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Regular paper

Be cautious during the interpretation of arterial blood gas analysis performed outside the intensive care unit

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Introduction. Reliable results of an arterial blood gas (ABG) analysis are crucial for the implementation of appropriate diagnostics and therapy. We aimed to investigate the differences (Δ) between ABG parameters obtained from point-of-care testing (POCT) and central laboratory (CL) measurements, taking into account the turnaround time (TAT). Materials and methods. A number of 208 paired samples were collected from 54 intensive care unit (ICU) patients. Analyses were performed using Siemens RAPIDPoint 500 Blood Gas System on the samples just after blood retrieval at the ICU and after delivery to the CL. Results. The median TAT was 56 minutes (IQR 39-74). Differences were found for all ABG parameters. Median Δs for acid-base balance were: ΔpH=0.006 (IQR –0.0070–0.0195), ΔBE_{ef}=–0.9 (IQR –2.0–0.4) and $\Delta HCO_{3\ act}^-$=–1.05 (IQR –2.25–0.35). For ventilatory parameters they were: ΔpO_2=–8.3 mmHg (IQR –20.9–0.8) and ΔpCO_2=–2.2 mmHg (IQR –4.2–-0.4). For electrolytes balance the differences were: ΔNa^+=1.55 mM/L (IQR 0.10–2.85), ΔK^+=–0.120 mM/L (IQR –0.295–0.135) and ΔCl^-=1.0 mM/L (IQR –1.0–3.0). Although the Δs might have caused misdiagnosis in 51 samples, Bland-Altman analysis revealed that only for pO_2 the difference was of clinical significance (mean: –10.1 mmHg, ±1.96SD –58.5; +38.3). There was an important correlation between TAT and ΔpH (R=0.45, p<0.01) with the safest time delay for proper assessment being less than 39 minutes. Conclusions. Differences between POCT and CL results in ABG analysis may be clinically important and cause misdiagnosis, especially for pO_2. POCT should be advised for ABG analysis due to the impact of TAT, which seems to be the most important for the analysis of pH.

Key words: arterial blood gas analysis, point-of-care testing, turnaround time, reliability

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Abbreviations: ABG, arterial blood gas; BE, base excess; CL, central laboratory; ICU, intensive care unit; IQR, interquartile range; POC(T), point-of-care (testing); TAT, turnaround time

INTRODUCTION

Laboratory blood tests help to establish the diagnosis and may influence the treatment decisions in everyday clinical practice. Their reliability is of key importance in the critical care setting as far as acid-base, electrolyte and ventilatory equilibrium are concerned. Although intensive care units (ICU) have the access to point-of-care testing (POCT), many non-ICUs still need to rely on the results from the central laboratory (CL). POCT is quick, accessible, easy-to-use, allows to reduce the possibility of pre-analytical and post-analytical errors, and significantly minimizes the turn-around-time (Nichols JH *et al.*, 2007). Despite the improvements in sample delivery, processing and report dispatch as a result of technological advancements, the analytical turnaround time (TAT) is considered one of the crucial indicators of laboratory effectiveness and continues to be a bone of contention between the clinicians and laboratorians (Goswami B *et al.*, 2010).

We aimed to investigate the extent of differences between major ABG parameters obtained from point-of-care (POC) and central laboratory (CL) measurements, taking into account the time delay in blood sample analysis.

MATERIALS AND METHODS

A number of 208 paired samples were collected from 54 ICU patients hospitalized in 2018 and 2019. Blood samples were retrieved via an arterial line into two 5 mL heparinized probes. The paired samples were always taken by the same investigator. Measurements of pH, pO_2, pCO_2, HCO_3^-, base excess (BE), Na^+, K^+ Cl^- were performed using the Siemens RAPIDPoint 500 Blood Gas System in the ICU (as POCT) and in the CL. The time gap between the measurements (i.e. TAT) was recorded. Differences were calculated (i.e. $\Delta = Value_{POC} - Value_{CL}$) and POCT value was concerned as the reference one.

The project was approved by the local Ethical Committee (KNW/0022/KB1/16/I/18) and the patients gave their informed consent for participation.

Statistical analysis was performed using MedCalc for Windows v15.8 (MedCalc Software, Ostend, Belgium). Quantitative variables were presented as median and interquartile ranges (IQR, i.e. 25–75 percentile), whereas qualitative variables were depicted as relative values. All quantitative variables were tested for normal distribution using the Shapiro-Wilk test. Between-group comparisons were verified using Kruskal-Wallis test with post-hoc analysis. The correlation was assessed using Spearman's rank correlation coefficient. Bland-Altman plots were drawn to analyse the agreement between POCT and CL results. A p-value of <0.05 was considered statistically significant.

