 20 cm, inserted in femoral artery. System calibration was done with 15 mL saline, temperature <7 °C, administered *via* central venous catheter placed in internal jugular vein. The measurement was repeated five times and the mean value was taken for calibration[5].

In the LiDCO method, the LiDCO Cardiac Sensor System with lithium electrode attached on radial artery was employed. Calibration was done by single administration of 0.3 mmol lithium chloride and washing with 20 mL saline[6,7]. Continuous output monitoring by Q-vue PAK and Abbott Q-vue monitor served as reference monitoring. The Q-vue PAK 7.5 Fr was placed in pulmonary artery and its location corrected by radiological and clinical testing. In both cases, the PiCCO and LiDCO systems were analog plugged on the Dräger Infinity basic monitor for invasive pressure monitoring.

Measurement results and numerical data were compared and processed by the Bland Altman method using the MedCalc software and by descriptive statistics including Wilcoxon method of ranked pairs using the Statistica 6 software[8].

Results

Upon statistical processing, measurement data were classified in Tables 1-4, reporting descriptive statistics of the data obtained on cardiac output measurement by use of the PAK-CO, PiCCO and LiDCO methods. Each table is followed by statistical analysis of the respective data (measurement) by Wilcoxon pair test and Bland Altman diagram of comparison of two methods.

Table 1 shows results of statistical analysis of 269 pairs of cardiac output measurement by the PAK and PiCCO methods.

Bland Altman analysis, used for comparison of measurement compatibility between the two methods, is shown in Figure 1.

Table 2 shows descriptive statistics of measurements by the same methods immediately after PiCCO system calibration.

Figure 2 shows Bland Altman statistical analysis for pairs of PAK-CO and PiCCO measurements.

In the next step, measurements done with lithium dilution method by calibration pulse contour technique and PAK-CO by the reference technique of pulmonary catheter measurement in the phase of calibration and between calibrations were compared.

Table 1. Pairs of cardiac output measurement by PAK-CO and PiCCO

Number of pairs 269	Maximal value	Minimal value	Arithmetic mean	Median	Standard deviation	Standard error of arithmetic mean
PAK-CO (L/min/m^2)	6.80	3.10	4.35	4.30	0.65	0.04
PiCCO (L/min/m^2)	6.12	2.2o	3.73	3.57	0.64	0.03

Statistical analysis of the pairs of measurement by Wilcoxon pair test:
PAK-CO and PiCCO
Variable: PAK-CO
Sample size = 269
Lowest value = 3.1000
Highest value = 6.8000
Median = 4.3000
95% CI for median = 4.1000 to 4.4000

Variable: PiCCO
Sample size = 269
Lowest value = 2.2000
Highest value = 6.1200
Median = 3.5700
95% CI for median = 3.4900 to 3.6500

Wilcoxon test (paired samples)
Number of positive differences = 50
Number of negative differences = 217
Large sample test statistics Z = 10.102348
Two-tailed probability P<0.0001

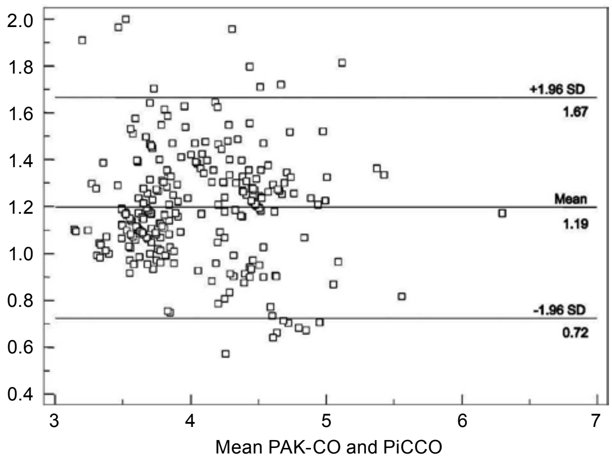

Fig. 1. Comparative measurement PAK-CO vs. PiCCO.

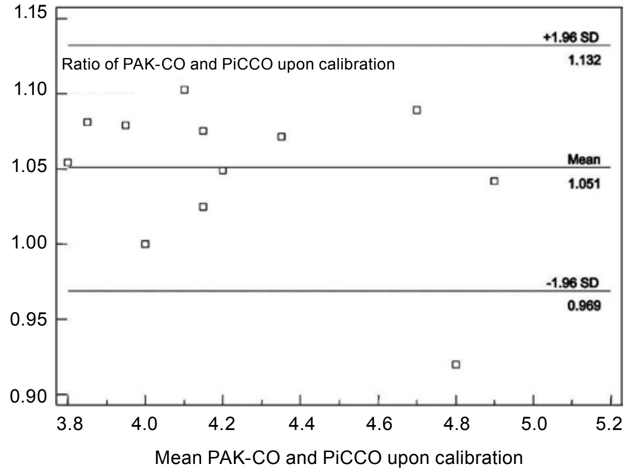

Fig. 2. PAK-O vs. PiCCO upon calibration.

