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The influence of undetected hemolysis on POCT potassium results in the emergency department

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Abstract

Objectives: This study aimed to evaluate discrepancies in potassium measurements between point-of-care testing (POCT) and central laboratory (CL) methods, focusing on the impact of hemolysis on these measurements and its impact in the clinical practice in the emergency department (ED).
Methods: A retrospective analysis was conducted using data from three European university hospitals: Technische Universitat München (Germany), Hospital Universitario La Paz (Spain), and Erasmus University Medical Center (The Netherlands). The study compared POCT potassium measurements in EDs with CL measurements. Data normalization was performed in categories for potassium levels (kalemia) and hemolysis. The severity of discrepancies between POCT and CL potassium measurements was assessed using the reference change value (RCV).
Results: The study identified significant discrepancies in potassium between POCT and CL methods. In comparing POCT normo- and mild hypokalemia against CL results, differences of −4.20 % and +4.88 % were noted respectively. The largest variance in the CL was a +4.14 % difference in the mild hyperkalemia category. Additionally, the RCV was calculated to quantify the severity of discrepancies between paired potassium measurements from POCT and CL methods. The overall hemolysis characteristics, as defined by the hemolysis gradient, showed considerable variation between the testing sites, significantly affecting the reliability of potassium measurements in POCT.
Conclusions: The study highlighted the challenges in achieving consistent potassium measurement results between POCT and CL methods, particularly in the presence of hemolysis. It emphasised the need for integrated hemolysis detection systems in future blood gas analysis devices to minimise discrepancies and ensure accurate POCT results.

Keywords: point-of-care testing (POCT); blood gas analysis (BGA); preanalytical error; hemolysis; potassium

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Introduction

Point-of-care testing (POCT) can be defined as the clinical laboratory tests conducted close to the site of patient care by personnel untrained in laboratory skills, that can lead to a possible change in the care of the patient with the ability to reduce turnaround time but without compromising the quality [1].

There are well-recognised advantages to the usage of these tests, particularly the rapid availability of results that allow for prompt clinical decision-making. The possibility of using unprocessed specimens with a small sample volume, preservation of sample quality, the possibility for more lean processes, and the ability to provide laboratory testing in a wider variety of sites or circumstances are other advantages of implementing POCT [2].

There are, however, some challenges associated with these types of tests, which could impact on patient care, including, in some cases, questionable reliability of POCT results [3].

Healthcare professionals running these tests are not necessarily qualified in laboratory discipline, but they need to be adequately trained and certified by laboratory professionals [2]. Nurses are the main users of POCT devices. During the last decades, an international shortage of qualified nurses has developed. Collaborative working is key to ensure that improvements made to the preanalytical process reflect users' needs, and optimising preanalytical processes may enable best use of nurses' time to focus on other clinical priorities [4, 5].

We can divide POCT errors like central laboratory (CL) errors into the three main phases of the process: preanalytical, analytical, and postanalytical. Similar to the CL process, most errors occur in the preanalytical phase [6]. Even though the whole preanalytical phase is much simpler in POCT, there are several steps prone to error like test ordering, patient and specimen identification, and specimen collection and finally, specimen evaluation or assessment of specimen attributes [7, 8].

POCT programs properly led and organized by the clinical laboratory can help to prevent these errors. Also, strategies that guarantee operator identification before analysis and adequate performance with quality assurance plans and data transfer (connectivity) are essential [9]. Development, implementation, and validation of performance using reliable key performance indicators (KPIs) is recommended. The evaluation of KPIs over time could determine a set of quality indicators and the implementation of improvement actions with POCT governance led by laboratory medicine, to achieve safer and better patient care [3, 10, 11].

Blood gas analysis (BGA) devices are one of the most commonly used methods for POCT testing in emergency departments (ED) and for acutely ill patients in hospital or hospitalised patients, and represents an essential part of the diagnosis and treatment of acute critically ill patients [12].