RESULTS

The study group comprised of 34 males and 20 females.

The medians of differences in parameters of acid-base balance were as follows: ΔpH=0.0060 (IQR –0.0070–

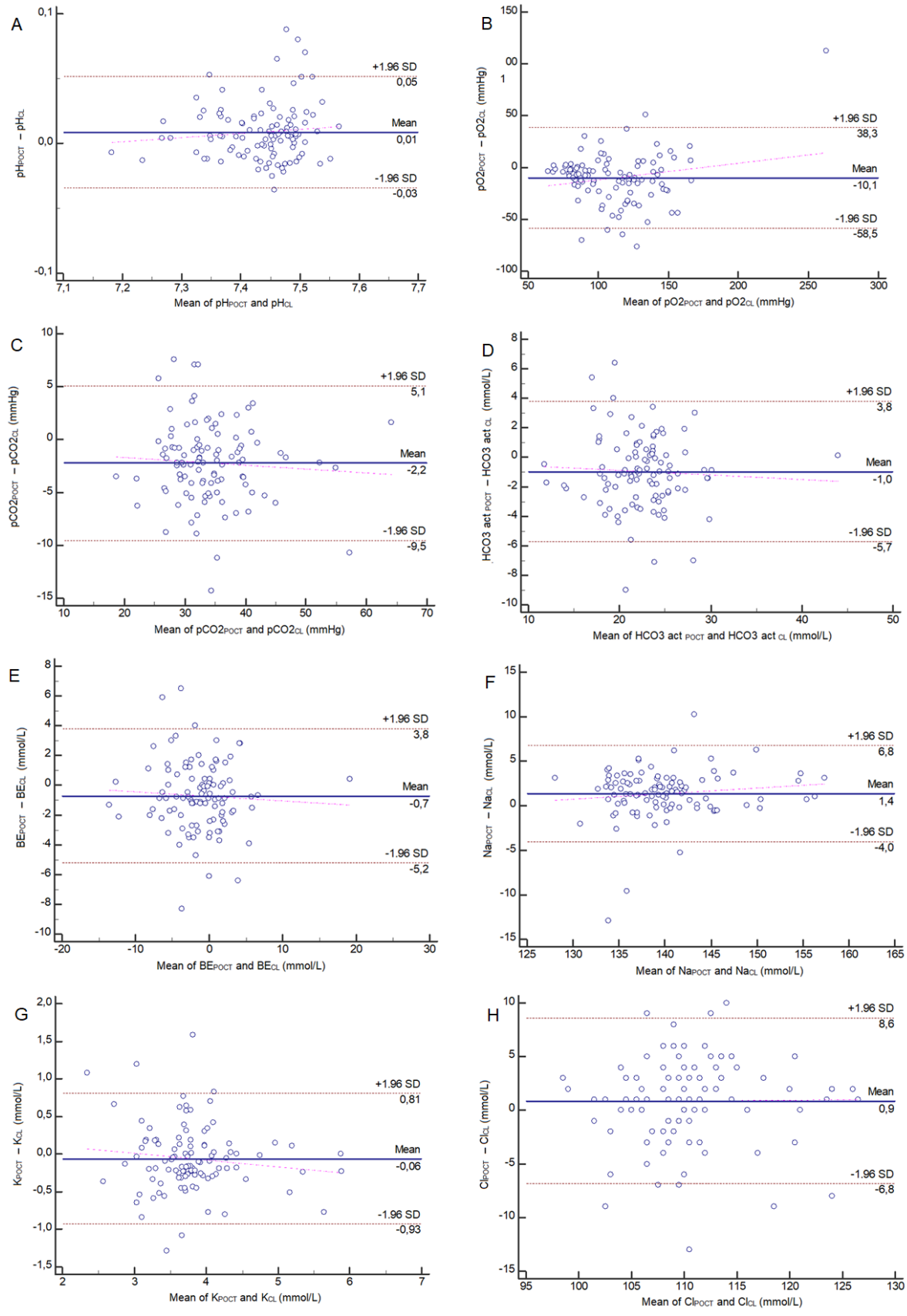

Figure 1. Bland-Altman analysis investigating differences between values obtained just after blood retrieval (POCT) and after delivery to the central laboratory (CL)
(A) pH; (B) pO_2; (C) pCO_2; (D) HCO_3^-; (E) BE; (F) Na^+; (G) K^+; (H) Cl^-

