



Research paper

The relationship between elevated prehospital point-of-care lactate measurements, intensive care unit admission, and mortality: A retrospective review of adult patients



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Objective: To determine whether prehospital point-of-care lactate (pLA) is associated with mortality, admission, and duration of hospital stay.

Design: A retrospective clinical audit, where elevated lactate was defined as ≥ 2 mmol/L.

Setting: The ambulance service and primary referral hospital in the Australian Capital Territory from 1st July 2014 to 30th June 2015.

Participants: Adult patients (≥ 18 years) who had pLA measured and were transported to the primary referral hospital.

Main outcome measures: Mortality, admission, and duration of hospital stay.

Results: Two hundred fifty-three patients with a median pLA of 2.5 mmol/L (interquartile range [IQR]: 1.5–3.7) were analysed. Overall mortality was 8.3%; 68% were admitted to the hospital; 8.3% to the intensive care unit (ICU). pLA was non-significantly higher in those who died compared to survivors (3.5 [IQR: 2.75–5.85] vs 2.4 [1.5–3.6]; $W = 1631.5$; $p = 0.053$). pLA was higher for those admitted to the hospital (2.9 [1.9–3.9] vs 2.0 [1.4–3.1]; $W = 5094.5$, $p = 0.001$) and the ICU (3.2 [2.4–5.7] vs 2.4 [1.5–3.6]; $W = 1578.5$; $p = 0.008$). There was no relationship between pLA and duration of stay. Considered as a screening tool, at a cut-off of 2.5 mmol/L, pLA had a likelihood ratio+ of 1.61 for mortality and 1.44 for ICU admission; the odds ratio for mortality was 3.76 (95% confidence interval = 1.30, 13.89).

Conclusions: Elevated prehospital lactate was associated with significantly increased ICU and hospital admissions. There may be value in pLA as a screening tool.

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1. Introduction

Critical illness and use of intensive care units (ICUs) are associated with increased burden of disease and economic cost.¹ Early recognition of serious illness and patient deterioration leads to a

reduction in mortality.² Point-of-care lactate measurement in the Emergency Department (ED) has been shown to decrease mortality and ICU admission rates³ and accurately reflects serum lactate.^{4,5} Prehospital point-of-care lactate (pLA) has been shown in several small studies to be useful as a predictor of outcome in trauma patients,⁶ carbon monoxide poisoning,^{7,8} paracetamol overdose,⁹ burns,¹⁰ and for diagnosing sepsis.^{11–13} However, the utility of pLA as a prognostic tool has not been established. Hyperlactataemia can occur from multiple conditions,^{14–16} so it is uncertain what value pLA has in critical illness.

The aim of this study was to determine the association between elevated pLA and mortality, ICU admission rates, and duration of hospital stay. It was hypothesised that patients with an elevated

Abbreviations: ACT, Australian Capital Territory; ACTAS, Australian Capital Territory Ambulance Service; AUC, area under the curve; CRIS, Clinical Research Information System; ED, Emergency Department; ePCR, electronic Patient Care Record; ICU, Intensive Care Unit; pLA, prehospital point-of-care lactate; LR+, likelihood ratio +; IQR, interquartile range.

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pLA would have significantly higher rates of ICU admissions, mortality, and longer overall length of hospital stay.

2. Method

2.1. Study design

A retrospective research review using data linkage was conducted at the Canberra Hospital and Health Services, in the Australian Capital Territory (ACT) from 1st July 2014 to 30th June 2015. This project was approved by the ACT Health Human Research Ethics Committee (submission number ETHLR.15.171).

2.2. Setting

The ACT has an estimated population of 392,000 people.¹⁷ Calls for emergency medical assistance are attended by the ACT Ambulance Service (ACTAS), a publicly funded service that attended 44,544 cases during the study duration.¹⁸ The primary referral centre in the ACT and its surrounding regions is the Canberra Hospital. It is a 600 bed public teaching hospital, which contains a 31 bed ICU.¹⁹