In vitro, hemolysis typically occurs during the preanalytical phase particularly during the collection process itself especially in those clinical scenarios with a high stress environment such as the EDs and CCUs, or while transporting the sample to the analyser [13, 14]. There are well-recognised sources of hemolysis that can cause falsely elevated potassium results. Some of them are inherent to the process of taking samples for BG analysis (venous or arterial) and how the staff use the phlebotomy equipment [7, 15]. Hemolysis can alter the result of different parameters, including potassium with abnormally high results or masking low levels (hypokalemia) when reporting normal concentrations. Hyperkalemia is conventionally defined as a serum or plasma potassium concentration >5.5 mmol/L or >5.0 mmol/L, respectively. Severe hyperkalemia, usually defined as plasma or serum potassium greater than 6.5–7.0 mmol/L respectively is associated with a risk of potentially fatal cardiac arrhythmia and requires emergency clinical intervention [16]. We can divide its causes into [7, 15–17]:

- Decreased renal excretion or increased intake of K^+ (renal failure, increased potassium intake, or administration of certain drugs such as β-blockers, digoxin and potassium-sparing diuretics among others)
- Decreased cellular entry of K^+ or increased exit of K^+ from cells (metabolic disorders)
- Preanalytical problems such as blood sample hemolysis, prolonged tourniquet placement, fist clenching, high speed of drawing blood into a syringe, sample contamination from infusive routes, prolonged storage of uncentrifuged blood, or leukocytosis or thrombocytosis

Unlike chemistry analysers in CLs, almost no BGA analysers can detect the presence of hemolysis in the sample or report the hemolysis index, and due to the characteristics of the sample, we cannot visually detect hemolysis either [18–20]. Some alternatives have been published to solve this problem using machine learning algorithms [21]. There is already an external option for a hemolysis detection available, the Hemcheck Helge H10 system, which is a CE-marked hemolysis test at the POC with sensitivity/specificity data of 80 and 95 % based on a free hemoglobin concentration cut-off of 0.5 g/L, as shown by Duhalde et al. [20]. According to Pradhan et al. clinicians should be aware of these circumstances and the authors recommend the confirmation of elevated potassium concentrations by CL methods [22].

This study aims to highlight the importance of the influence of undetected *in vitro* hemolysis on the results of blood potassium analysed in POCT analysers and to demonstrate the possible impact it may have on an incorrect diagnosis. It was primarily designed to evaluate and quantify the discrepancies in potassium measurements between POCT and CL methods and to assess how these discrepancies could potentially impact patient management and treatment decisions in the fast-paced, high-stakes environment of the ED.

Materials and methods

Sites and analysers

For this retrospective study, data from three comparable European university hospitals ("Technische Universitat München, Munich, Germany", "Hospital Universitario La Paz, Madrid, Spain" and "Erasmus University Medical Center, Rotterdam, The Netherlands") were analysed (Supplemental Table 1). The three sites are tertiary hospitals, and their emergency departments treat patients with similar characteristics. All laboratories operate according to ISO 15189 and ISO 22870 for POCT, and POCT is organized by the CL with an active POCT committee. Table 1 shows the description of POCT and CL equipment as well as the used matrix for analysis.

Table 1: Distribution of POCT and CL equipment as well as the used matrix for analysis.

Site (no. of patients)	Madrid (n=7,073)	Munich (n=10,838)	Rotterdam (n=3,172)
Period	2020	2020	2019–2021
BGA equipment	Radiometer ABL90+ Flex	Siemens RAPIDPoint 500	Radiometer ABL90+ Flex
BGA site	ED	CL	ED
BGA sample	Whole blood	Whole blood	Whole blood
Chemistry analyser	Siemens Atellica	Roche Cobas c8000	Roche Cobas c8000
Potassium site	CL	CL	CL
Type of sample	Plasma	Serum	Plasma

Inclusion criteria

We assessed the potential impact of hemolysis on the potassium (K) analysis at the emergency department (ED) as measured with a blood gas analyser (BGA). Additionally, matched K and hemolysis-index (H-I) results as measured in the CL were extracted. The following inclusion criteria were formulated:

(1) Only data from adults admitted to the ED were acceptable.
(2) All BGA measurements must be paired with an order with K and H-I measurements in the CL.
(3) The timeframe between the paired BGA POCT K, and CL K and H-I measurements must be within 45 min; and
(4) BGA must be performed before CL K and H-I measurement.