0.0195), ΔBE_{ef}=–0.9 (IQR –2.0–0.4) and $HCO_{3\ act}^{-}$=–1.05 (IQR –2.25–0.35). Median Δs values for ventilatory parameters were: ΔpCO_2= –2.2 mmHg (IQR -4.2–0.4) and ΔpO_2= -8.3 mmHg (IQR –20.9–0.8). As far as electrolytes were concerned, the differences were: ΔNa^+= 1.55 mM/L (IQR 0.10–2.85), ΔK^+=–0.120 mM/L (IQR –0.295–0.135) and ΔCl^-=1.0 mM/L (IQR –1.0–3.0). The Bland-Altman analysis revealed that only for pO_2 the difference was noteworthy from the clinical and practical point of view (mean: –10.1 mmHg, ±1.96SD –58.5; +38.3) (Fig. 1A–H). CL overestimated also the value of pCO_2, $HCO_{3\ act}^{-}$, BE_{ef} and K^+ but the variations were too small to be clinically significant.

We found a correlation only between the time delay and ΔpH (R=0.45, $p<0.01$), and ΔpCO_2 (R=0.22, $p=0.02$). The median TAT was 56 minutes (IQR 39–74). Differences across the quartiles for TAT (i.e. <39 *vs.* 39–56 *vs.* 57–74 *vs.* >74 minutes) were statistically significant only for pH (Fig. 2A–H) with the safest time interval not exceeding 39 minutes.

The differences might have caused misdiagnosis in 51 samples for acid-base analysis, 49 for ventilatory parameters and 51 for electrolytes (Table 1A–C).

DISCUSSION

In this short study we showed that the delay in ABG analysis in our hospital was intolerably high, might interfere with the results and result in misdiagnosis. The difference was of significant clinical importance especially for pO_2 (Δ of –8.3 mmHg and mean difference of 10.1 mmHg in the Bland-Altman analysis). The correlation between TAT and the ABG results seems the most important in case interpretation of pH, and TAT should not exceed 39 minutes to draw reliable therapeutic conclusions.

Although our findings are not novel in the field, this project sheds light on the proper analysis of ABG in the non-ICU setting, if POCT is inaccessible and the time delay may occur due to various local conditions (e.g. work overload in the ward, transportation problems, work overload in the CL). Different TAT may have an uncontrolled impact on ABG results which results in the risk of misdiagnosis. We found that some type of misdiagnosis occurred in 51 samples. Taking into account all the analyses, the effect was found only in case of pH – the longer the TAT, the higher the delta. The safety margin for proper assessment was in the first TAT quartile, i.e. <39 minutes. In this time period, a median difference was –0.003 (95%CI –0.14; 0.005), whereas in the second quartile it was statistically significantly higher and reached +0.003 (95%CI –0.006; 0.01) ($p<0.05$). The quantity of this difference is, however, clinically unimportant and should not impact the treatment decisions. Interestingly, although not statistically significant, the difference in pO_2 of –8.3 mmHg seems important from a practical perspective. The current guidelines recommend patient-oriented respiratory treatment with strict compliance with ABG findings. Both hypoxaemia and hyperoxaemia are harmful, so delivery of oxygen should be titrated and pO_2 of 75–100 mmHg is the goal in the vast majority of patients (de Jonge *et al.,* 2008).

Based on our findings, we may recommend using POCT in diagnostics and treatment of ABG abnormalities *via* a validated bedside tool. Unjustified postponement of the analysis may cause a delay in the implementation of suitable treatment in patients with respiratory failure, shock or electrolyte disequilibrium (Szczeklik *et al.*, 2019). The Siemens RAPIDPoint 500 Blood Gas Analyzer was found reliable in POCT and its results were found interchangeable with those obtained from the CL (where Beckman & Coulter AU 5800 and Beckman & Coulter UniCel DxH 800 were used) in 314 paired samples collected from 51 critically ill patients (Allardet-Servent *et al.*, 2017).