Table 3 shows descriptive statistics for 203 pairs of simultaneous PAK-CO and LiDCO measurements.

Figure 3 shows statistical analysis of measurements by Bland Altman method.

Table 4 shows numerical results obtained by descriptive statistics for pairs of cardiac output measurements upon LiDCO system calibration with lithium chloride in comparison with measurements done by PAK.

Figure 4 shows Bland Altman statistical analysis of pairs of cardiac output measurements by PAK-CO and LiDCO immediately upon calibration.

Accordingly, Bland Altman statistical analysis of the results obtained on cardiac output measurement by PAK and by the new methods of PiCCO and LiDCO yielded good compatibility between the two study methods and PAK in all phases of measurement, upon calibration and between calibrations. A low, clinically acceptable limit of compatibility was recorded between the two methods and PAK. Graphic presentation shows that the results of measurement obtained by different methods compared according to deviation from the mean (±1.96 SD) were grouped, falling in-between the limits, thus indicating good

Table 2. Pairs of PAK-CO and PiCCO measurements immediately after PiCCO system calibration

Number of pairs 18	Maximal value	Minimal value	Arithmetic mean	Median	Standard deviation	Standard error of arithmetic mean
PAK-CO (L/min/m^2)	5.00	3.90	4.31	4.30	0.35	0.08
PiCCO calibration (L/min/m^2)	5.00	3.70	4.11	4.00	0.40	0.09

Statistical analysis of pairs of measurements by Wilcoxon test: PAK-CO and PiCCO immediately upon calibration
Variable: PAK-CO
Sample size = 18
Lowest value = 3.9000
Highest value = 5.0000
Median = 4.3000
95% CI for median = 4.0000 to 4.5309

Variable: PiCCO immediately upon calibration
Sample size = 18
Lowest value = 3.7000
Highest value = 5.0000
Median = 4.0000
95% CI for median = 3.7691 to 4.2926

Wilcoxon test (paired samples)
Number of positive differences = 1
Number of negative differences = 16
Smaller total of ranks = 16.50
Two-tailed probability *P*=0.0026

Table 3. Pairs of cardiac output PAK-CO and LiDCO measurements

Number of pairs 203	Maximal value	Minimal value	Arithmetic mean	Median	Standard deviation	Standard error of arithmetic mean
PAK-CO (L/min)	9.60	6.50	8.06	8.00	0.54	0.03
LiDCO (L/min)	9.20	6.20	7.81	7.80	0.59	0.04

Statistical analysis of the pairs of measurements by Wilcoxon test: PAK-CO and LiDCO
Variable: PAK-CO
Sample size = 203
Lowest value = 6.5000
Highest value = 9.6000
Median = 8.0000
95% CI for median = 7.9000 to 8.0000

Variable: LiDCO-CO
Sample size = 203
Lowest value = 6.2000
Highest value = 9.2000
Median = 7.8000
95% CI for median = 7.7000 to 7.8000

Wilcoxon test (paired samples)
Number of positive differences = 40
Number of negative differences = 158
Large sample test statistics Z = 8.478611
Two-tailed probability $P<0.0001$

compatibility of the methods compared. Based on the Wilcoxon rank method and pair comparison, PAK to LiDCO comparison yielded better compatibility of results immediately upon calibration, whereas PAK to PiCCO comparison showed better result compatibility between calibrations ($P<0.001$ both).

Discussion

Cardiovascular instability is a common cause of morbidity and mortality in critically ill patients. Appropriate choice of therapy requires thorough understanding of the pathophysiological impairments, which can frequently be revealed by use of advanced

Table 4. Pairs of cardiac output measurements by PAK-CO and LiDCO immediately upon calibration

Number of pairs 21	Maximal value	Minimal value	Arithmetic mean	Median	Standard deviation	Standard error of arithmetic mean
PAK CO (L/min)	9.0	6.50	8.03	8.10	0.53	0.11
LiDCO calibration (L/min)	8.80	6.80	7.89	7.90	0.45	0.09

Statistical analysis of the pairs of measurement by Wilcoxon test: PAK-CO and LiDCO immediately upon calibration
Variable: PAK-CO
Sample size = 21
Lowest value = 6.5000
Highest value = 9.0000
Median = 8.1000
95% CI for median = 7.9000 to 8.3000

Variable: LiDCO_upon calibration
Sample size = 21
Lowest value = 6.8000
Highest value = 8.8000
Median = 7.9000
95% CI for median = 7.8000 to 8.0171

Wilcoxon test (paired samples)
Number of positive differences = 2
Number of negative differences = 17
Smaller total of ranks = 17.50
Two-tailed probability $P=0.0008$

