Treball de Recerca

Convocatòria Setembre 2012

Autor:

Sergi Vaquer Araujo

Servei de Medicina Intensiva. Corporació Sanitària Universitària Parc Taulí de Sabadell.

Departament de Medicina. Universitat Autònoma de Barcelona.

Títol:

Estimating arterial blood gases with the EABC® System ("Earlobe Arterialized Blood Collector") in critically ill patients. A validation study.

CERTIFICAT DEL DIRECTOR O CO-DIRECTOR DEL TREBALL DE RECERCA

Dr. Antoni Artigas Raventós, Cap del Servei de Medicina Intensiva de la Corporació Sanitària Parc Taulí de Sabadell i Professor del Departament de Medicina de la Universitat Autònoma de Barcelona

FA CONSTAR,

que el treball titulat: "**Estimating arterial blood gases with the EABC® System ("Earlobe Arterialized Blood Collector") in critically ill patients. A validation study.**" ha estat realitzat sota la meva direcció pel llicenciat **Sergi Vaquer Araujo** trobant-se en condicions de poder ser presentat com a treball d'investigació de 12 crèdits, dins el programa de doctorat en Medicina Interna/Diagnòstic per la Imatge (curs 2011-2012), a la convocatòria de **Setembre**.

Barcelona, 20 d'Agost de dos mil dotze.

1. INDEX

2. ABSTRACT

The EABC® is a minimally invasive system able to perform arterialized capillary blood gas analysis from the earlobe (EL). A prospective study to validate EABC® system in critical ill patients was performed. 55 ventilated patients, admitted to a polyvalent Intensive Care Unit (ICU), with an arterial catheter, were sequentially included. Patients with severe coagulopathy or anticoagulant therapy were excluded. Performance of the EABC® system was compared to Radiometer ABL 700® system. Demographic and clinical variables, vasoactive drug treatment, problems in the procedure and complications were registered. Qualitative variables were analysed using Chi-square test, quantitative variables were evaluated with Student's t test for paired variables and a multivariate analysis using logistic regression method was performed. A concordance analysis was performed using Pearson's linear regression, Student's t test for mean comparison, agreement evaluation using Bland-Altman method, and evaluation of the β coefficient from the correlation equation. Bilateral significance was established at $p < 0.05$. Arterialised blood sample from EL was obtained in 31 patients (56.4%) in an average time of 11 minutes. Risk factors were age > 65, diabetes, vasoactive drug therapy and noradrenaline (NA) doses above 0.22 μg / kg / min. Multivariate analysis showed age > 65 years was the only factor independently associated with failure. Concordance analysis and Bland-Altman agreement evaluation were insufficient for validating the new system for all gasometrical variables.

3. BACKGROUND

The use of arterialized capillary blood from the earlobe (EL) to perform blood gas analysis was firstly introduced by Drs. Lilenthal and Rilley [1]. The technique is based on the hypothesis blood from dilated capillaries of the EL, collected by a small incision and a capillary tube, contains a higher proportion of arterial blood than venous blood, being therefore a good estimator of arterial gas content. Several potential advantages of EL capillarized blood sampling compared to arterial puncture have been postulated, such as a lower risk of bleeding, minimized ischemic complications, less invasiveness and better patient tolerance. Nevertheless, studies have shown discordant results on the reliability of the technique to estimate arterial blood gases, which has limited its implementation in current clinical practice. Furthermore, a certain training degree is required to ensure appropriate anaerobic sampling and there is a low but relevant risk of needle stick injury by health care professionals. An especially designed prototype for arterialized capillary blood collection from the EL (Earlobe Artrialized Blood Collector, EABC®) has proven to be safe, with comparable results to arterial puncture in healthy volunteers, in various experimental situations such as head venous congestion, hypoxia and in microgravity [2,3]. Additionally, it has been reported to be virtually painless, especially compared with arterial puncture, easy to use, had no complications and eliminate the risk of accidental puncture or direct blood contact by the operator. These advantages make the EABC® a useful system able to be operated safely by non-trained caregivers and provide analytical capabilities in remote and isolated environments. A preliminary validation study in patients with chronic renal failure and haemodialysis showed adequate correlation with direct arterial sampling for blood gas measurement [4]. Further testing is required for ensuring accuracy and applicability in a wider range of pathological situations, especially in the critically ill patient.

This project aims to evaluate the ability to estimate arterial blood gases from the analysis of arterialized earlobe blood obtained and measured using the EABC® + i-Stat® system in critically ill patients, determine the possible adverse effects and its applicability in routine clinical practice as a part of its validation process before being implemented into the ISS health care system.

4. MATERIALS & METHODS

Patients

From November 2010 to May 2012, ventilated patients admitted to a polyvalent Intensive Care Unit (ICU), who had an arterial line, were sequentially included into the study. Patients with severe coagulopathy (Prothrombine Time > 2.5 ratio, Platelet count <10.000 units / dl) were excluded.

Ethical issues

The study protocol was accepted by local ethics committee (IRB: 2009593. Comité Ètic d'Investigació Clínica, Corporació Sanitària Universitària Parc Taulí. Sabadell, Spain) and informed consent was always obtained from the patient or next of a kind.

Blood collection procedure

A new prototype device, the Earlobe Artrialized Blood Collector (EABC®) developed by the microgravity Centre / FENG-PUCRS (Brazil) in collaboration with King's College of London (United Kingdom) was used for collecting samples of arterialized capillary blood from the EL. The EABC® system consisted of a plastic shell containing a small blade, a capillary heparinised tube and a sensor cartridge which could be interchangeable. The collecting device was coupled to the i-Stat® portable analyser (Abbot, United States of America), which received arterialized blood directly from a small skin cut, through a capillary tube, always under anaerobic conditions. Arterialisation was performed by massaging the EL for 2.5 min initially (first 20 patients) and later during 5 minutes (remaining 35 patients), with vasodilation cream (2% nitroglycerine cream) to ensure arterio-venous capillary shunting and sufficient blood congestion. Simultaneous blood samples were withdrawn and analysed. EL arterialized blood was collected and analysed using the EABC® + i-Stat® (CG4+ cartridges) (Abbot, United States of America) and arterial blood samples were analysed using ABL 700® system (Radiometer, Denmark). Both the i-STAT® and ABL 700® were calibrated, maintained and updated periodically as indicated by the producer. After blood collection from the EL a gentle pressure was applied until haemostasis was achieved.

Measures

Demographic variables, diagnostic at ICU admission, illness severity determined by Acute Physiology and Chronic Health Evaluation II (APACHE II) score, general analytical variables, hemodynamic and respiratory variables, mechanical ventilation parameters, vasoactive therapy and drug dose (noradrenaline - NA, dopamine - Dp, dobutamine - Db, Nitroglycerine - NTG, Nitroprusiate - NTP, Levosimendan - LVD, Terlipressine - TLP, alone or in combination), presence of sepsis (as determined by the Surviving Sepsis Campaign [5]), complications, total time to results, problems / difficulties during the procedure, sampling success / failure ratio and its cause were registered. High heart rate (HR > 130 beats per minute), low mean arterial pressure

(MAP < 65 mmHg), low cardiac output index (CI < 2.5 l/min/m^2) measured by thermodilution or arterial pulse contour analysis, high lactate levels (> 22mg/dl) or vasoactive drug treatment were considered as markers of hemodynamic instability. pH, PO_2, PCO_2, HCO_3, BE and lactate were determined in arterial and capillary samples.

Data analysis

Association between study variables and sampling success / failure ratio was evaluated and is presented as relative risk (RR) of sampling failure for the presence of a given variable. Confidence interval 95% (CI 95%) is provided whenever possible. Qualitative variables were analysed using Chi-square test whereas Student's t test for paired variables was used in the case of quantitative variables. Hemodynamic instability variables were analysed individually and in combination using a linear by linear association test, which evaluated the additive effect of having two, three, four or five variables over sampling success ratio. Vasoactive, vasopressor and especially NA treatment effects were also studied. In order to estimate critical drug dose, a ROC (Receiving Operator Curve - Sampling Success / Drug Dose) was generated upon which a Youden test [6] was applied. Finally, using logistic regression method a multivariate analysis was performed to ascertain which variables were independently associated with sampling success / failure.

Whenever sampling was possible, concordance analysis between the two methods consisted of a correlation test using Pearson's linear regression method and its quadratic coefficient, mean difference comparison using Student's t test, evaluation of β coefficient from the regression equation, and an agreement evaluation using the Bland-Altman method [7]. We applied this analysis procedure to the whole study population and for a subgroup of patients < 45 years old. Two tailed significance threshold was established at $p < .05$ and the 95% confidence interval was calculated whenever possible. Sample size calculation was made based upon previous reports. For a desired correlation coefficient of 0.85 with a minimum accepted ratio of 0.75, an alpha error of .05, and a statistical power above 0.8 sample size required was 79 patients. Statistical analysis was performed using SPSS version 19 (International Business Machines – IBM. Armonk, New York. United States of America) statistical software.