On one hand, many investigators advise being cautious in the interpretation of electrolytes using various POC tools (Morimatsu *et al.,* 2003; Leino *et al.*, 2011; Budak *et al.*, 2012; Gavala & Myrianthefs, 2017). On the other hand, Zhang with colleagues found that the differences for electrolytes were within USCLIA-determined limits (Zhang *et al.*, 2015) and Dashevsky et al. confirmed an excellent agreement between POC and CL for electrolytes in a cohort of almost 15 000 subjects at the emergency department (Dashevsky *et al., 2017*). This inconsistency is difficult to explain but may arise from the analytical errors due to implementation of different tools. The strength of our study was the use of the same Siemens ABG analyzer in the ICU and in the CL. Clinicians should always be aware of the limitations of the assays they use (Uyanik *et al.*, 2015).

There are some limitations of the study. Firstly, we focused on the selected ABG parameters. It has been revealed that the most noticeable differences between POCT and CL measurements usually concern haemoglobin, hematocrit and metabolic parameters (Allardet-Servent *et al.*, 2017; Gavala & Myrianthefs, 2017). Clinicians should be aware of this fact when interpreting the data if the time delay occurs. Secondly, based on our project we were unable to investigate the reason for the variations. We assumed that they were caused by the TAT. To reduce the bias, the preparation of blood samples and blood retrieval were standardized and performed by three trained investigators. But the storage of the sample and the transportation conditions may play some role. According to Srisan and coworkers (Srisan P *et al.*, 2011), if the blood is kept in room temperature, the time delay should not exceed 20 minutes, but Mohammadhoseini and coworkers (Mohammadhoseini E *et al.*, 2015) concluded that the results should still be reliable within 60 minutes after blood collection. Finally, we did not attempt to investigate the impact of the study group characteristics on the results. Extreme variations in ABG parameters in critically ill subjects with multiorgan failure may deliver some new interesting observations. The patients' clinical profile was of lower importance for us. However, we included only conscious patients who gave their informed consent.

CONCLUSION

We may conclude that long TAT is unacceptable and adequate urgent action is needed in the organization of work and training of employees to reduce or at least minimize this pre-analytical error. Differences between POCT and CL results in ABG analysis may be clinically important and cause misdiagnosis, especially for analysis of pO_2. POCT should be advised for ABG analysis due to the impact of TAT, which seems to be the most important for the analysis of pH.

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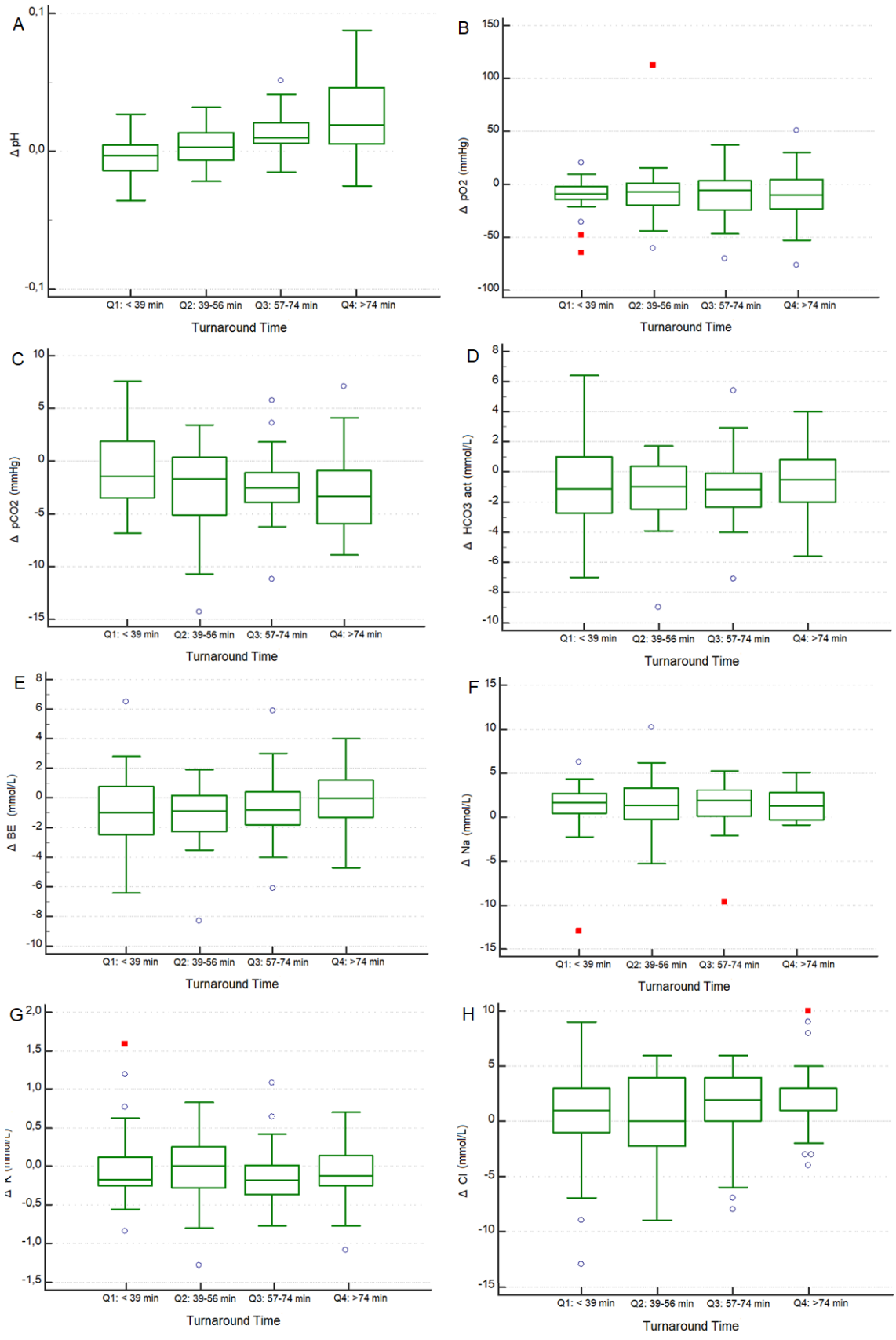