Potassium and hemolysis gradient

To differentiate between the levels of K, results were divided into five classes: severe hypokalemia (<3.0 mmol/L), mild hypokalemia (3.0–3.4 mmol/L), normokalemia (3.5–5.0 mmol/L), mild hyperkalemia (5.1–6.5 mmol/L), and severe hyperkalemia (>6.5 mmol/L). This differentiation applied to both POCT as well as CL K (Figure 1).

To differentiate between the levels of hemolysis, all three sites conducted individual analysis and set their own cutoff values according to their local clinical standard. Thus, H-I was divided into three categories: normal, mild, and severe hemolysis (Table 2).

Site differences

Besides differences in analysers and hemolysis cut-offs, the two most significant differences between the sites are: (1) the location of POCT potassium measurements, and (2) the used matrix to measure potassium in the CL. In Munich the BGA is in the CL, with the patient laboratory request and POCT blood gas request arriving simultaneously, meaning that potassium and hemolysis are measured from the same draw. In Rotterdam and Madrid, potassium POCT is done in the ED. In addition, Munich analyses potassium in the CL in serum while Rotterdam and Madrid measure it in plasma.

Table 2: Hemolysis gradient and normalization criteria.

	Madrid	Munich	Rotterdam
Equipment	Siemens Atellica	Cobas c8000	Cobas c8000
Type of sample	LiHep plasma	Serum	LiHep plasma
Normal	<100 mg/dL	<50	<42
Mild	100–200 mg/dL	50–150	42–100
Severe	>200 mg/dL	>150	>100

Data extraction and analysis

One year of data was extracted from the three different LIS (Madrid: Trakcare, Intersystems, USA; Munich: Swisslab, Nexus AG, Germany; Rotterdam: Labtrain, Bodegro, The Netherlands) using custom SQL scripts. Analysis was performed using RStudio v2022.12.0+353 and Microsoft Excel v16.72.

Due to the differences described above, CL POCT potassium measurements (Munich) were compared with the ED POCT measurements (Rotterdam and Madrid). Data were normalised into five categories for "kalemia" and three for hemolysis as described above. Additionally, to assess the severity of the observed discrepancies between potassium measurements as done by POCT and CL, the RCV was determined using an analytical CV of 2 %. This was performed between the paired samples as discussed above.

Results

General characteristics

Paired samples and kalemia

As described above, due to differences in the physical location of K-POCT analysis and differences in the matrix used in the CL for the K-measurement, Rotterdam, and Madrid (decentral), data (n=10,245) were pooled and compared with the Munich (central) data (n=10,840). The analysed samples and the distribution of the potassium gradient are shown in Table 3. The most noticeable difference between Madrid/Rotterdam and Munich can be seen in the POCT normo- and mild hypokalemia with deltas of −4.20 % and +4.88 % respectively. In the CL, the biggest difference is +4.14 % and is seen in the mild hyperkalemia group. The individual findings per location are available in the Supplemental Table 2.

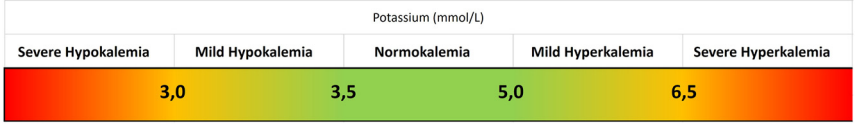

Figure 1: Potassium gradient as defined within the study showing the normokalemic, mild hypo-/hyperkalemic, and severe hypo-/hyperkalemic zones.

