



Reducing pain by using venous blood gas instead of arterial blood gas (VEINART): a multicentre randomised controlled trial

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Handling editor Edward Carlton

► Additional material is published online only. To view, please visit the journal online (<http://dx.doi.org/10.1136/emered-2019-209287>).

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Received 11 November 2019

Revised 23 June 2020

Accepted 24 June 2020

Published Online First

5 August 2020

ABSTRACT

Introduction Venous sampling for blood gas analysis has been suggested as an alternative to arterial sampling in order to reduce pain. The main objective was to compare pain induced by venous and arterial sampling and to assess whether the type of sampling would affect clinical management or not.

Methods We performed an open-label randomised multicentre prospective study in four French EDs during a 4-week period. Non-hypoxaemic adults, whose medical management required blood gas analysis, were randomly allocated using a computer-generated randomisation list stratified by centres with an allocation ratio of 1:1 using random blocks to one of the two arms: venous or arterial sampling. The primary outcome was the maximal pain during sampling, using the visual analogue scale. Secondary outcomes pertained to ease of sampling as rated by the nurse drawing the blood, and physician satisfaction regarding usefulness of biochemical data.

Results 113 patients were included: 55 in the arterial and 58 in the venous sampling group. The mean maximal pain was 40.5 mm±24.9 mm and 22.6 mm±20.2 mm in the arterial group and the venous group, respectively, accounting for a mean difference of 17.9 mm (95% CI 9.6 to 26.3) ($p<0.0001$). Ease of blood sampling was greater in the venous group as compared with the arterial group ($p=0.02$). The usefulness of the results, evaluated by the prescriber, did not significantly differ ($p=0.25$).

Conclusions Venous blood gas is less painful for patients than ABG in non-hypoxaemic patients. Venous blood gas should replace ABG in this setting.

Trial registration number NCT03784664.

INTRODUCTION

Pain is one of the major complaints of patients during medical care, blood sampling being one of the most frequent causes.¹ Sampling can be performed in a vein or in an artery. Arterial sampling is mostly used for blood gas and acid-base analysis (pH, HCO₃⁻, PaCO₂, PaO₂). However, it is a painful procedure that can be challenging to perform.² It may rarely be responsible for major vascular damage such as thrombosis or pseudoaneurysm formation.^{3,4}

To reduce pain related to arterial blood sampling, a variety of methods have been studied such as local application of anaesthetic cream (lidocaine,

Key messages

What is already known on this subject

- The performance characteristics of venous blood gas (VBG) sampling, and the clinical utility of the results, is often sufficient to safely guide treatment decisions in the ED.
- Venous sampling for VBG analysis has been suggested as an alternative to ABG analysis in order to reduce pain.
- No randomised controlled trial specifically evaluated the contribution of VBG versus ABG to the pain experienced by patient in EDs.

What this study adds

- In this randomised controlled trial with 113 patients comparing arterial and venous sampling for blood gases analysis, we demonstrated that VBG are less painful than ABG.
- The physicians felt the biological results equally useful.
- This is a strong argument in favour of using VBGs as standard care in non-hypoxaemic patients in ED.

xylocaine) or subcutaneous lidocaine injection before procedure. Since ABGs are often performed in emergent situations, and because anaesthetic cream must be applied at least 1 hour before puncture, this method is not likely to be used in the ED. In a prior study, subcutaneous lidocaine anaesthesia did not provide a significant reduction of pain before radial artery puncture.⁵ In a study using ultrasound guidance for ABG, there was no significant reduction in the pain, the rate of immediate complications or the physician's satisfaction.⁶

Venous blood gas (VBG) analysis has been suggested as an alternative to ABG analysis in order to reduce pain. Agreement between venous and arterial samples for pH makes them clinically interchangeable, and agreement for bicarbonate is satisfactory.⁷ The performance characteristics of VBG sampling, and the clinical utility of the results, is thus often sufficient to safely guide treatment decisions in the ED. However, most EDs in France perform ABG when acid-base disorder is suspected.