2.3. Materials and procedure

ACTAS Clinical Management Guidelines²⁰ recommend paramedics to measure pLA particularly in cases of suspected sepsis. To be diagnosed with sepsis by ACTAS, a patient must have an infection risk factor or symptom, plus at least two alterations in vital signs. These alterations include systolic blood pressure ≤ 100 , respiratory rate ≤ 10 or ≥ 25 , peripheral oxygen saturation $< 95\%$, heart rate ≤ 50 or ≥ 120 , temperature ≤ 35.5 or ≥ 38.5 , altered level of consciousness, and hyperlactataemia. Prehospital lactate measurement is not compulsory and is at the discretion of the treating paramedic.

pLA samples are obtained using either a finger prick to draw capillary blood or from venous blood obtained via a Protectiv® Plus Safety I.V. Catheter (Smiths Medical International Ltd, Lancashire UK). All ACTAS emergency ambulances are equipped with the Lactate Pro 2 (ARKRAY, Shiga Japan) meter, which uses point-of-care enzymatic amperometric detection technique to measure pLA. The pLA is then recorded on an electronic patient care record (ePCR), along with the patient's personal details, history, examination findings, and any treatment provided. The ePCR record is completed by the treating paramedic as soon as the patient has been removed from the ambulance stretcher.

2.4. Participants

Participants were all patients attended by ACTAS during the study period who had a pLA obtained and were transported to the Canberra Hospital. Paediatric patients (< 18 years) and patients who had a cardiorespiratory arrest before pLA measurement were excluded. Cardiorespiratory arrests cause total body ischaemia and result in significant hyperlactatemia.²¹ Single lactate measurements in the early period after return of spontaneous circulation are therefore of limited usefulness.²¹ Patient who were transferred to another hospital were counted as lost to follow-up and were removed from the analysis.

2.5. Data collection

A search was conducted by one author (TK) on the ACTAS ePCR database for any cases within the specified date range with a recorded pLA. From these records, the case number, first name,

surname, date of birth, gender, date and time of pLA collection, pLA, date and time of hospital arrival, and the date and time of cardiac arrests were recorded. The patients extracted from ePCR were then linked to the Clinical Research Information System (CRIS), which is the primary database used by the Canberra Hospital. The data linkage criteria were the patient's first name, surname, date and time of admission, date of birth, and gender. Deterministic record linkage was conducted by one author (KS), with four of the five data linkage criteria required to match for establishment of an accurate data link.

The CRIS database is managed by the Clinical Records Department at the Canberra Hospital. It includes both electronic data entered by administration staff and clinicians, plus scanned copies of patient medical files (including triage forms, ICU progress notes, discharge summaries, and death certificates), but does not routinely include ambulance data or pathology results. From the CRIS electronic database, the following data were extracted: medical record number, first name, surname, date of birth, gender, and date and time of arrival at hospital. If related to the hospital admission in question, the date and time of a patient's in-hospital death and the final diagnosis were collected from the scanned death certificate. From the scanned discharge summaries, the following were recorded: final diagnoses of patients who were alive at hospital discharge, discharge location, date and time of hospital discharge, and discharge destination. Date and time of ICU admission and ICU discharge were collected from the scanned ICU progress notes. After data linkage, the patient identifiers (first name and surname) were removed before storage and analysis to protect patient identity. No follow-up was attempted for patients after hospital discharge.

2.6. Statistical analyses

Owing to the disagreement regarding classification of hyperlactataemia in the literature,^{22–24} this study used a cut-off of ≥ 2 mmol/L for elevated lactate and < 2 mmol/L for normal lactate to reflect current ACTAS guidelines.²⁰ IBM SPSS Statistics, version 20, for Windows (IBM Corp, Armonk USA) was used for statistical analysis. The data for pLA did not follow a normal distribution; therefore, non-parametric statistical analysis was employed; group comparisons were performed with Wilcoxon rank sign tests with continuity correction or Spearman's rho rank correlations. All statistical tests used a two-tailed alpha level of < 0.05 . The median age, pLA, and the gender breakdown were determined using descriptive statistics. A frequency histogram was produced for the pLA, as a visual description of variance in pLA and to demonstrate skew. Statistics are reported as median (interquartile range [IQR]), odds ratio (95% confidence interval [CI]), or mean (standard deviation).