Table 3: General characteristics of the kalemic gradient as presented per site. The delta displays the percentage difference between the compared groups.

	POCT			CL		
	Madrid and Rotterdam (n=10,245)	Munich (n=10,840)	Delta	Madrid and Rotterdam (n=10,245)	Munich (n=10,838)	Delta
Severe hypokalemia	1.54 %	2.39 %	0.85 %	1.23 %	0.61 %	−0.62 %
Mild hypokalemia	8.82 %	13.70 %	4.88 %	7.54 %	5.11 %	−2.43 %
Normokalemia	83.40 %	79.20 %	−4.20 %	84.21 %	83.36 %	−0.85 %
Mild hyperkalemia	5.55 %	4.60 %	−0.95 %	6.47 %	10.61 %	4.14 %
Severe hyperkalemia	0.68 %	0.20 %	−0.48 %	0.54 %	0.30 %	−0.24 %

Mild/severe hemolysis and potassium

In Table 4 the overall hemolysis characteristics are shown as defined by the hemolysis gradient. To gain insights into the potential role of hemolysis on the POCT potassium levels, we analysed the POCT K- and the lab-measured hemolysis levels from the paired samples. We focused on mild and severe hemolysis as they have the biggest implications for the interpretation of POCT potassium in clinical practice. Table 5 shows that despite being mild or severe hemolytic, most samples as measured in POCT were normokalemic.

Potassium hemolysis matrix

In clinical practice, hemolysis can lead to discrepancies between POCT-K and CL-K results which, in turn, might lead to erroneous over/undertreatment. We studied this impact utilising a POCT-K/CL-K concordance matrix as shown in Table 6 and Supplemental Tables 3 and 4. The matrix has been divided according to severity of alteration into three distinct zones/categories. The green zone/nominal where POCT-K corresponds with the CL-K result i.e., POCT-normokalemia = CL-normokalemia, the orange/subnominal zone where POCT-K corresponds with a step before or after the CL-K i.e., POCT-normokalemia = CL-mild hypo/hyperkalemia, and the red/severe subnominal zone where POCT-K shows severe discrepancy as compared to CL-K i.e., POCT-normokalemia = CL-severe hyperkalemia. From a clinical perspective, a change in category to abnormal might warrant further investigation or treatment, whilst a wrongful alteration into the normokalemic category might result in missing potential disease.

Table 4: General characteristics of the assessed hemolysis gradient as presented per site in the CL.

	Madrid and Rotterdam (n=10,245)	Munich (n=10,842)
Normal	84.8 % (n=8,695)	96.9 % (n=10,504)
Mild hemolysis	15.1 % (n=1,545)	2.7 % (n=291)
Severe hemolysis	0.1 % (n=5)	0.4 % (n=47)

In the Munich dataset, 79 % (n=8,572) of the paired samples showed a good correlation in the green/nominal zone between POCT-K and the CL-K. The remaining 21 % (n=2,262) were in the orange/subnominal zone and 0 % (n=5) were in the red/severe subnominal zone. Those five patients in the red/severe subnominal zone might have received erroneous over- or undertreatment options. In the Madrid/Rotterdam location, 89.4 % (n=9,254) of the paired samples are in the green/nominal zone. Unfortunately, 9.9 % (n=1,018) and 0.7 % (n=73) were categorized in the orange/subnominal and red/severe subnominal zone respectively. This means that 1,018 patients' diagnosis and treatment (9.9 %) might have been impacted by erroneous results and

Table 5: The kalemic gradient measured on POCT is represented against mild and severe hemolysis as measured in the CL.