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To cite: Chauvin A, Javaud N, Ghazali A, et al. *Emerg Med J* 2020;**37**:756–761.



Table 1 Characteristics of patients on inclusion in the VEINART study

	All patients n (%) n=113	Patients with arterial sampling n (%) n=55	Patients with venous sampling n (%) n=58
Age (median (min to max))	62 (19 to 103)	69 (19 to 95)	59 (19 to 103)
Male	56 (49.6)	29 (52.7)	27 (46.6)
Medical history			
Heart disease	47 (41.6)	23 (41.8)	24 (41.4)
Chronic lung disease	36 (31.9)	11 (20.0)	25 (43.1)
Neoplastic disease	11 (9.7)	9 (16.4)	2 (3.4)
Metabolic disease	45 (39.8)	26 (47.3)	19 (32.8)
Hospitalisation after ED consultation	74 (65.5)	38 (69.1)	36 (62.1)
Diagnosis hypotheses motivating the blood sampling*			
No lactic metabolic acidosis	27 (24.1)	14 (25.5)	13 (22.8)
Lactic metabolic acidosis	25 (22.3)	14 (25.5)	11 (19.3)
Metabolic alkalosis	11 (9.9)	2 (3.6)	9 (15.8)
Respiratory acidosis	24 (21.4)	13 (23.6)	11 (19.3)
Respiratory alkalosis	25 (22.3)	12 (21.8)	13 (22.8)
Predictive criterion of difficulty in sampling			
Intravenous drug abuse	5 (4.4)	3 (5.5)	2 (3.4)
Others	4 (3.5)	2 (3.6)	2 (3.4)
Analgesic within 4 hours previously sampling†			
None	83 (74.8)	41 (75.9)	42 (73.7)
Level 1	21 (18.9)	10 (18.5)	11 (19.3)
Level 2	5 (4.5)	2 (3.7)	3 (5.3)
Level 3	2 (1.8)	1 (1.9)	1 (1.7)

*One missing data in arterial group.

†Two missing data: one in each group.

There is some controversy as to whether venous sampling is less painful. A multicentre observational study did not show reduction of pain with venous sampling.⁸ In contrast, a prospective cohort study of patients with chronic obstructive pulmonary disease found less pain when VBG was performed as compared with ABG.⁹ A randomised control study was therefore needed.

We hypothesised that, in the absence of hypoxaemia (normal oxygen saturation evaluated by pulse oximetry), a VBG would be less painful, easier to perform and would provide sufficient data for treatment decisions in comparison to ABG in the ED.

The main objective of this study was to compare venous and arterial sampling in terms of pain at the time of blood draw in the ED. Secondary objectives were to evaluate the ease of venous sampling for the sampler and the usefulness of biochemical results for physicians.

METHODS

Study design and setting

We performed an open-label, multicentre, randomised controlled study comparing venous and arterial sampling when blood gas analysis was judged necessary for optimal care among patients with normal pulse oximetry (>95%) breathing room air. Recruitment took place in four university-affiliated hospitals in Paris during a 4-week period between 21 January 2019 and 22 March 2019. Each ED receives between 45 000 and 90 000 annual visits. Before this study, blood gas analysis was routinely performed on arterial blood whatever the diagnostic hypothesis in these four EDs.

Patient and public involvement

This research was designed without direct patient involvement. Discussions with patients in the EDs regarding the pain related to arterial sampling were the basis of our project. Patients were not invited to comment on the study design and were not consulted to develop patient relevant outcomes or interpret the results.

Selection of participants

Inclusion criteria were: blood gas analysis prescribed by an emergency physician, percutaneous oxygen saturation higher than 95% with room air, age ≥ 18 years, GCS of 15. Exclusion criteria were patients under legal protection or unable to receive information, or with no social security insurance or who refused to participate.

Patients received verbal and written information about the study by an investigator. In case of verbal consent from the patient, inclusion was notified in the medical file followed by randomisation performed by the investigator.

Randomisation

The study was designed as a two-arm trial for evaluating the pain felt by the patient during the sampling. The subjects were randomly allocated using a computer-generated randomisation list stratified by centres with an allocation ratio of 1:1 using random blocks.