3. Results

During the study duration, 44,544 patients were attended by ACTAS paramedics. Of those, 290 patients met the inclusion criteria, which equates to 0.65% of the total attended cases. Of the 290 patients who met the inclusion criteria, only 253 patients were analysed because of exclusions (Fig. 1). Table 1 describes the participants and summarises the results for mortality and ICU admission. Fig. 2 shows the overall distribution of pLA, which is positively skewed. The median pLA was 2.5 mmol/L (IQR: 1.5–3.7). The median time from measurement of pLA to ED admission was 38 min (IQR: 30–46).

Overall mortality was 7.5%. Participants who died were more likely to be male (63% vs 49%) and older (85 years [IQR: 78.5–90.5] vs 74 [IQR: 57.25–84]; $W = 1314$, $p = 0.003$). The difference in pLA

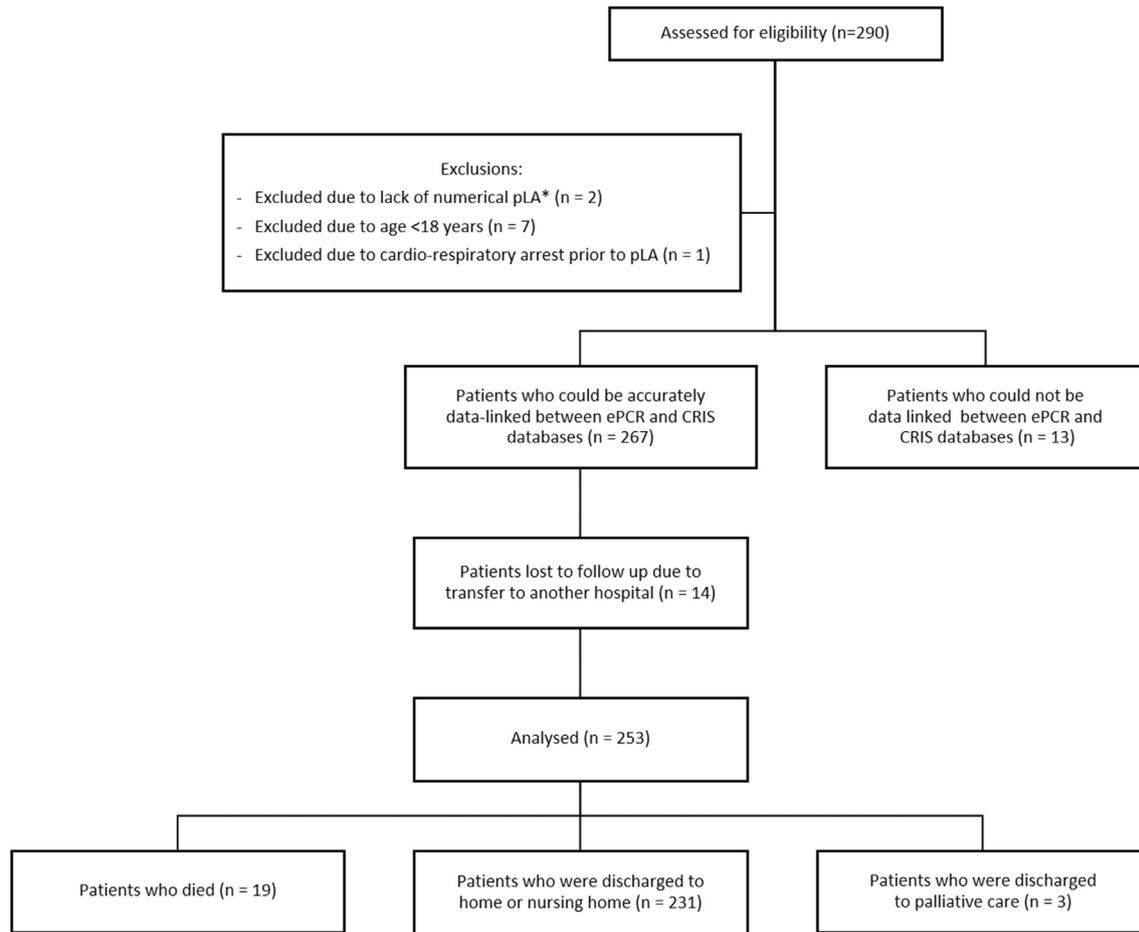


Fig. 1. Study population inclusions and exclusions. pLA = prehospital point-of-care lactate; ePCR = electronic patient care record; CRIS = Clinical Research Information System. *In place of numerical lactate, “lactate monitor malfunction” and “inaccurate reading” were recorded.