5. RESULTS

Study population

A total of 55 patients were included in this study. Patients were predominantly males (72.7%), with mean age of 62 years old. Arterial hypertension and diabetes were most prevalent comorbidities (41.8% and 34.5%) and severe sepsis was the most frequent cause of ICU admission (38.1%). Mean APACHE II score was 18.28 (3 - 34). All patients were in mechanical ventilation with mean PEEP (Positive End Expiratory Pressure) of 7.13 (4 - 12) and received oxygen at mean FiO_2 of 0.36 (0.21 - 0.66). Patients received treatment with vasoactive drugs in 65.5% of the cases, being noradrenaline the most used drug (83.3%). Complete patient demographic, clinical characteristics, and additional study variables are described in *tables 1* & *2*.

Blood collector performance

EL blood samples were obtained in 31 patients (56.4%). The most prevalent cause of sampling failure was low blood flow (78.1%). Failure was more frequent in patients older than 65 years (RR= 1.93, p = 0.04) and with diabetes (RR = 1.90 p = 0.03). Success rate was 100% in patients younger than 45 years old. There was a non-significant trend to higher failure rates in patients treated with vasoactive drugs (RR = 2; p = 0.06), this trend was also observed in a subgroup of patients treated with vasoconstrictor drugs (NA, Dp, TLP) but with weaker intensity (RR = 1.75; p = 0.094). NA treatment was not related with failure rate (RR = 1.66; p = 0.112) and dose was not different between patients with successful or failed blood collection (Mean Dif. = 0.172; p = 0.805; CI 95% = -0.35 - 0.69). In contrast, NA doses above 0.22 μg/kg/min were associated with increased failure rates (RR = 2.37; p = 0.024). Additional factors thought to modify capillary blood flow and therefore increase failure rate were evaluated. Neither was the presence of sepsis (RR = 1.43; p = 0.262), nor were the presence of analytic signs of tissue hypoperfussion (lactate > 22mg/dl) (RR = 1.42; p = 0.382), severe alteration of MAP in either of its extreme values (<65 or >90 mmHg) (RR = 0.83; p = 0.573) and remaining variables associated with hemodynamic instability (HR > 130 beats per minute and CI < 2.5 l/min/m^2). Linear by Linear analysis showed a trend to failure ratio increase the more variables were associated (*Figure1*) but without reaching significance (p=0.146). Severity at admission (APACHE II) was not different between patients with successful or failed blood collection (Mean Dif. = 4.22; p = 0.165; CI 95% = -2 - 10.4). Vasodilation and massage time (2.5 min. vs. 5 min.) did not affect sampling success rate, nor did fluid balance 3 hours before the procedure (*Table 3*). Finally multivariate analysis demonstrated age > 65 years was the only variable independently associated with sampling success ratio from the EL using the EABC® system in critical ill patients (*Table4*).

Learning curve

Study population was divided chronologically in groups of 5 patients in order to determine whether there was a learning curve for the procedure or not. Success / failure percentages were recorded and its evolution throughout the study timeline is shown in *Figure 2*. Successes and failures stabilized after 35 sampling attempts at around 60% of success rate. In the last 5 patients success rate rose up to 80% unexpectedly. Density of patients older than 65 years in the group with the highest failure rate was higher but not significantly different form the group with the lowest failure rate (52.4% vs. 20%)

Complications and bleeding time

Serious complications did not occur during this study. There was one case of wound infection (2%), which evolved satisfactorily without specific treatment, and bleeding time was <10 min. in 92.7% of cases. The average time to results was 11 min. (range 6 - 28 min.). No association was found between bleeding time and antiplatelet treatment (bleeding > 2 min. p = 0.374 ; bleeding > 10 min. p = 0.452), prophylactic anticoagulation (bleeding > 2 min. p = 0.957 ; bleeding > 10 min. p = 0.924) or combination of both (bleeding > 2 min. p = 0.407 ; bleeding > 10 min. p = 0.462). Neither were any differences in platelet count (mean dif.= 26.8 pl x 10^3/dl, CI 95% = -58 - 111, p = 0.529) or Prothrombine Time (mean dif. = 0.008, CI95% = -0.8 - 0.1, p = 0.792) between patients bleeding for > 2 min. from those who did not.

Concordance analysis

In the 31 cases where samples were obtained from the EL, correlation equation coeficients and mean difference comparisons between EABC® + i-Stat® system and ABL 700® for all study patients is presented in *Table 4* and for patients < 45 years old in *Table 5*. PO_2, SO_2 and pH correlations were poor, acceptable for PCO_2 and HCO_3, and remarkable for BE and lactate. Regression equation β coefficient showed PO_2, SO_2, pH and PCO_2 values were underestimated at higher values. Additionally, there were statistically significant mean differences for PO_2, SO_2, HCO_3^-, and lactate, representing a systematic error, which always underestimated values. Concordance did not improve in the subgroup of patients younger than 45 years old albeit outstanding sampling success rates.

Agreement evaluation using Bland-Altman methods evidenced high variability in mean differences between arterial and capillary blood samples for all gasometrical variables and lactate. Furthermore, in all cases except for HCO_3^-, mean differences overcame tolerance limits at least in one occasion. Bland-Altman plots also revealed the EABC® + i-Stat® system always underestimated gasometrical variables. In PO_2 and SO_2 measures the magnitude of this error approximated 25% in both cases. Finally, mean difference dispersion pattern confirmed capillary PO_2 measures were underestimated the higher the mean arterial - capillary PO_2, however it was

not the case for SO_2, pH and PCO_2. HCO_3^- and BE mean differences showed a dual distribution being underestimated by capillary samples at lower values and overestimated at higher values (approximate threshold of 25 mEq/L for HCO_3^- and 2 mEq/L for BE).

6. DISCUSSION

This study has demonstrated the EABC® + i-Stat® system for estimating arterial gas values from EL arterialized capillary blood is not suitable for routine clinical use in critically ill patients. We found an excessive failure rate and age > 65 years old was a determinant factor. Vasoactive drugs, especially noradrenaline, and cumulative effect of hemodynamic instability could also be associated with increased failure rates. Whenever sampling was possible, concordance analysis and Bland-Altman agreement evaluation were insufficient for validating the new system.

Arterialized capillary blood gas measurement has numerous potential advantages over direct arterial sampling, such as lower bleeding risk, smaller sample size, minimized ischemic complications, reduced invasiveness and better patient tolerance. This technique has been extensively evaluated in healthy volunteers at rest and during sub-maximal exercise [8,9], in outpatients attending to a pulmonary function laboratory [10] and for the purpose of long-term oxygen therapy prescription [11], in patients with chronic obstructive and restrictive respiratory conditions [12] and with hypoxia from varied causes with [13] or without [14] tissue hypoperfussion signs. Some studies found good concordance of capillary gas measures with standard direct arterial sampling while others did not. To address the question whether EL capillary blood gas analysis was an accurate and reliable substitute for arterial gasometrical measures, applicable in routine clinical practice, a meta-analysis was performed [15]. The study concluded PO_2 measurement from the EL could be appropriate as a replacement for arterial PO_2 unless precision was required. Pooled analysis of capillary PO_2 measures showed improved agreement the lower the arterial PO_2 (from < 123mmHg) with mean difference being markedly reduced when arterial PO_2 was below 70mmHg. Other blood gasometrical variables like pH and PCO_2 were in good agreement with arterial samples over a wide range of values. Poor arterialisation of the EL despite the utilisation of means for capillary bed arterialisation was hypothesised to be responsible, causing an increase in venous blood percentage when sampling at the EL. At low arterial PO_2, the effect of venous blood admixture is depreciable whereas it becomes more evident at high arterio-venous PO_2 differences. Since arterio-venous PCO_2 differences are comparatively smaller, poor arterialization does not affect its measurement. Furthermore, collection protocols among studies included were varied and its quality could not be determined in all cases. Direct capillary sampling always implies a certain degree of room air contamination thus insufficient “anaerobical” blood collection could have significantly affected blood sample

quality and meta-analysis results.