Intervention

As per usual care, each patient presenting to a participating ED first sees an intake nurse who records the reason for consultation and vital parameters: BP, pulse rate, RR, temperature, pulse oximetry and pain if present, on a visual analogue scale (VAS). All these elements were recorded in the emergency file prior to any procedures.

After consent and enrolment in the study, the patient was randomly allocated to one of the two arms: venous or arterial sampling. Sampling technique was performed according to local standards without specific recommendation. In the four EDs, venous sampling is obtained using a tourniquet. The arterial blood sampling material was similar in each centre. The nurse in charge of drawing blood performed either venous or arterial sampling (on the radial site exclusively for the later). The diameter for arterial puncture needle was 22 G, whereas the diameter for venous puncture varied between 20 and 25 G. Prior to sampling, the nurse recorded a prediction for the difficulty of the blood draw in an electronic case report form.

Within 3 min of the blood draw, the nurse who drew the blood asked the patient to rate their maximal pain during the blood sampling, using a VAS. The VAS is a self-measurement scale in the form of a plastic strip of 10 cm graduated in mm.¹⁰ On the side of the strip presented to the patient, a cursor can be moved along a straight line, with one end corresponding to 'absence of pain' and the other to 'worst pain imaginable'. The patient is asked to position the cursor at the place that best describes their level of pain. On the other side of the plastic strip, there are millimetre graduations seen only by the assessor to allow quantitative evaluation of pain intensity expressed in millimetres. A higher score indicates a more intense pain.

The nurse recorded the patient's score in the electronic form, as well as whether or not ultrasound was used, number of sampling attempts, change of provider, failure of sampling, ease of sampling; ease of sampling was rated on a 4-point Likert scale (easy, moderately easy, difficult, very difficult) by the first nurse who attempted the blood draw. Later, the physician recorded