	Madrid and Rotterdam (n=1,550)		Munich (n=338)	
	Mild (n=1,545)	Severe (n=5)	Mild (n=291)	Severe (n=47)
POCT severe hypokalemia	2.07 %	0.00 %	0.00 %	0.00 %
POCT mild hypokalemia	6.47 %	0.00 %	16.84 %	0.00 %
POCT normokalemia	82.85 %	80.00 %	76.98 %	89.36 %
POCT mild hyperkalemia	7.06 %	20.00 %	5.15 %	8.51 %
POCT severe hyperkalemia	1.55 %	0.00 %	1.03 %	2.13 %

Table 6: Summary of the concordance matrix.

	Madrid & Rotterdam (n=10,245)	Munich (n=10,839)
Nominal	89.4 % (n=9,254)	79.1 % (n=8,572)
Subnominal	9.9 % (n=1,018)	20.9 % (n=2,262)
Severe subnominal	0.7 % (n=73)	0.0 % (n=5)

The green zone/nominal where POCT-K corresponds with the CL-K result i.e., POCT-normokalemia = CL-normokalemia, the orange/subnominal zone where POCT-K corresponds with a step before or after the CL-K i.e., POCT-normokalemia = CL-mild hypo/hyperkalemia, and the red/severe subnominal zone where POCT-K shows severe discrepancy as compared to CL-K i.e., POCT-normokalemia = CL-severe hyperkalemia.

could get an expectant attitude (wait and see and eventually treat) while 73 patients (0.7 %) may have received erroneous over- or undertreatment.

Reference change value

The RCV was calculated as described above. Our data show that ±8 % of all paired potassium results as analysed on POCT and in the CL were outside the RCV ranges (Figure 2). This implies that these patients could have been given an incorrect diagnosis potentially resulting in a lack of the correct needed care.

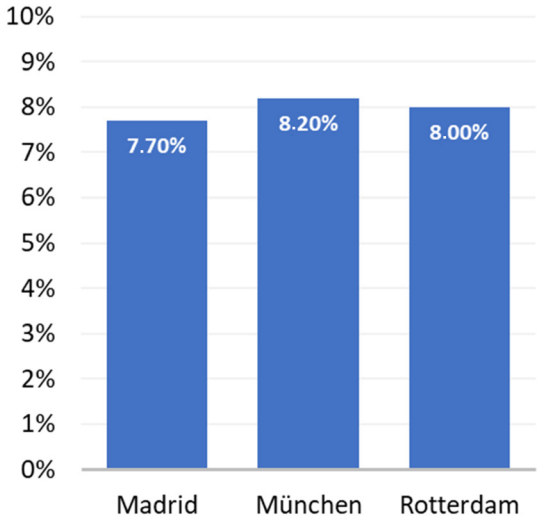

Figure 2: The RCV between POCT-K and CL-K. The graph depicts the percentage (%) of the paired K+ results outside the RCV.

Discussion

Our retrospective study conducted in EDs of three different European university hospital centers clearly shows that *in vitro* hemolysis is a common and potentially serious problem for POCT potassium results. From our big data analysis, we were able to describe the proportion of patients having a significantly altered potassium plasma/serum concentration (>5.0 mmol/L), presumably caused by sample hemolysis.

The normalized data sets from the Madrid plus Rotterdam (total n=10,245) sites were compared with those from Munich (n=10,842) with comparable total analysis numbers (10,245 vs. 10,842; Table 1). When focusing on the mild and severe hyperkalemia cases in Table 3, the percentages between Madrid plus Rotterdam, and Munich for the POCT measurements were comparable (6.23 vs. 4.8 %), whereas for the CL determinations, a significantly higher percentage of Munich vs. Madrid plus Rotterdam (10.91 vs. 7.01 %) can be stated. Since in Munich most of these cases are mild hyperkalemia (10.61 vs. 6.47 %), it can be presumed that the use of serum instead of plasma can explain this difference.