The new EABC® system together with an enhanced EL arterialization protocol were designed to overcome aforementioned problems. The EABC® permits procedure standardization, high reproducibility of collection and minimizes air contamination. Preliminary validation studies showed good correlation between arterial and EL capillary samples in physiological conditions simulating austere environments [2], in microgravity [3] and in a reduced group of patients with chronic renal insufficiency [4]. In order to confirm its applicability in routine clinical practice, our study was proposed to test the system in a population of critically ill patients with a wider variety of diagnostics at admission, different hemodynamic status and treatments. We were able to find only one preceding study evaluating the accuracy of EL capillary blood gas analysis in an ICU environment [16]. In this study, authors reported reliable arterial PCO_2 estimation from the EL as well as for pH, HCO_3^- and BE measures. Nonetheless, arterial PO_2 estimation showed the same limitations as previously reported. It has to be emphasised severe hemodynamic alterations, hypothermia or hyperthermia, chronic respiratory disease, high FiO_2 or PEEP values, severe sepsis and multi-organ failure were exclusion criteria, representing an important limitation for its applicability to real critically ill patients. Conversely, our objectives were not only to validate the EABC® + i-Stat® system as an estimator of arterial blood gas values from EL arterialized capillary blood, but also evaluate its applicability in a wide spectrum of critically ill patients into a real ICU environment.

Despite promising preliminary data, we were unable to validate the new system for various reasons. Firstly, a high sampling failure rate was observed due to low blood flow from the EL, representing an unexpected finding not evidenced in preliminary studies. Interestingly, age > 65 years old was the only patient characteristic associated with such failure rate. Aging is responsible for vascular function impairment [17] and increased capillary rigidity. It may have limited vascular blood flow and blood delivery causing the observed low blood flow through EABC® capillary tube which eventually led to blood coagulation and sampling failure. The impact of age is evidenced in patient subgroup < 45 years old where success rate increased to 100%. Vasoactive drugs, moderate NA doses (> 0.22 μg/kg/min) and cumulative effect of haemodynamic instability variables had an effect on sampling success, although it was not always statistically significant. Vasodilation cream and EL rubbing were not able to overcome this problem. On the contrary, signs of frank tissue hypoxia such as elevated blood lactate and conditions known to cause vascular dysfunction such as severe sepsis were not associated with increased sampling failure ratio.

Insufficient training of operators could have also explained observed failure rates. However there were two qualified operators who received two training sessions during the study and had the possibility of interacting with the EABC® producer whenever required. Furthermore, two interim analyses were performed to identify possible reasons for sampling failures. Success/failure ratio stabilized after 35 sampling attempts suggesting a learning period had been overcome around the mid part of the study. Nevertheless, this hypothetical learning curve was probably disrupted by differential age distribution among study phases. Our opinion is provided the procedure simplicity sufficient skills and expertise were already acquired at early stages of the study.

The statistical procedure used in this study for assessing concordance between the new system and the standard permitted a more accurate analysis of results than in previous reports. Not only correlation coefficients and mean differences were considered but also Bland-Altman plots and correlation equation β coefficient were evaluated. PO_2 was not concordant with standard, neither was SO_2. Both variables showed poor correlation and were underestimated by the system up to 25%, which represents a clinically significant error. Furthermore, its mean differences with the standard were high and overcame tolerance limits in Bland-Altman plots. These results are similar to those previously reported in literature and could represent an insufficient capillary bed arterialisation and venous blood admixture. We also detected an increase in PO_2 underestimation the higher the arterial PO_2 (β coefficient < 1 and specific mean difference scattering distribution in Bland-Altman plots) in all patients, showing the effect of higher arterio-venous differences when venous blood admixture occurs. In the case of PCO_2 and pH, concordance analysis was better but mean differences were excessive and also overcame tolerance limits, which was a new finding from previous reports. Correlation coefficient was acceptable for HCO_3^- and good for BE and Lactate however, mean differences were again excessive. Interestingly, HCO_3^- and BE showed a bimodal distribution in Bland-Altman plots being underestimated at lower values and overestimated at higher values but no explanation has been found for this finding.

It could be argued results presented in this study depict the inability of the EABC® for collecting an adequate blood sample. Three previous studies using this device had never encountered such sampling difficulties and correlation seemed to be acceptable, nonetheless, these studies included fewer patients and its statistical analysis was limited. Furthermore, study results point age of critically ill patients as the main factor affecting sampling success with a possible effect of vasoactive drugs, especially NA. We would like to emphasise, concordance analysis did not improve in patients < 45 years old in spite of outstanding successful sampling rates, which suggests results are not influenced by the collecting system but by the

characteristics of the population being studied and the limitations of EL arterialized capillary blood gas analysis technique itself.

Limitations of this study were the unexpected high failure rates, which significantly slowed inclusion rate, and poor concordance of the new system with the standard, which was already observed in first patients and continued invariable despite sample size increases. Combination of these factors invalidated initial sample size calculations, which was based upon previous studies with a different population.

Despite presented results the EABC® + i-Stat® system is a safe, fast and easy to use point of care device. These advantages warrant further investigation on its applicability in specific environments, and in selected populations of patients. Points to be addressed in the future are the ability of the EABC® + i-Stat® system to estimate gas partial pressure variations in arterial blood from the analysis of EL arterialised capillary blood, which could be in fact more informative than actual values in certain situations, and the exploration of extended analytical possibilities of the system by exchanging the EABC® cartridge.

7. CONCLUSSIONS

The EABC® + i-Stat® system for the estimation of arterial blood gases is fast and secure. An age > 65 years old, vasoactive drugs (especially moderate doses of NA) and hemodynamic instability seem to affect sampling success rates in critically ill patients. There is an insuficient concordance with the standard for all gasometrical variables and lactate. Concordance is not improved in patients < 45 years old albeit outstanding success rates. These results limit the applicability of this new system in routine clinical practice of critically ill patients and questions the validity of arterialized capillary blood samples from the EL as an estimator of arterial values. Other advantages, such as safety, easiness of use, quickness and portability make this system potentially applicable to other scenarios on selected patients.

8. DISCLOSURES

This study has been funded by the European Space Agency via the Medical Projects and Technology Unit from the Crew Medical Support Office, European Astronaut Centre, Cologne (Germany). Funds were administered by the Fundació Parc Taulí, Sabadell (Spain) and delivered to the Critical Care Center, Corporació Sanitària Universitària Parc Taulí, Sabadell (Spain), were the project was developed. Main authors are employees of the Corporació Sanitària Universitària ParcTaulí.

9. APPENDIX

Demographic and clinical characteristics

Patients	**55**	
Male / Female	40 / 15	72.7 / 27.3%
Age	62.75	(24 - 83)
Comorbidities		
Arterial hypertension	23	41.8%
Diabetes	19	34.5%
Chronic cardiac failure	4	7.3%
Severe vasculopathy	4	7.3%
Renal insufficiency	5	9.1%
Diagnostic at ICU admission		
Severe sepsis	21	38.1%
Respiratory insufficiency	7	12.7%
Polytrauma	7	12.7%
Neurological	6	10.8%
Cardiogenic shock	5	9.1%
Other	5	9.0%
Cardiac arrest	3	5.4%
Haemorrhagic shock	1	1.8%
Mechanical ventilation variables		
PEEP (cm H_2O)	7.13	(4-12)
FiO_2	0.36	(0.21 - 0.66)
Minute Volume (L/min)	9	(5.5 - 19)

Table 1: Demographic and clinical characteristics of study patients.

Study clinical variables

Apache II	18.28	(3 - 34)
Mean arterial pressure (mmHg)	80	(57-113)
Cardiac index (l/min/m2)	3.23	(1-5.9)
Fluid balance 3h *	0.80	(-4.8 - 4.6)
Lactate (mg/dl)	18.75	(6-71)
Lactate >22mg/dl	10	18%
Sepsis	32	58.2%
Platelets (pq x 10^3 / dl)	226	(54 - 669)
Prothrombine time (ratio)	1.2	(1 - 1.9)
Prophylactic Anticoagulant	40	72.7%
Antiplatelet drugs	6	10.9%
Vasoactive drugs	36	65.5%
Noradrenaline	30	83.3%
NA dose μ g/kg/min	0.49	0.02 - 3.02
Other Vasoconstriction drugs	3	8.2%
Inotropic drugs	5	13.8%
Vasodilation drugs	2	5.5%

Table 2: Clinical variables * Fluid balance 3h before sampling (ml/Kg/h).

Univariate analysis

	RR	p value
Age > 65 years	1.93	0.04
Diabetes	1.9	0.03
Vasoactive drugs	2	0.06
Vasoconstrictors	1.75	0.09
NA > .22 μ g/kg/min	2.37	0.02
Sepsis	1.43	0.26
Lactate > 22mg/dl	1.42	0.38
MAP (<65 or >90 mmHg)	0.83	0.57
APACHE II	4.22*	0.16
NA dose (μ g/kg/min)	0.17*	0.80

Table 3: Relative Risk of sampling failure for main studied variables. No CI 95% is available for qualitative variables using Chi-square test.
*For quantitative variables APACHE II and NA dose, mean difference is presented.