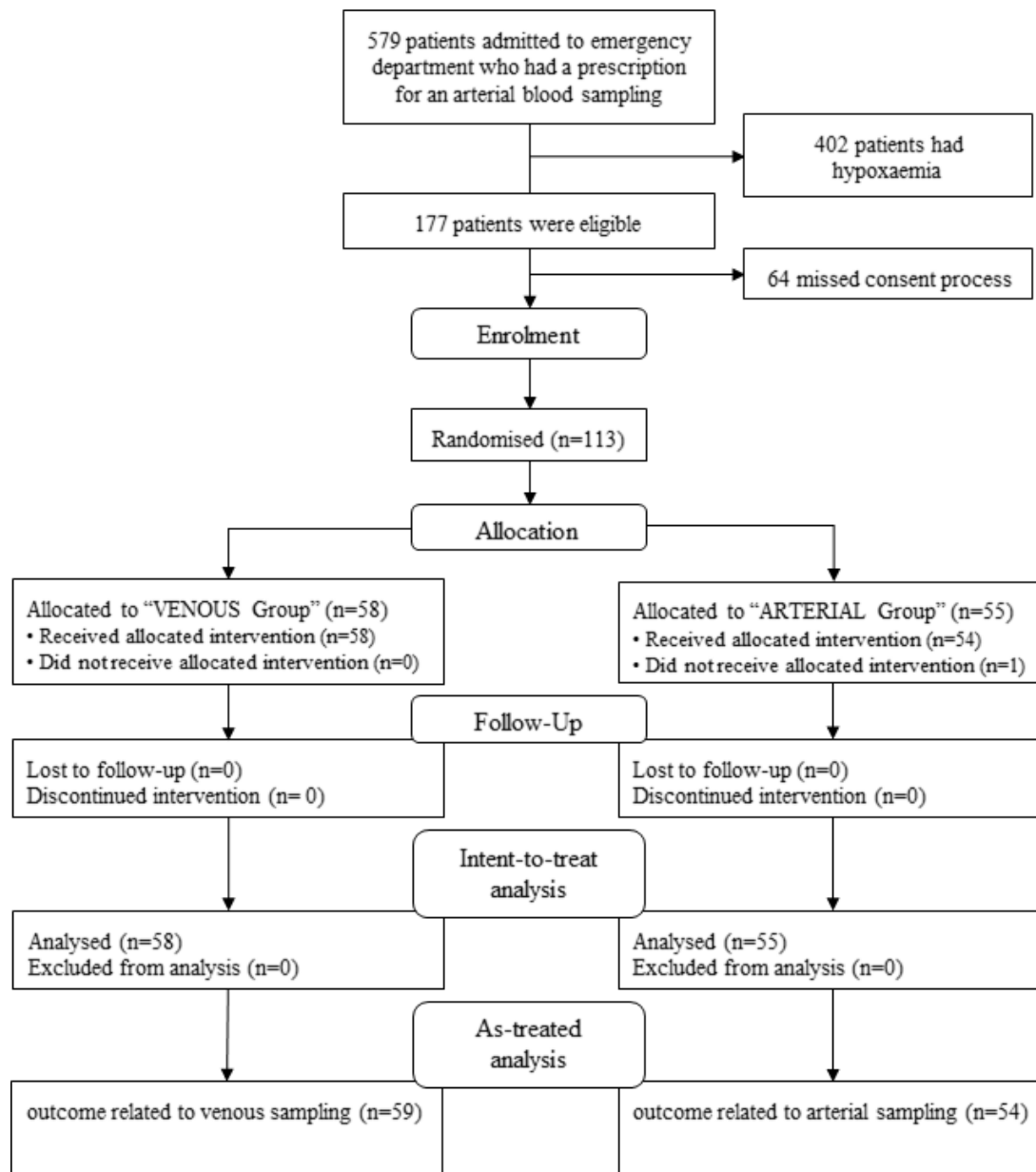


Figure 1 Flow chart.

the indication of the blood gas, usefulness of biochemical results (Likert scale 1–4, not at all satisfied, partly satisfied, satisfied, to very satisfied) and necessity to perform a second blood gas analysis. Outcomes assessments were not blinded.

Outcomes

The primary outcome was the maximal pain during blood sampling, recorded within 3 min after blood sampling, using the VAS.

Secondary outcomes pertained to sampling ease and physician satisfaction regarding usefulness of the biochemical data. Sampling ease was evaluated using number of sampling attempts to obtain a sufficient quantity of blood for analysis, number of providers involved in the sampling (change of provider) and failure of sampling. Physician rating of usefulness was based on the 4-point Likert scale completed in the Case Report Form (online supplementary file 1).

Sample size estimation and statistical analysis

To assess a clinically relevant difference in VAS of at least 20 mm and an SD of the difference of 28 mm, with a power of 90% and an alpha risk of 5%, 43 patients per arm were required for the study.^{11 12} Considering that the primary end point could be unavailable in 10%–15% of patients, we planned to enrol 100 patients (50 patients in each group).

Baseline variables are expressed as median with IQR and minimum and maximum for quantitative variables and as number and percentage for categorical variables.

Outcomes were compared between the two study arms using t-test for quantitative variables and Fisher's exact test for qualitative variables. In the intent-to-treat analysis, patients were analysed according to the group to which they were originally assigned. Two post hoc sensitivity analyses were performed. The first was an as-treated analysis where patients were analysed in the group corresponding to which actual blood sampling technique the recorded VAS was related to. The second was an