Table 1
Summary of results.

	N (%)	Gender, n (%)	Age (years), median (IQR)	pLA (mMol/L), median (IQR) [Wilcoxon rank sum test]
Analysed	253	Female: 126 (49.8%). Male: 127 (50.2%)	75 (58–85)	2.5 (1.5–3.7)
Mortality				
Alive at discharge	234 (92.5%)	Female: 119 (50.9%). Male: 115 (49.1%)	74 (57.25–84)	2.4 (1.5–3.6)
Died	19 (7.5%)	Female: 7 (36.8%). Male: 12 (63.2%)	85 (78.5–90.5)	3.5 (2.75–5.85); [W = 1631.5; p = 0.053]
ICU				
Admitted	21 (8.3%)	Female: 8 (38.1%). Male: 13 (61.9%)	72 (51–76)	3.2 (2.4–5.7)
Not admitted	232 (91.7%)	Female: 118 (50.9%). Male: 114 (49.1%)	76 (60–85)	2.4 (1.5–3.6); [W = 1578.5; p = 0.008]
Hospital admission				
Admitted	172 (68%)	Female: 79 (45.9%). Male: 93 (54.1%)	76 (66–85.3)	2.9 (1.9–3.9)
Not admitted	81 (32%)	Female: 47 (58%). Male: 34 (42%)	73 (43–83)	2.0 (1.4–3.1); [W = 5094.5, p = 0.001]

pLA = prehospital point-of-care lactate; IQR = interquartile range; ICU = intensive care unit.

between those who died and survivors approached but did not reach statistical significance (3.5 [IQR: 2.75–5.85] vs 2.4 [1.5–3.6]; $W = 1631.5$; $p = 0.053$). Sixty-eight percent of participants were admitted to hospital; 8.3% were admitted to the ICU. pLA was higher for those admitted to the hospital (2.9 [1.9–3.9] vs 2.0 [1.4–3.1]; $W = 5094.5$, $p = 0.001$) and the ICU (3.2 [2.4–5.7] vs 2.4 [1.5–3.6]; $W = 1578.5$; $p = 0.008$).

Overall, participants spent a median of four days in hospital (IQR: 1–9). Those admitted to the ICU had a median length of stay of 11 days (8–25); hospital admission resulted in a median stay of seven days (4–12). For those admitted to hospital, length of stay was uncorrelated with pLA (Spearman rho: 0.031). Similarly, there

was no relationship between pLA and length of stay in those admitted to the ICU (Spearman rho: 0.226).

To assess the value of pLA as a screening tool, test statistics were calculated for pLA against mortality and ICU admission at a range of cut-off values between 1 and 3 mmol/L (Table 2). Sensitivity for mortality ranged from 0.74 to 0.95 depending on the proposed cut-off; specificity ranged from 0.01 to 0.61 (see Table 2). For ICU admission, sensitivity varied from 0.62 to 1.0; specificity ranged between 0.02 and 0.60 (Table 2). Receiver operating characteristic curves were calculated for pLA on mortality (area under the curve (AUC): 0.633 [95% CI: 0.479–0.787]) and ICU admission (AUC: 0.676 [95% CI: 0.5606–0.7914]).