The gross differences in the sum of mild and severe hemolysis determined in the CLs between Madrid plus Rotterdam vs. Munich, described in Table 4, can be explained as effect of the sum of different complex conditions and circumstances connected with preanalytical issues, as described by Buño et al. and Schlüter et al. [7, 8], organizational and operational issues, the use of different specimens (plasma in Madrid and Rotterdam vs. serum in Munich), as well as selection and handling of admitted patients. Using a pneumatic tube system to transport the samples in Munich does not seem to influence these differences as previously demonstrated by Zanner et al. [23].

However, despite the above-described differences between the three study sites, the found percentages of hyperkalemia in hemolyzed samples, measured by POCT, are rather comparable (Table 5). These data impressively confirm the observations of other authors (see below) for hemolysis in BGA samples [12, 14, 20, 24–29].

The data from the concordance matrix showed differences between Madrid plus Rotterdam vs. Munich, leading to an over- or under-estimation of the potassium level. Fortunately, a good agreement was found for the RCV analysis (±8 %) in the three sites of the paired potassium concentrations analysed either in the CL or at the POC.

Our findings are consistent with several other studies confirming the observation of hemolyzed patient samples as a common problem with BGAs under stressful and fast-paced conditions in the ED. Also important is the fact that the blood collection procedures and the preanalytical sample handling are undertaken by a variety of medical professionals with different training statuses [4]. It has already been pointed out that preanalytical POCT errors are inversely correlated with user experience [30, 31]. When assessing these studies, one must first determine which patient population and clinical setting the evaluation refers to in each case: outpatients, inpatients at an ED or ICU or on a normal ward.

We found five studies investigating the prevalence of hemolysis or hyperkaliemia in blood samples drawn in the ED. Singer et al. found 3.6 % hyperkalemic and 3.6 % hemolytic samples in 48,827 ED-patient visits [25]. The study of Tazmini et al. reports on 62,991 ED visits and found in 3.3 % of all samples a hyperkalemic status [26]. Another already mentioned trial found that a rate of 7.9 % hemolysis was found in 1,270 observed blood gas analyses from an ED [20]. Differences were seen between different sites in terms of hemolysis in a trial of Wilson et al. [27]. They observed 100 blood gas analyses and found a hemolysis rate of 13 % in the ED and 4 % in an ICU. Finally, Nigro et al. reported that in 472 arterial samples hemolysis was present in 12 % [28].

Casati et al. [12] found 5 % hemolysis in 1,244 observed BGAs, samples from different hospital wards and the ED, whereas Salvagno et al. reported a rate of 4 % hemolysis in 487 observed BGAs from routine and stat samples from a hospital [24].

An interesting study by O´Hara et al. deals with hyperkalemic specimens, showing that in consecutively collected 100 hyperkalemic samples, 40 % showed significant hemolysis [14]. Grieme et al. investigated the impact of various interferences on parameters in POCT and found a similar result: there was evidence of hemolysis in 60 % of samples with potassium serum concentrations from 6.0 to 6.9 mmol/L [29]. The discrepancy in the study of O'Hara is likely due to the application of different hyperkalemia cutoffs.

A critical issue for considering measured hyperkalemia as an indicator of hemolysis is knowledge of the incidence of true hyperkalemia cases (caused by acute or chronic renal failure, heart failure, potassium supplementation, certain drug effects, insulin deficiency, or metabolic acidosis) in patients admitted to the ED. Singer et al. found an incidence of hyperkalemia of 3.6 % in 47,089 patients [25], whereas Kuo et al. only found 0.92 % in 602 investigated patients [32]. Lemoine et al. summarized data from the literature with incidence rates between 1 and 10 % [33]. In our study, we found a tendency to hyperkalemia but even normokalemia in a significant proportion of samples with severe hemolysis analysed with POCT. Whilst hyperkalemia and hemolysis have been observed and discussed for decades, the high incidence of hemolysis resulting in "normal" readings might be a concern. Hypokalemia is a common clinical finding in the ED (for example in frail elder patient), and pseudo-normalized results due to hemolysis seem to be common. In consequence, patients with clinically relevant hypokalemia might be missed and left untreated.