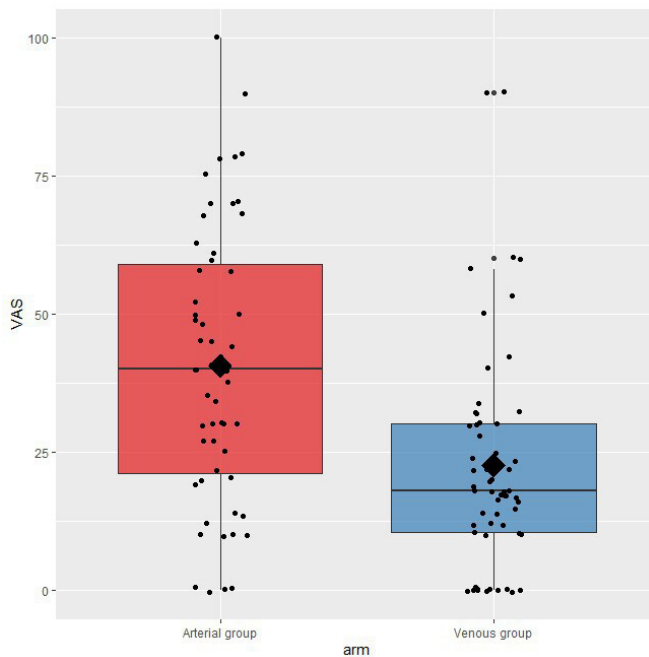


Figure 2 Box plot of visual analogue scale (VAS) according to randomised arm. Each plot represents an individual value. Diamonds represents the mean.

adjusted analysis that accounted for baseline imbalance despite randomisation, using a linear regression model.

All statistical analyses were two-tailed and performed on R V.3.5.2 (2018 The R Foundation for Statistical Computing). A *p* value <0.05 was considered statistically significant. The design, conduct and reporting of this study were done in compliance with the Consolidated Standards of Reporting Trials guidelines.¹³

RESULTS

A total of 113 patients were enrolled from the 4 EDs during the recruitment period: 55 (49%) in the arterial group and 58 (51%) in the venous group. In two patients, arterial sampling failed and they ultimately received VBG. For one patient, artery was not perceived and not punctured, and thus no pain score for the ABG was recorded. A pain score for the VBG was obtained. For the second patient, initial artery puncture failed and a pain score for arterial puncture was obtained.

The age ranged from 19 to 103 years, with median age 62 years. Half of the participants were male (*n*=56; *table 1*). Suspicion or exploration of metabolic acidosis was the main reason for blood gas analysis. Three-quarters of patients recruited in the study did not receive analgesics before the sampling and none had application of an anaesthetic cream. None of the providers used ultrasound for sampling.

Primary outcome

One hundred and thirteen patients were included in the intent-to-treat analysis. Both patients who ultimately had venous instead of arterial sampling were included in the as-treated analysis, one in the ABG group (because he received two blood sampling and the recorded VAS related to the arterial sampling) and the other in the VBG group (because artery was not punctured in the failed ABG attempts so the recorded VAS related to venous sampling) (*figure 1*).

In the intent-to-treat analysis, the mean maximal pain experienced by the patients during sampling was significantly lower in

patients undergoing VBG compared with ABG: $22.6 \text{ mm} \pm 20.2 \text{ mm}$ vs $40.5 \text{ mm} \pm 24.9 \text{ mm}$, respectively (*figure 2*). The mean difference was 17.9 mm (95% CI 9.6 to 26.3) (*p*<0.0001).

Secondary outcomes

Success on the first attempt was high and not statistically different between venous and arterial sampling groups (53 (91%) and 44 (80%), respectively; *p*=0.073). The provider doing the sampling was changed in three cases in each arm. Blood sampling for VBG was more frequently assessed as easy (*n*=40; 69%) by the nurse as compared with sampling for ABG (*n*=24; 44%; *p*=0.02). Eight samples (15%) were assessed as difficult or very difficult to obtain in the arterial group as compared with two samples (3%) in the venous group (*table 2*).

The physician's satisfaction with the usefulness of the information from the blood gas did not differ between groups, with most physicians describing the usefulness of the results as satisfying or very satisfying: 56 (97%) in the venous and 52 (95%) in the arterial groups (*p*=0.25, *table 2*).

One patient in each group had a second prescription of blood gas analysis. The patient in the venous group had an ABG whereas the patient in the arterial group had a VBG.

As-treated analyses

A sensitivity analysis moving one patient to the venous blood draw group showed that the mean maximal pain experienced was respectively $40.0 \text{ mm} \pm 24.8 \text{ mm}$ during the arterial blood draw and $23.3 \text{ mm} \pm 20.9 \text{ mm}$ during the venous blood draw. The mean difference was 14.3 mm (95% CI 8.1 to 25.3) (*p*=0.0002).