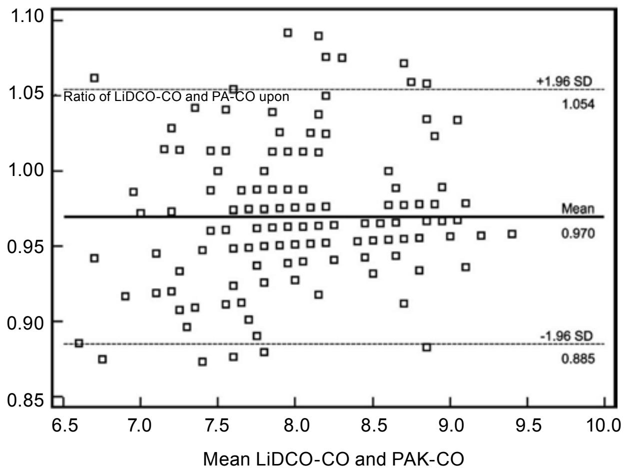

Fig. 3. PAK-CO vs LiDCO.

hemodynamic monitoring. The methods applied cannot influence the outcome, but do represent a tool for active intervention, depending on the data collected. With this in mind, we tried to compare cardiac output measurement by use of the two novel pulse contour methods, PiCCO and LiDCO, with the reference PAK-CO method as a gold standard, immediately upon calibration and between calibrations.

The results obtained were consistent with literature reports comparing the two methods (PiCCO and LiDCO) with standard measurement by the PAK thermodilution method[9-11]. However, there are not many studies comparing these methods in septic patients. In comparison with PAK, both methods showed good compatibility in the results of cardiac output measurement immediately upon calibration and between calibrations. A recent consensus conference on the efficacy and utility of the new generation of less invasive hemodynamic monitoring in critically ill patients pointed to the paucity of data and studies in the field[12]. Most validation studies of pulse contour methods were conducted in patients undergoing cardiac surgery, whereas data on septic patients are rather insufficient[13,14]. Therefore, our study included septic patients having undergone non-cardiac surgery and free from any history of cardiac disease, thus eliminating the impact of cardiac disease on measurement results. Good compatibility and the trend of cardiac output hemodynamic measurement by the study methods enables a simpler and less invasive approach as well as faster acquisition of data, along with a lower risk of complications for the patient. Although thermodilution measurement by pulmonary catheter remains the gold standard of hemodynamic monitoring, these new methods, even though inadequately evaluated as yet, have gradually taken their place in daily routine.

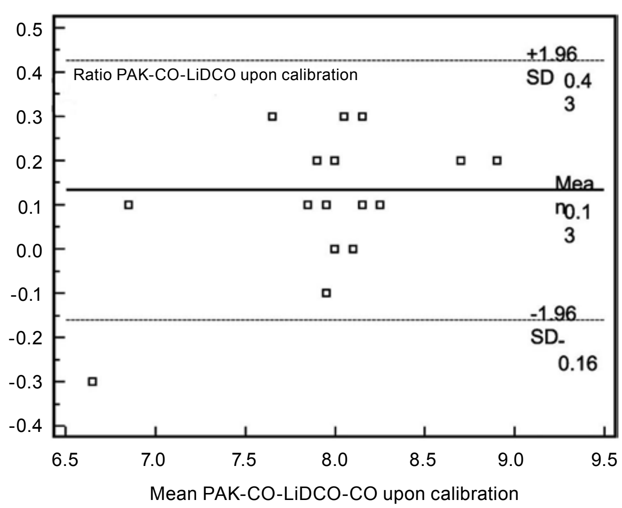

Fig. 4. PAK-CO vs. LiDCO

Conclusion

In this preliminary study, the LiDCO and PiCCO methods of cardiac output measurement were compared with the reference PAK technique of continuous cardiac output monitoring and showed a good level of compatibility in septic patients. Therefore, LiDCO and PiCCO as less invasive methods, thus associated with a lower rate of complications, could replace PAK in continuous real-time monitoring of cardiac output in septic patients.

When using either of these methods in hemodynamic monitoring of hemodynamically stable septic patients, calibration can be done at longer intervals, thus decreasing the risk of complications associated with manipulation and reducing the cost of treatment, while having a beneficial effect on the quality of patient management.

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Sažetak

STALNI NADZOR SRČANOG IZBAČAJA METODAMA PiCCO I LiDCO PREMA PAK-u U SEPTIČNIH BOLESNIKA: KALIBRIRATI ILI NE?

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U ovom radu uspoređivala se točnost mjerenja srčanog izbačaja pomoću dviju najčešće upotrebljavanih metoda manje invazivnog hemodinamskog nadzora i standardnom tehnikom termodilucije plućnim kateterom. Mjerenje je provedeno kod septičnih kirurških bolesnika u razdoblju neposredno nakon i između kalibracija sustava. Rezultati su pokazali zadovoljavajuću podudarnost mjerenja u obje faze primjenom obiju metoda i pomoću plućnog katetera, pa se kalibriranje sustava preporuča u hemodinamski nestabilnih septičnih bolesnika.

Ključne riječi: *Srčani izbačaj – fiziologija; Nadzor, fiziološki – metode; Sepsa; Jedinice intenzivne skrbi*