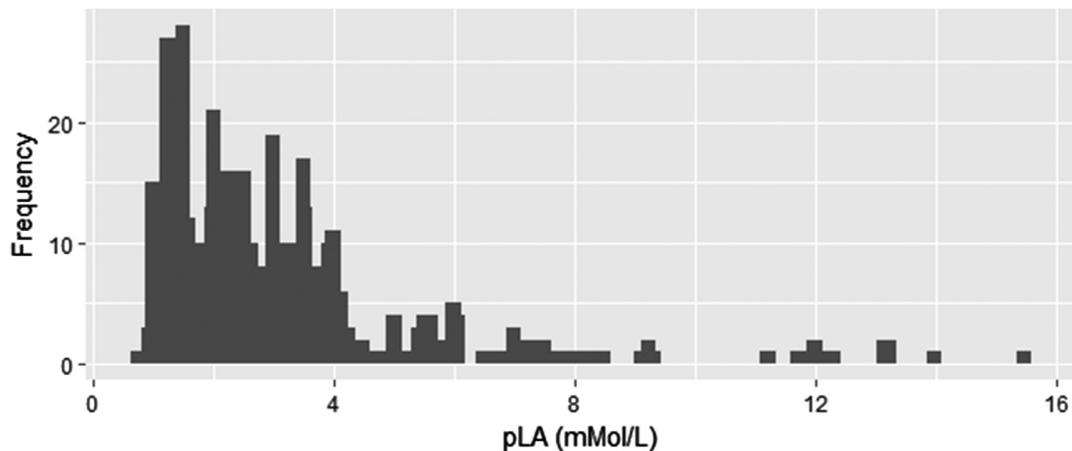


Fig. 2. Histogram of pLA value frequency (n = 253). pLA = prehospital point-of-care lactate.

Table 2

Summary of results for pLA as a screening test at cut-offs between 1 mmol/L and 3 mmol/L.

	pLA ≥ 1 mmol/L	pLA ≥ 2 mmol/L	pLA ≥ 2.5 mmol/L	pLA ≥ 3 mmol/L
Sensitivity (95% CI)				
Mortality	0.95 (0.74, 1.00)	0.79 (0.54, 0.94)	0.79 (0.54, 0.94)	0.74 (0.49, 0.91)
ICU admission	1.00 (0.84, 1.00)	0.90 (0.70, 0.99)	0.71 (0.48, 0.89)	0.62 (0.38, 0.82)
Specificity (95% CI)				
Mortality	0.01 (0.00, 0.04)	0.36 (0.30, 0.42)	0.51 (0.44, 0.57)	0.61 (0.54, 0.67)
ICU admission	0.02 (0.00, 0.04)	0.37 (0.31, 0.44)	0.50 (0.44, 0.57)	0.60 (0.53, 0.66)
LR+ (95% CI)				
Mortality	0.96 (0.86, 1.07)	1.23 (0.96, 1.58)	1.61 (1.23, 2.10)	1.87 (1.37, 2.56)
ICU admission	1.02 (1.00, 1.04)	1.44 (1.21, 1.70)	1.44 (1.07, 1.95)	1.54 (1.07, 2.24)
LR- (95% CI)				
Mortality	4.11 (0.45, 37.59)	0.59 (0.24, 1.42)	0.41 (0.17, 1.00)	0.43 (0.20, 0.93)
ICU admission	0.00	0.26 (0.07, 0.97)	0.57 (0.28, 1.13)	0.64 (0.36, 1.11)
PPV (95% CI)				
Mortality	0.07 (0.06, 0.08)	0.09 (0.07, 0.11)	0.12 (0.09, 0.15)	0.13 (0.10, 0.17)
ICU admission	0.08 (0.08, 0.09)	0.12 (0.10, 0.13)	0.12 (0.09, 0.15)	0.12 (0.09, 0.17)
NPV (95% CI)				
Mortality	0.75 (0.25, 0.96)	0.95 (0.90, 0.98)	0.97 (0.93, 0.99)	0.97 (0.93, 0.98)
ICU admission	1.000	0.98 (0.92, 0.99)	0.95 (0.91, 0.97)	0.95 (0.91, 0.97)
Odds ratio (95% CI)				
Mortality	0.22 (0.02, 6.48)	2.04 (0.70, 7.55)	3.76 (1.30, 13.89)	4.22 (1.54, 13.71)
ICU admission	NA	5.22 (1.46, 36.17)	2.50 (0.97, 7.33)	2.40 (0.96, 6.37)

LR+ = likelihood ratio +; LR- = likelihood ratio -; PPV = positive predictive value; NPV = negative predictive value; 95% CI = 95% confidence interval; ICU = intensive care unit; pLA = prehospital point-of-care lactate.

4. Discussion

This is the first Australian study we are aware of that has attempted to establish a relationship between paramedic collected pLA and patient outcome.