Despite randomisation, some baseline imbalance was observed between arms regarding age, medical history (namely chronic lung disease and neoplastic disease) and diagnosis hypotheses motivating the blood sampling. When adjusting for these imbalances, the mean difference between arterial and venous blood draw was 17.5 mm (95% CI 8.0 to 27.0) (*p*=0.0005).

DISCUSSION

The results of this study can be summarised as follows: venous sampling for blood gas analysis (i) is less painful for patients, (ii) is easier for the healthcare team and (iii) provides biochemical information considered sufficient by the physicians, in comparison with an arterial blood gas, for diagnosis and treatment decisions in non-hypoxaemic patients.

Our study is the first randomised controlled trial comparing the pain experienced during arterial or venous puncture in the context of an ED. An observational study which included 820 patients undergoing vein catheterisation or arterial puncture for blood gas was previously performed in EDs of two tertiary Spanish hospitals.⁸ This study did not observe a significant difference in pain between the groups. However, because of its observational design, comparison between the two groups was difficult and possibly biased. Two other studies performed in EDs confirmed the reliability of venous and arterial blood gas analysis for patients with diabetic ketoacidosis. However, pain and benefit for patients were not evaluated.^{14 15}

Eliminating pain is a cornerstone of patient care. Since the assessment of the acid-base balance and its evolution to guide treatment decisions for unstable patients is essential, we believe that research in this area is mandatory.¹⁶ Our study highlights the gap between recommendations on the management of pain and current practice.¹⁷

Agreement between venous and arterial samples is satisfactory for pH and bicarbonate level but, this agreement was poorer

Table 2 Primary and secondary outcomes of the VEINART study

	Arterial sampling n (%)	Venous sampling n (%)	P value	Effect size (95% CI)
Primary outcome				
Pain, mean±SD in mm	40.5±24.9	22.6±20.2	<0.0001	17.9 (9.6 to 26.3)
Pain, median (IQR 1–3) in mm	40.0 (21.0 to 59.0)	18.0 (10.5 to 30.0)		
Secondary outcomes				
Number of sampling attempts per patient*			0.07	
1	44 (80)	53 (93)		–13 (–25 to 0)
2	9 (16)	4 (7)		9 (–3 to 21)
3	2 (4)	0 (0)		4 (–3 to 10)
Change of sampling provider	3 (5)	3 (5)	1	0 (–9 to 10)
Failure of sampling	2 (4)	0 (0)	0.24	4 (–3 to 10)
Ease felt by the effector and the primary outcome				
			0.02	
Easy	24 (44)	40 (69)		–24 (–42 to –7)
Moderately easy	23 (42)	16 (28)		14 (–3 to 31)
Difficult	6 (11)	2 (3)		7 (–3 to 17)
Very difficult	2 (4)	0 (0)		4 (–3 to 10)
Prescriber's satisfaction				
			0.25	
Very satisfied	33 (60)	43 (74)		–14 (–31 to 3)
Satisfied	19 (35)	13 (22)		12 (–5 to 28)
Partly satisfied	3 (5)	2 (3)		2 (–7 to 11)
Not at all satisfied	0 (0)	0 (0)		0 (–5 to 5)

*One missing data in the venous group.

concerning lactate measurement.⁷ This discrepancy was previously described especially when peripheral venous lactate is found elevated whereas arterial blood lactate is normal.^{18–19} Arterial blood lactate concentration is a useful indicator of circulatory or liver failure, and of tissue hypoxia. Peripheral lactate determination cannot be substituted for arterial determination in all circumstances. Indeed, agreement between VBG and ABG values decline when venous lactate is ≥ 2 mmol/L. This results in a higher mean difference and broader limits of agreement between samples.²⁰ Then, determination of arterial lactate is more accurate for determining the magnitude of systemic lactic acidosis but a normal value of venous lactate concentration rules out increased arterial lactate concentration.²¹ This may prove useful for the screening of a hypoxic state such as severe sepsis. In the present work, clinicians suspected the occurrence of lactic metabolic acidosis in almost a quarter of the population (n=25). In all cases, physicians were satisfied or very satisfied by the usefulness of biochemical data in both groups and no 'rescue' arterial sampling was mandated in the venous group for lactic acidosis suspicion. This confirms the possibility of integrating VBG results with clinical findings to guide treatment decisions.^{9–22}