Multivariate analysis

Variable	Exp. B	CI 95%	p value
Age	0.95	0.9 - 1	0.05
Diabetes	0.42	0.1 - 1.4	0.17
Vasoactive drugs	0.40	0.1 - 14	0.17

Table 4: Multivariate analysis of variables which showed significance in univariate analysis. The variable Vasoactive drugs was also included for its proximity to signification but NA > 0.22 μ g/kg/min was not since it was implicit in the vasoactive drugs variable.

Sampling success / failure and hemodynamic instability

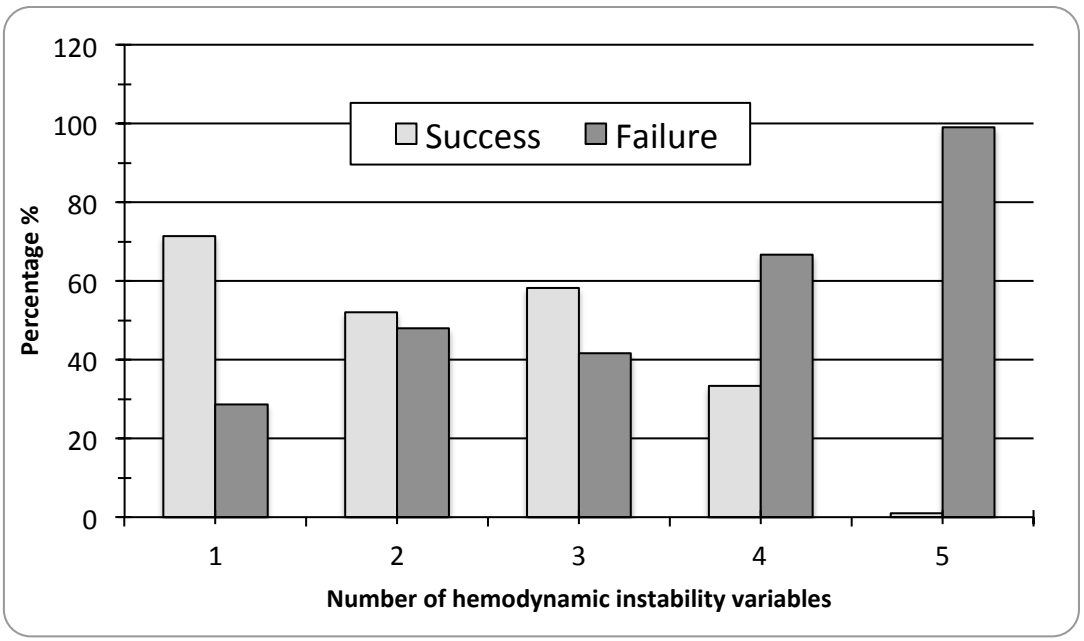


Figure 1: Change of sampling success / failure ratio depending on the number of variables of hemodynamic instability associated (HR > 130 beats x min., MAP < 65 mmHg, CI < 2.5 l/min/m2, Lactate > 22mg/dl, vasoactive drug treatment)

Evolution of success / failure ratio throughout the study

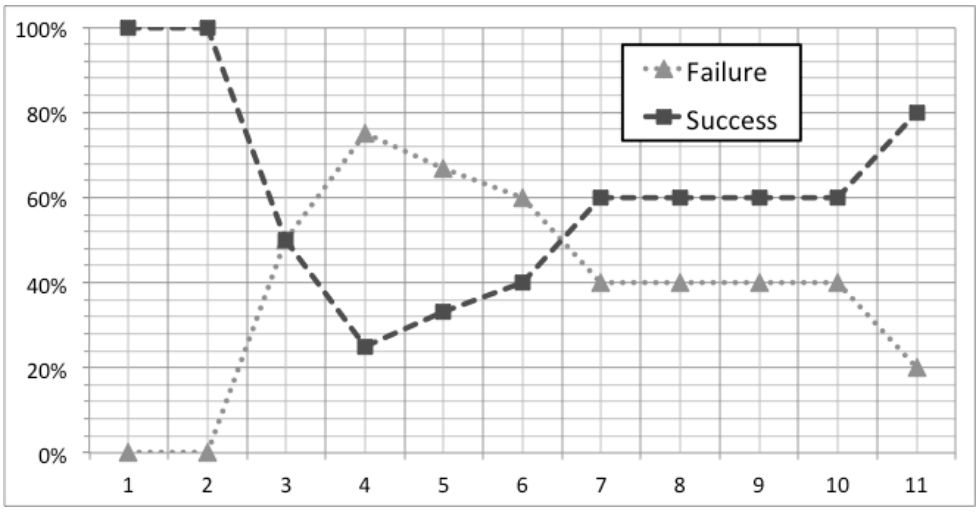


Figure 2: Success / failure percentages throughout the study. Groups of 5 patients were chronologically built (x-axis).

Table 4: Blood gas analysis and lactate in 31 ICU patients

	ABL700	EABC	SD	R^2	β	Mean dif.	CI 95%	p value
pH	7.44	7.44	0.05	0.75	0.86	0.006	- 0.004 / 0.015	0.21
PCO_2	37.4	37.3	6.39	0.80	0.86	0.08	- 1 / 1.1	0.87
PO_2	80.4	69.2	8.98	0.53	0.73	11.15	8.12 / 14.2	< 0.01
SO_2	95.9	93.8	2.38	0.37	0.60	2.1	1.3 / 2.8	< 0.01
HCO_3^-	26.0	25.4	4.17	0.88	0.94	0.63	0.05 / 1.2	0.03
BE	1.6	1.2	4.59	0.91	0.95	0.39	0.1 / 0.9	0.15
Lactate	13.3	12.2	6.47	0.95	0.97	1.1	0.6 / 1.6	< 0.01

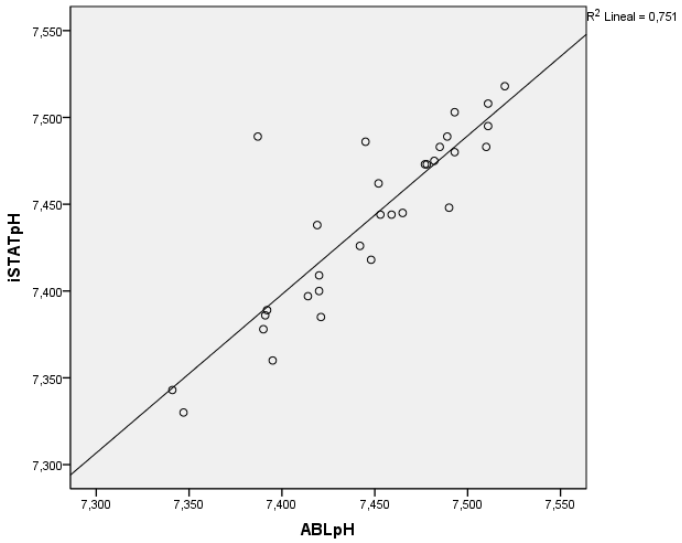
Concordance analysis between EABC® + i-Stat® and ABL 700® systems.

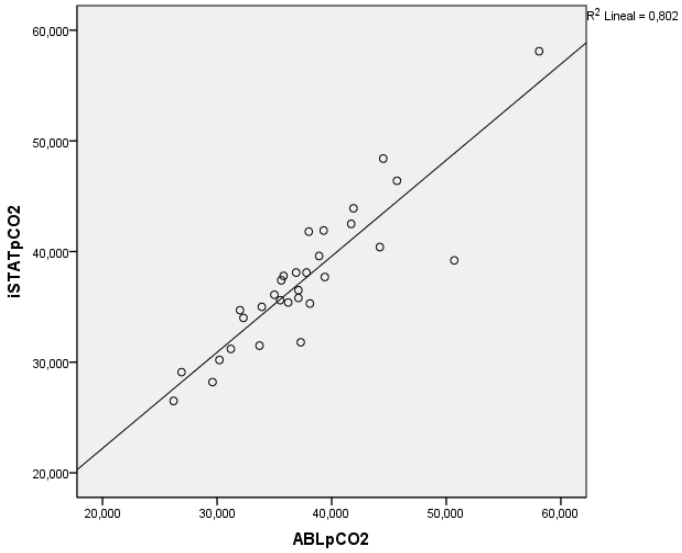
Table 5: Blood gas analysis and lactate in patients < 45 years