Figure 2. Differences between the values obtained just after blood retrieval (POCT) and after delivery to the central laboratory (CL) between quartiles of the turnaround time
(A) pH; (B) pO_2; (C) pCO_2; (D) HCO_3^-; (E) BE; (F) Na^+; (G) K^+; (H) Cl^-

Table 1. Number of possible misdiagnoses due to differences between values in samples just after blood retrieval (POCT) and after delivery to the central laboratory (CL)
A. Acid–base equilibrium

CL / POCT		pH			BE			$HCO_3^-{}_{act}$		
		↓	N	↑	↓	N	↑	↓	N	↑
pH	↓	10	0	0	–	–	–	–	–	
	N	4	29	7	–	–	–	–	–	–
	↑	0	8	46	–	–	–	–	–	–
BE	↓	–	–	–	32	15	0	–	–	–
	N	–	–	–	4	29	13	–	–	–
	↑	–	–	–	0	2	9	–	–	–
$HCO_3^-{}_{act}$	↓	–	–	–	–	–	–	22	14	1
	N	–	–	–	–	–	–	4	51	3
	↑	–	–	–	–	–	–	0	2	7

N means the norm; ↓ means below the norm; ↑ means over the norm. The norms were considered as follows: pH 7.35–7.45; BE –2.0–3.0 mmol/L; HCO_3^- 21–26 mmol/L

B. Ventilatory parameters

CL / POCT		pO2			pCO2		
		↓	N	↑	↓	N	↑
pO2	↓	4	1	2	–	–	–
	N	0	28	13	–	–	–
	↑	0	5	48	–	–	–
pCO2	↓	–	–	–	26	23	0
	N	–	–	–	6	39	3
	↑	–	–	–	0	1	6

N means the norm; ↓ means below the norm; ↑ means over the norm; The norms were considered as follows: pO_2 70–100 mmHg; pCO_2 35–46 mmHg

C. Electrolytes

CL / POCT		Na			K			Cl		
		↓	N	↑	↓	N	↑	↓	N	↑
Na	↓	6	6	0	–	–	–	–	–	–
	N	16	59	0	–	–	–	–	–	–
	↑	0	5	12	–	–	–	–	–	–
K	↓	–	–	–	20	15	0	–	–	–
	N	–	–	–	6	57	1	–	–	–
	↑	–	–	–	0	0	5	–	–	–
Cl	↓	–	–	–	–	–	–	0	0	0
	N	–	–	–	–	–	–	0	10	6
	↑	–	–	–	–	–	–	0	13	75

N means the norm; ↓ means below the norm; ↑ means over the norm; The norms were as follows: Na^+ 135–145 mmol/L; K^+ 3.6–4.8 mmol/L; Cl^- 95–105 mmol/L

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