Our study has some limitations. First, we did not standardise the material used for arterial and venous punctures. The diameter for arterial puncture needle was 22 G whereas the diameter for venous puncture varied between 20 and 25 G. Moreover, we did not collect patient characteristics, which could have influenced the pain experienced during arterial puncture (eg, obesity, smokers or anxiety before puncture).¹¹ However, the randomisation should have equally distributed patients' characteristics. Another point that should be considered is the professional qualification of the provider drawing the blood, evidenced by their years of professional experience. Pain of the puncture seems to be dependent to the nurse's technical skill, and so the results might differ based on professional experience. Another limitation related to the unblinded evaluation of the pain. In fact, the nurse in charge of the patient gave the VAS. All pain scales

are subjective but the analogical pain or numerical pain scales are the most reliable strategy for assessing or monitoring pain in ED. Finally, this study included only patients with normal pulse oximetry. The results of this study cannot be generalised to hypoxaemic patients.

CONCLUSION

For the evaluation of acid-base balance in the context of emergencies, VBG is less painful for non-hypoxaemic patients than arterial blood sampling. Considering patient's comfort, we believe VBG should be the standard of care when blood gas analysis is required in EDs. ABG sampling should be reserved for situations where knowledge of PaO₂ or precise lactate level is mandatory. Additional studies with broader inclusion criteria could help define the place of VBG analysis for hypoxaemic patients.

Dissemination declaration

The results will be presented at international congresses and summarised on ClinicalTrials.gov. Dissemination to study participants is not possible since emergency departments do not follow patients in a long-term manner. In addition, no patient organisation dedicated to emergency departments exists in France.

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Acknowledgements We thank all patients who participated to the study. We thank Professor Didier Dreyfuss for critically revising the manuscript. We thank the Medical School Paris Diderot and the Dean Philippe Ruzsniwski for encouraging new pedagogical learning methods and for supporting the course "Initiation to Clinical Research".

Contributors TA, NB, JB, ACh, LD, DD, NK, CO, YS, MW, SG, JL, ACo and DR conceived the study and designed the trial. DR, ACh and JL supervised the conduct of the trial and data collection. TA, NB, JB, ACh, LD, DD, NK, CO, YS, MW, SG and DR undertook recruitment of participating centres. ACh, NJ, AG, SC, AA, PP and EC undertook recruitment of patients and managed the data, including quality control. JL provided statistical advice on study design and analysed the data. ACh and DR drafted the manuscript, and all authors contributed substantially to its revision. All authors approved the final manuscript. DR takes responsibility for the paper as a whole.

Funding This study has been designed and conducted in the context of an optional learning course ('Initiation to clinical research') from Paris Diderot Medical School, Université de Paris, Paris. Collection, analysis and interpretation of data were done under the supervision of an associate professor of the Biostatistics Department of Saint Louis Hospital, Assistance Publique—Hôpitaux de Paris, Paris, France (JL), who participated to the learning course. Overall, Université de Paris and Assistance Publique—Hôpitaux de Paris financially supported the research.

Disclaimer The sponsors had no other role regarding the trial.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval Authorisation by the institutional review board (Comité de Protection des Personnes) of the ethics committee Ile de France IV (IRB 00003835) was obtained (registered 24 December 2018; <https://clinicaltrials.gov/ct2/show/NCT03784664>). Patients received verbal and written information about the study by an investigator. In absence of opposition to participate, inclusion of the patient was notified in the medical file followed by randomisation.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request. Deidentified participant data are available on reasonable request (Anthony.chauvin@aphp.fr).

Author note Ten medical students developed the protocol under supervision during the university learning course "initiation to clinical research". Student authorship, identified in the title page, is in alphabetical order.

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