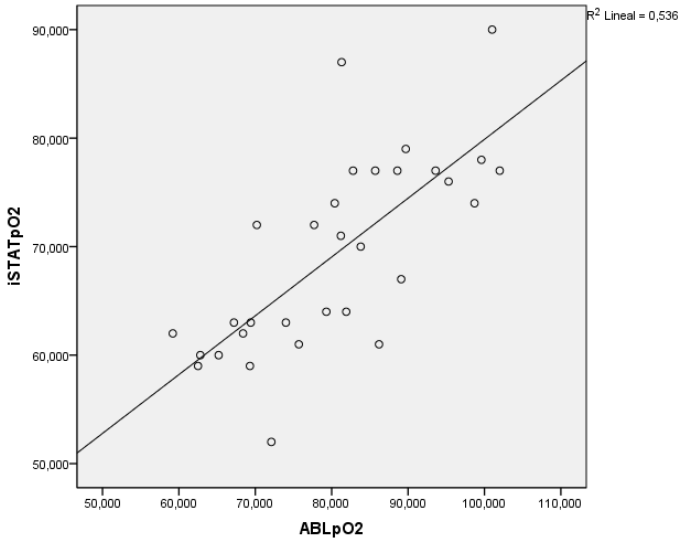
	ABL700	EABC	SD	R^2	β	Mean dif.	CI 95%	p value
pH	7.45	7.46	0.03	0.12	0.34	- 0.008	- 0.04 / 0.02	0.55
PCO_2	39.2	37.9	3.82	0.18	0.43	1.23	- 2.8 / 5.3	0.49
PO_2	84	72.5	13.2	0.49	0.70	11.53	3.5 / 19.5	0.01
SO_2	96.5	94.3	2.82	0.40	0.63	2.18	0.3 / 4	0.02
HCO_3^-	27.5	27.3	2.32	0.73	0.85	0.25	- 1.1 / 1.6	0.68
BE	3.4	3.6	2.50	0.80	0.89	- 0.15	- 1.5 / 1.2	0.81
Lactate	11.8	10	3.45	0.84	0.92	1.72	0.5 / 2.8	0.01

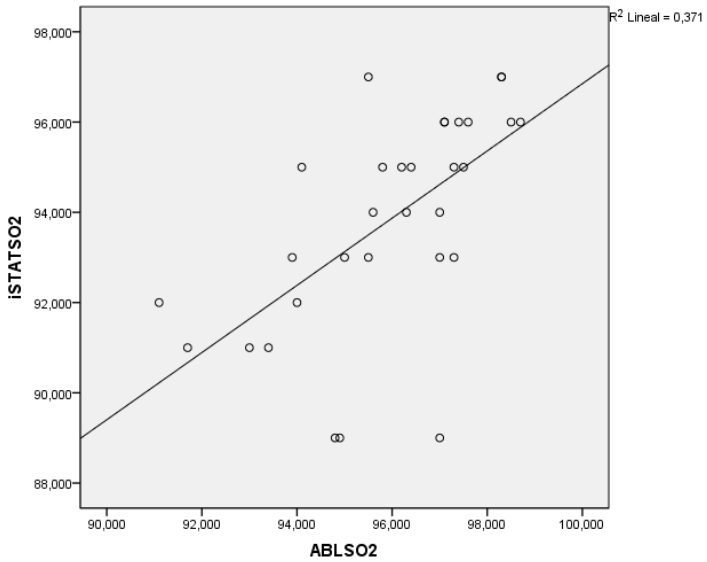
Concordance analysis between EABC® + i-Stat® and ABL 700® systems in patients < 45 years old

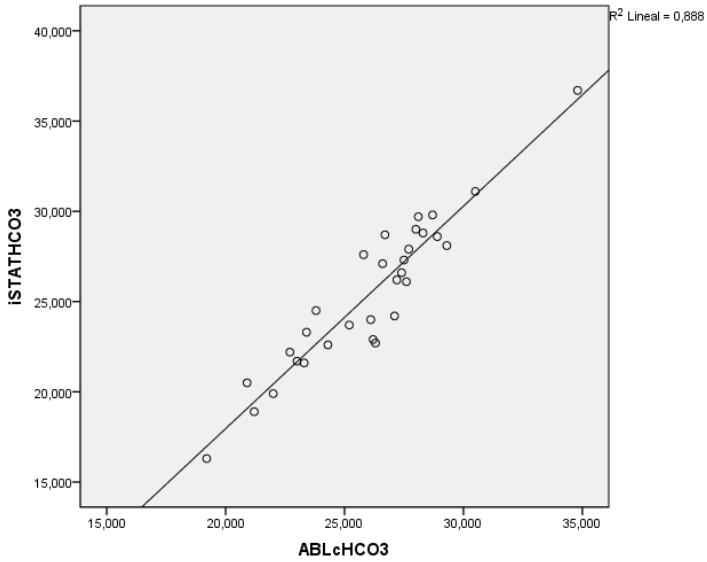
Regression plots - All patients

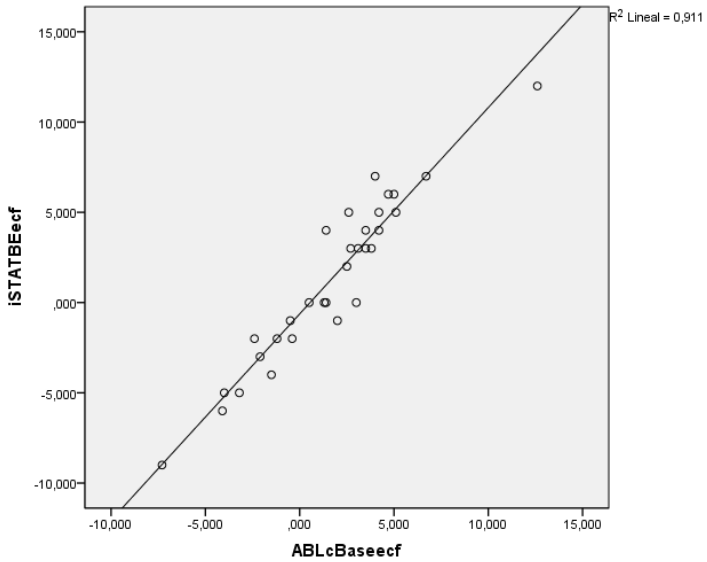


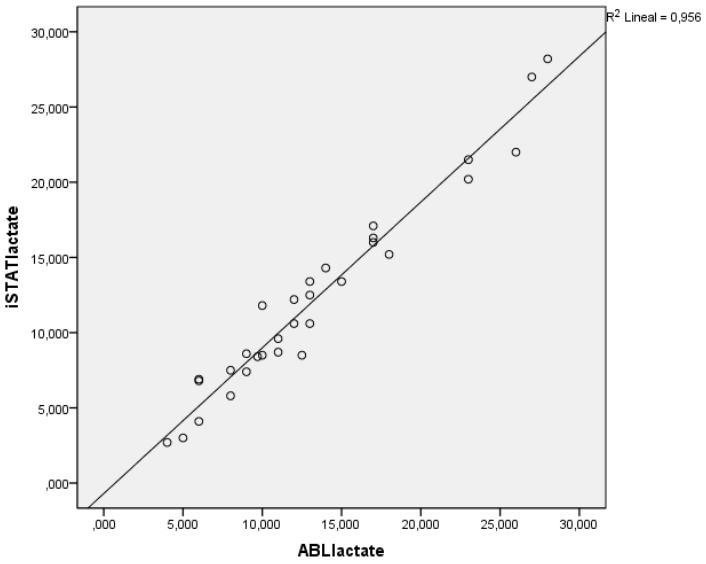




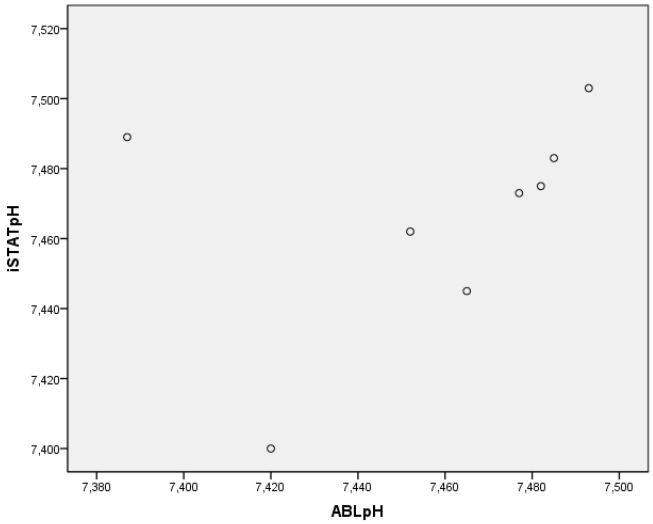

R² Lineal = 0,371
iSTATSO2
ABLSO2
98,000
96,000
94,000
92,000
90,000
88,000
90,000
92,000
94,000
96,000
98,000
100,000