These clinical studies indicate that among hyperkalemic BGA samples, the percentage of falsely elevated potassium concentrations is alarmingly high, and this finding is disproportionally often in the ED. The underlying reasons were already mentioned above. Therefore, it is not surprising that Lippi et al. reported 1.2 % hemolytic samples in 1,228 BGAs from clinical wards with the exclusion of ED and ICU sites [34]. This also fits with the observation from Jose and Preller et al. that clinicians – in particular, intensivists – trust more the potassium results from the CL than their own POCT results [35]. Hemolyzed samples at the BGA pose also additional problems. First, pseudohyperkalemia may mimic low serum potassium concentrations. In this case, the BGA reports normokalemia whereas the patient is hypokalemic (Supplemental Tables 3 and 4). Hypokalemia is found often in hospitalized patients and is associated with excess morbidity and mortality. The lower the potassium serum concentrations, the higher the risk, starting at potassium <4.0 mmol/L, with a significant risk increment when the potassium levels are <3.5 mmol/L, as described by Ferreira et al. [36]. Secondly, spurious hemolysis affects also various other BGA parameters, such as pO_2, pCO_2 or Ca^{2+} [29, 37].

In the literature, the prevalence of unsuitable specimens referred for BGA is given at 1.2–3.7 % [24, 34, 37], with hemolysis accounting for 40–70 % of the cases [38]. The Clinical and Laboratory Standards Institute (CLSI) C46-A2 guideline [39] generically advises against processing unsuitable blood samples for BGA. However, this requirement can only be met by providing the best possible training for operating personnel to accurately identify and appropriately manage spurious sample hemolysis [34].

Regarding the limitations of our study, different points compromise the value of our data: first, the paired blood samples for BGA at Munich were sent to the CL while in Madrid and Rotterdam were analysed as POCT. Also, the time frame of 45 min between the POCT BGA measurement and CL is questionable, although were considered a pragmatic and realistic approach. Second, the majority of over 21,000 samples were venous samples. However, we do not know the minor portion of arterial samples. Third, the three sites used different chemistry analysers for the measurement of potassium and used also different cut-offs for the HIL indices (even between Madrid and Munich, due to the use of plasma or serum) defining the hemolysis rate. These cut-offs had been previously established for routine analysis in all three sites and had proved successful in daily measurements by providing an effective screening tool for checking specimen quality concerning hemolysis, hyperbilirubinemia, and lipidemia [40]. In addition, the cut-offs had been compared and harmonized with measurements of free hemoglobin in plasma (data not shown). Fourth, the design of the study is retrospective and can be more susceptible to bias and confounding variables compared to prospective studies. Fifth, we cannot assure that the patient population at the three hospitals were comparable in terms of the pathology presented at the ED.

Conclusions

This multicenter study is the largest to date investigating the true incidence of hyperkalemia in hemolyzed samples in POCT in the ED. The observed rate of 7–9% is in good accordance with previous reports concerning hemolysis in BGA specimens. However, this study has much more statistical power due to the enormous number of evaluated data sets and its multicenter design.

The hemolysis rates presented in this trial and the other published clinical studies shows that there is still a major need for improvements in the preanalytical phase of BGA [41, 42]. There are important demands for dedicated training and revalidation for ICU and ED personnel in terms of preanalytics [31]. Another mandatory requirement for future BGA devices is the implementation of an inbuilt hemolysis detection system [12, 43], a request that is sustainably endorsed by our study. Until then other alternatives could be used to minimize the problem such as the use of predictive analytics, or the Hemcheck Helge H10 system and the stringent application of a Failure Mode and Effects Analysis (FMEA) protocol by the POCT quality management team [20, 21, 44].

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