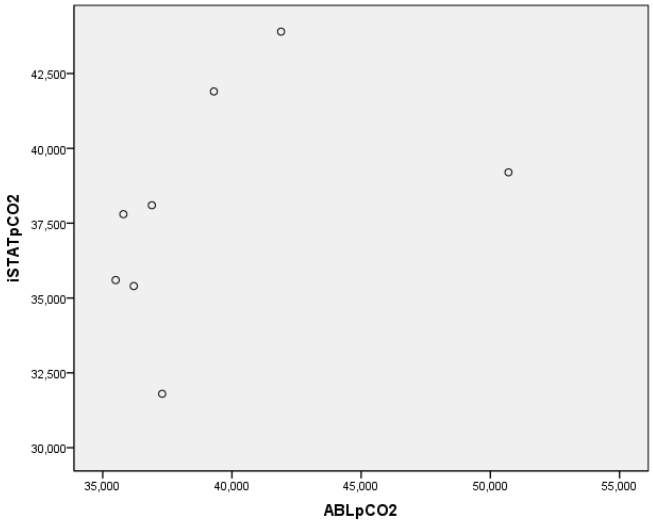

R² Lineal = 0,888
iSTATHCO3
ABLcHCO3
40,000
35,000
30,000
25,000
20,000
15,000
15,000
20,000
25,000
30,000
35,000

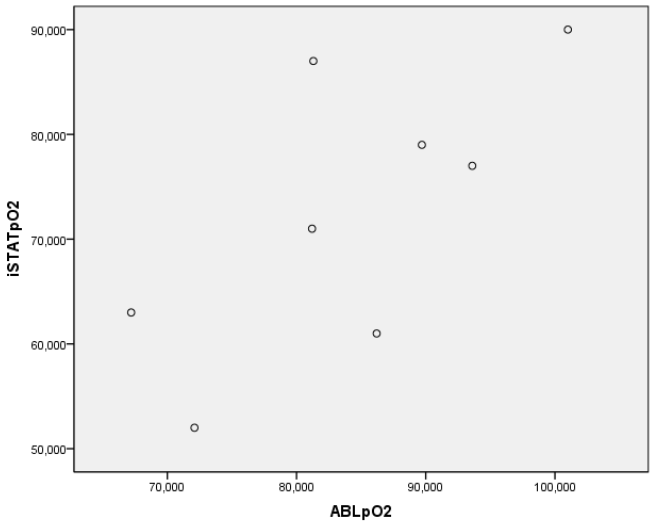

R² Lineal = 0,911
iSTATBEecf
ABLcBaseecf
15,000
10,000
5,000
,000
-5,000
-10,000
-10,000
-5,000
,000
5,000
10,000
15,000

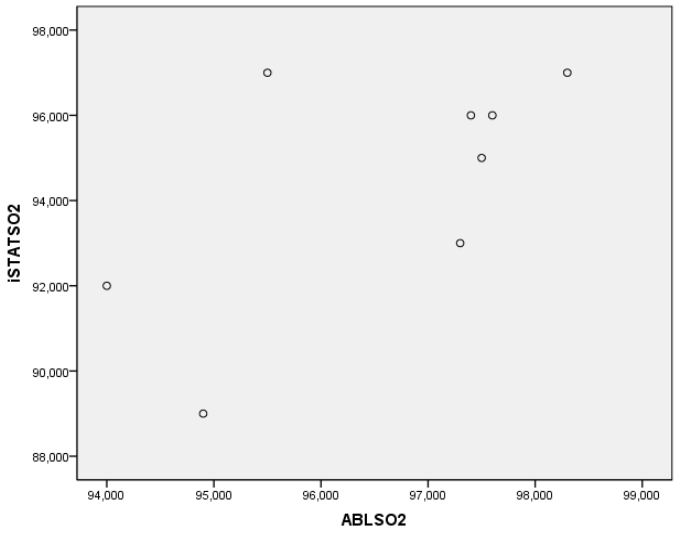

R2 Lineal = 0,956
30,000
25,000
20,000
15,000
10,000
5,000
,000
iSTATlactate
,000
5,000
10,000
15,000
20,000
25,000
30,000
ABLlactate

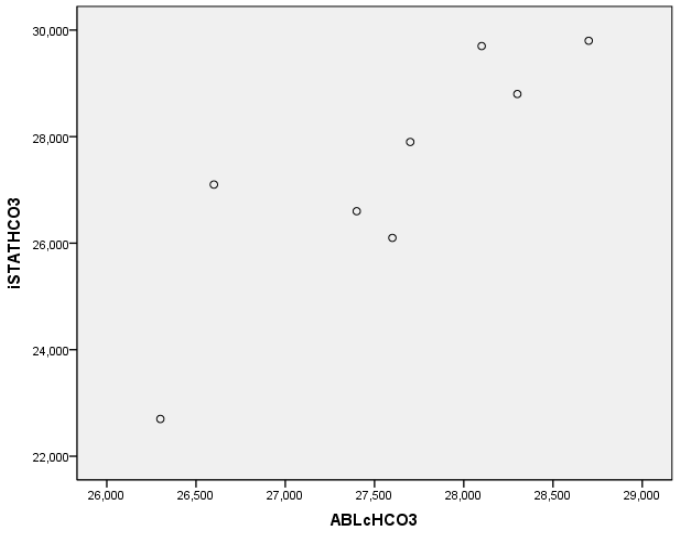
Regression plots - Patients < 45 years old (n=8)

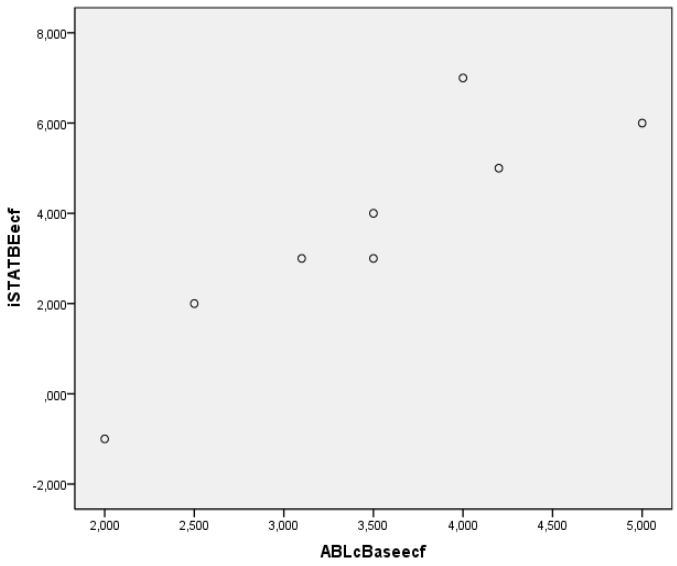


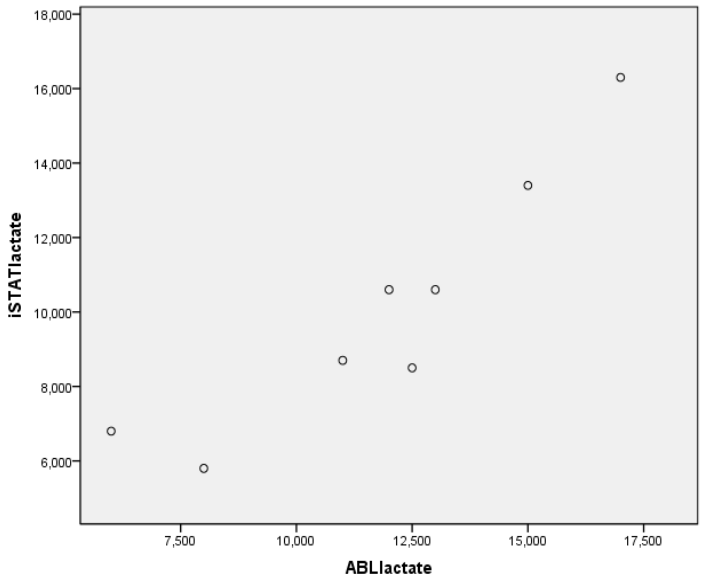




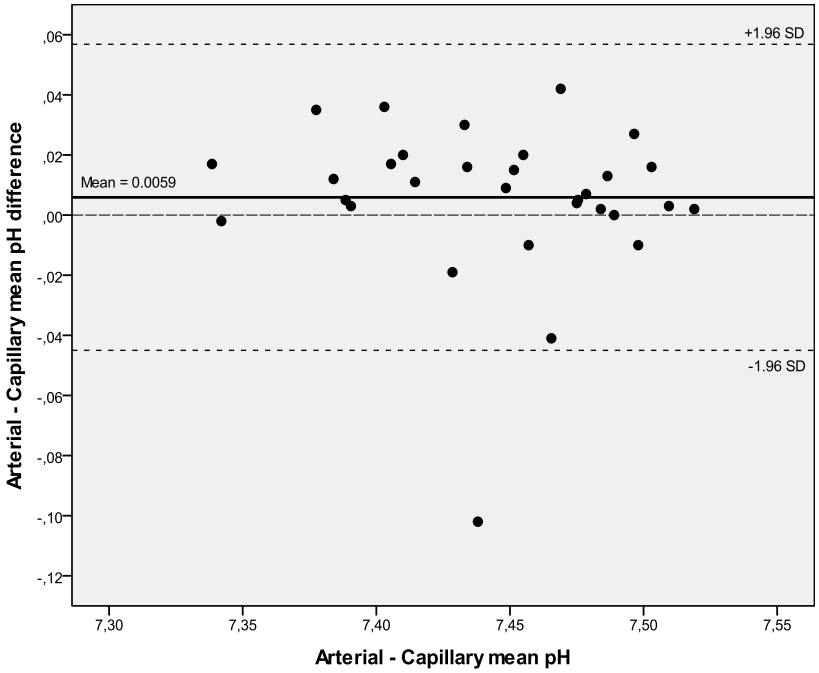

iSTATSO2
98,000
96,000
94,000
92,000
90,000
88,000
94,000
95,000
96,000
97,000
98,000
99,000
ABLSO2

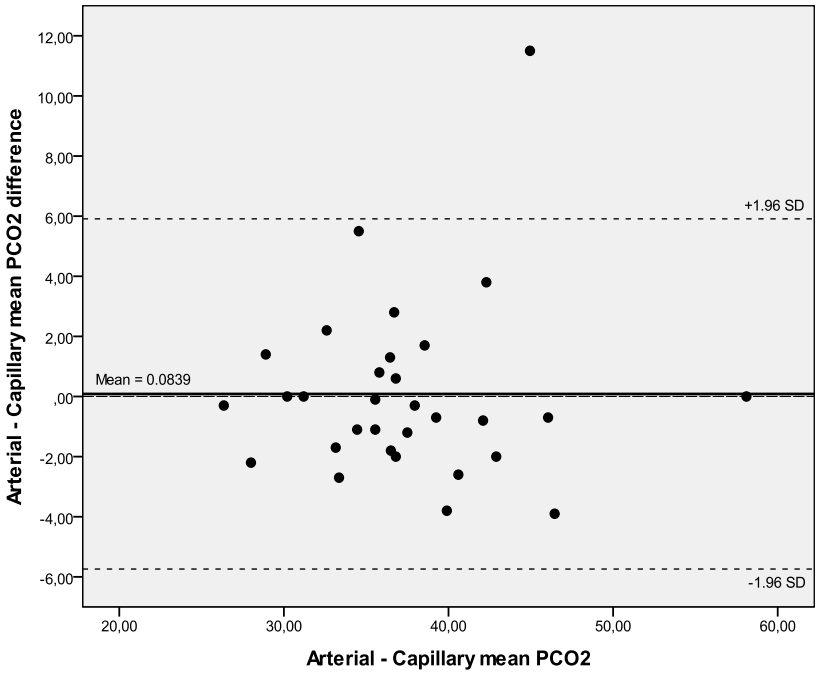

iSTATHCO3
30,000
28,000
26,000
24,000
22,000
26,000
26,500
27,000
27,500
28,000
28,500
29,000
ABLcHCO3

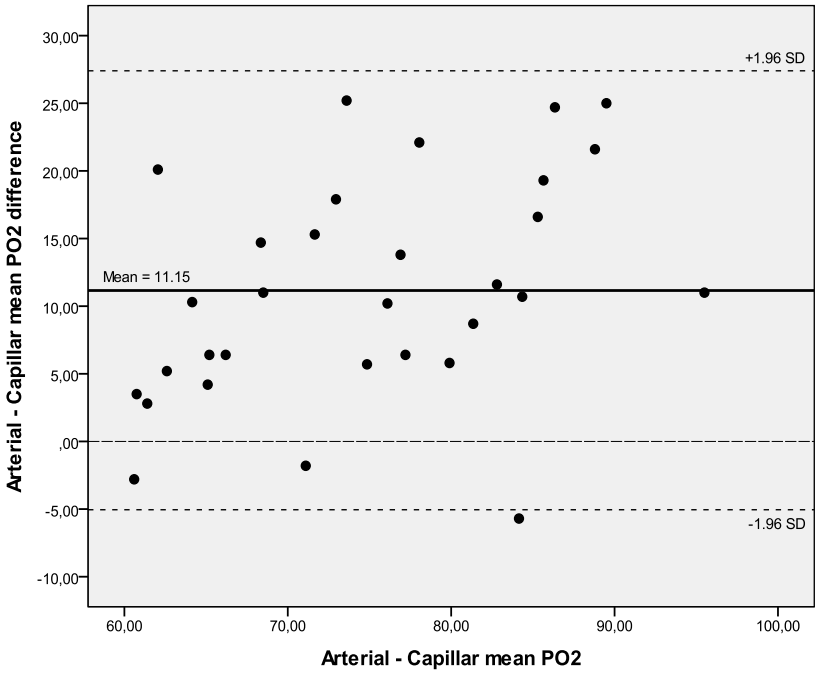

iSTATBEecf
8,000
6,000
4,000
2,000
,000
-2,000
2,000
2,500
3,000
3,500
4,000
4,500
5,000
ABLcBaseecf

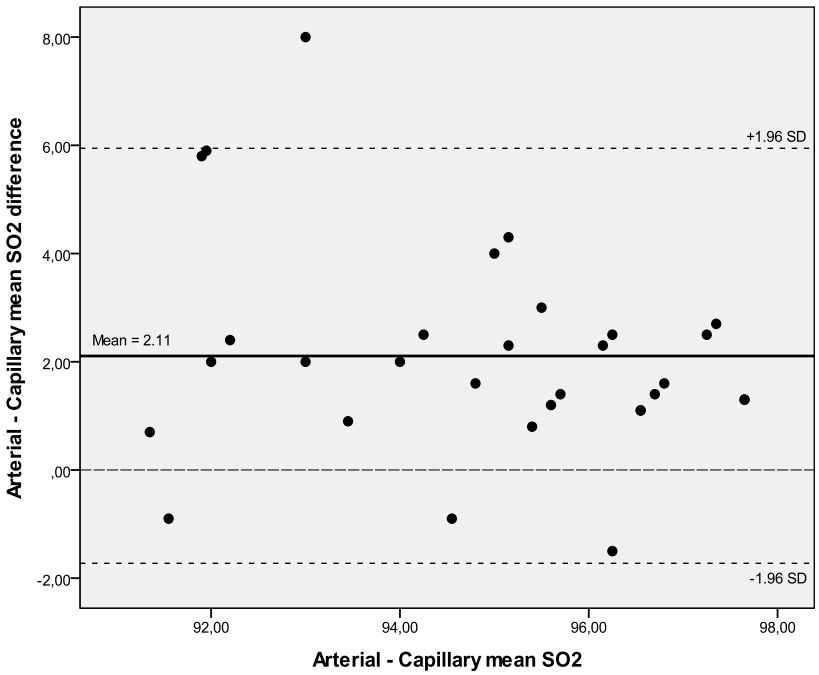

18,000
16,000
14,000
12,000
10,000
8,000
6,000
iSTATlactate
7,500
10,000
12,500
15,000
17,500
ABLlactate

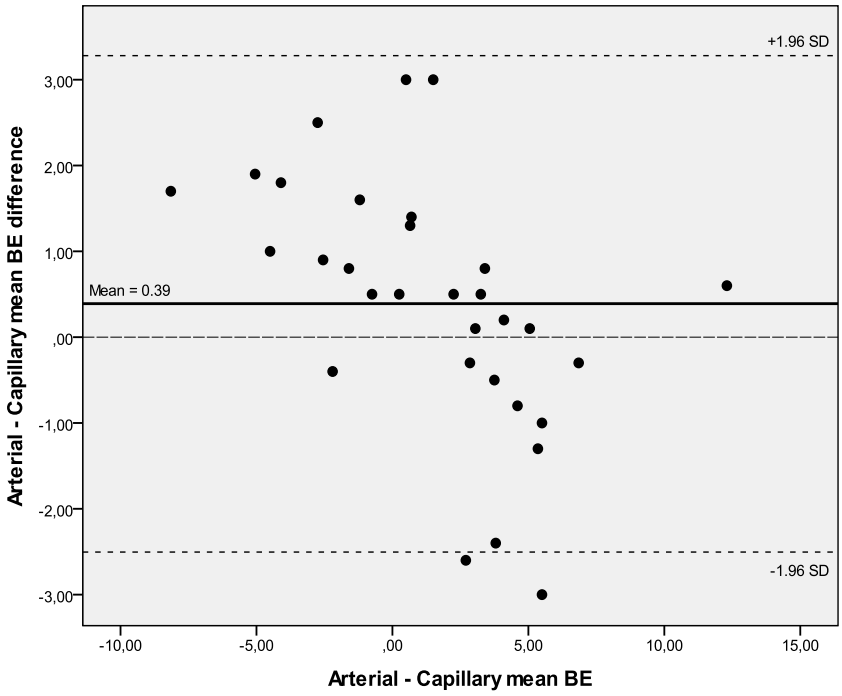
Bland-Altman plots

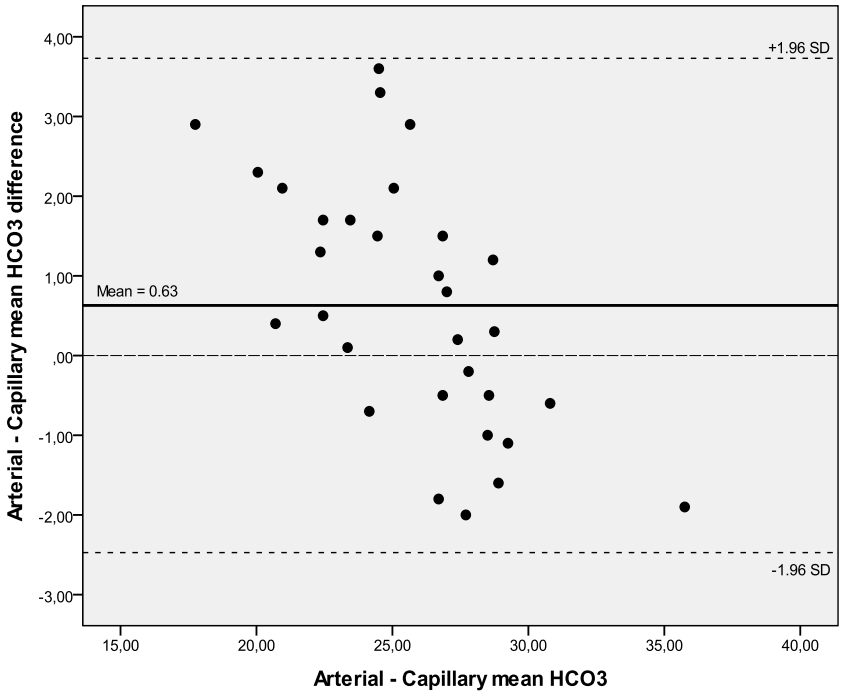


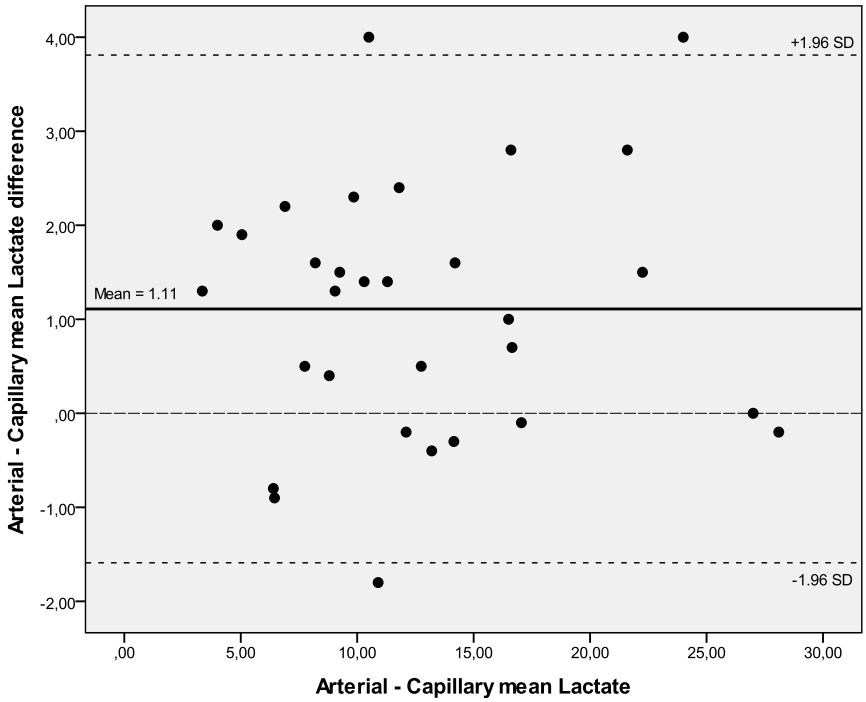



30,00
25,00
20,00
15,00
10,00
5,00
,00
-5,00
-10,00
+1.96 SD
Mean = 11.15
-1.96 SD
60,00
70,00
80,00
90,00
100,00
Arterial - Capillar mean PO2 difference
Arterial - Capillar mean PO2


8,00
6,00
4,00
2,00
,00
-2,00
+1.96 SD
Mean = 2.11
-1.96 SD
92,00
94,00
96,00
98,00
Arterial - Capillary mean SO2 difference
Arterial - Capillary mean SO2


+1.96 SD
Mean = 0.39
-1.96 SD
Arterial - Capillary mean BE difference
Arterial - Capillary mean BE
3,00
2,00
1,00
,00
-1,00
-2,00
-3,00
-10,00
-5,00
,00
5,00
10,00
15,00


+1.96 SD
Mean = 0.63
-1.96 SD
Arterial - Capillary mean HCO3 difference
Arterial - Capillary mean HCO3
4,00
3,00
2,00
1,00
,00
-1,00
-2,00
-3,00
15,00
20,00
25,00
30,00
35,00
40,00


+1.96 SD
Mean = 1.11
-1.96 SD
4,00
3,00
2,00
1,00
,00
-1,00
-2,00
,00
5,00
10,00
15,00
20,00
25,00
30,00
Arterial - Capillary mean Lactate difference
Arterial - Capillary mean Lactate

10. REFERENCES

[1] Lilienthal JI, Riley RL. On the determination of arterial oxygen saturations from samples of capillary blood. J Clin Invest 1944; 23:904-6

[2] Russomano T. A device for sampling arterialized earlobe blood in austere environments. Aviat Space Environ Med. 2006 Apr;77(4):453-5

[3] Russomano T, Ernsting J. The arterialized ear lobe blood samples for blood gas tensions - a technique for medical emergencies in microgravity. IAF Proceedings, 47th IAC Congress, Beijing, China. International Astronautical Federation, October 1996

[4] Falcão F. Clinical validation of the earlobe arterialized blood collector. Aviation, Space, and Environmental Medicine x Vol. 81, No. 11 x November 2010

[5] Dellinger RP, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2008. Crit Care Med. 2008 Apr;36(4):1394-6

[6] Youden WJ. Index for rating diagnostic tests. Cancer. 1950 Jan;3(1):32-5

[7] Altman DG, Bland JM. Measurement in Medicine: the Analysis of Method Comparison Studies. The Statistician. 1983;32:307-317

[8] McEvoy JD, Jones NL. Arterialized capillary blood gases in exercise studies. Med Sci Sports. 1975 Winter;7(4):312-5

[9] Fajac I, et al. Blood gas measurement during exercise: a comparative study between arterialized earlobe sampling and direct arterial puncture in adults. Eur Respir J. 1998;11:712-15

[10] Dall'Ava-Santucci J, et al. Is arterialized earlobe blood PO_2 an acceptable substitute for arterial blood PO_2?. Eur Respir J. 1996;9:1329-30

[11] Eaton T, et al. The clinical utility of arterialized earlobe capillary blood in the assessment of patients for long-term oxygen therapy. Respir Med. 2001;95(8):655-60

[12] Pitkin A, Roberts C, Wedzicha J. Arterialised earlobe blood gas analysis: an underused technique. Thorax 1994; 49:364-6

[13] MacIntyre J, Norman JN, Smith G. Use of capillary blood in measurement of arterial PO2. Br Med J. 1968 Sep 14;3(5619):640-643

[14] Sauty A, et al. Differences in PO_2 and PCO_2 between arterial and arterialized earlobe samples. Eur respir J. 1996;9:186-9

[15] Zavorsky GS, et al. Arterial versus capillary blood gases: a meta-analysis. Respir Physiol Neurobiol. 2007 March;155(3):268-279

[16] Honarmand. Prediction of arterial blood gas values from earlobe arterialized blood gas values in patients treated with mechanical ventilation. Indian J Crit Care Med. 2008. Jul;12(3):96-101.

[17] Phillip E, et al. Human endothelial function and microvascular ageing. Exp Physiol. 2009;94(3):311–316