4.1. Mortality

This study found no statistically significant relationship between pLA and mortality. Although there have been three other studies^{25–27} which support this finding, the majority of studies using a cut-off of 2 mmol/L found a statistically significant relationship between lactate and mortality.^{28–31} Australian ICUs have lower mortality rates when compared with international ICUs^{32,33} and perform particularly well in the treatment of septic patients.³⁴ The mortality rate in our study was relatively low at 7.5%. The unexpectedly low mortality rate may have resulted in this study being underpowered to detect a statistical difference in pLA. Additionally, earlier studies measured lactate at admission to ED or ICU,^{28–31} whereas our study measured prehospital lactate.

A systematic review³⁵ concluded it was the trend in serial lactates and lactate clearance which had the greatest and most

consistent prognostic significance for mortality. The review recommended that either persistent hyperlactataemia or the time required to normalise lactate should be used in place of a single lactate measurement. However, serial hyperlactataemia and lactate clearance could not be assessed in this research as ACTAS paramedics only obtain single point-of-care lactate measurements. The review also concluded that an interval of 2–6 h is a sufficient time period to follow the lactate trend³⁵ which is far shorter than for most patients who are in paramedic care. However, pLA may serve as a useful baseline measurement for subsequent ED measurements.³⁶

4.2. Hospital and ICU admission rates

Our results reveal a statistically significant relationship between elevated pLA levels and admission to both ICU and the hospital generally. This suggests that elevated pLA levels could serve as an early indicator of clinical deterioration and organ failure in critical situations. Several authors have reported a relationship between hyperlactaemia and ICU admission.^{37–41} This study gathered insufficient data to calculate an acute physiology and chronic health evaluation score that would allow comparisons of illness severity

across studies. Future research should consider illness severity as a potential confounder. The ICU admission rate of 8.3% was lower than expected, given that paramedics were selecting for patients with suspected sepsis. However, 68% of participants were admitted to the hospital, possibly indicating the paramedics had some accuracy in selecting unwell patients.

4.3. Length of hospital stay

Our results show no significant relationship between pLA and length of ICU stay, unlike other studies^{24,42,43} A study by van Beest et al²⁴ on patients with confirmed shock demonstrated an additional 6 days of hospital stay in patients with elevated lactate levels. This may be due to the higher lactate cut-off of ≥ 4 mmol/L being used in the van Beest study.²⁴

4.4. Other findings

The median pLA was higher than expected, which could either suggest the Lactate Pro 2 meter is not as accurate in a prehospital setting as it was in laboratory¹⁵ and hospital⁴ testing or that ACTAS paramedics are accurately identifying critically ill patients. ACTAS paramedics are authorised to use clinical judgement in deciding when to collect lactate measurements but are encouraged to do so when there are signs of infection with abnormal vital signs. Traditional vital signs are known to be unreliable for early detection of sepsis, so there is likely some selection bias. Future research should consider the value of lactate in the early detection of occult shock.

ACTAS guidelines recommend paramedics use a cut-off of 2 mmol/L to determine if a pLA value is elevated. The results here suggest that, if used as a screening tool, a cut-off of 2.5 mmol/L would perform better than 2 mmol/L. At a cut-off of 2.5 mmol/L, pLA had a likelihood ratio + of 1.61 for mortality and 1.44 for ICU admission; participants with pLA of 2.5 mmol/L or greater were 3.74 times more likely to die than those with a lower pLA. The assessment of pLA as a screening tool was compromised by low rates of mortality and ICU admission. However, there is sufficient evidence here to consider pLA as a useful screening tool for serious illness, particularly given the unreliability of traditional vital signs for early detection.

4.5. Strengths and limitations

There are several limitations to this study. Firstly, generality may be limited as it is based on a 12-month period in a small ambulance service and a single hospital. The study relied on data linkage and is therefore limited by the 13 patients who had to be excluded as they could not be accurately cross-matched. Additionally, 14 participants were lost to follow-up after they were transferred to other hospitals. Given the relatively low mortality and ICU admission rates, the outcomes for these 14 participants could have significantly altered the outcomes.

Measurement of pLA was at the discretion of the treating paramedic. Paramedics were recommended to measure pLA in patients with suspected sepsis as indicated by signs of infection and alteration of vital signs. Combined with the retrospective nature of the study, this paramedic discretion may have led to a selection bias, limiting the generality of the results. Future research should prospectively collect pLA in all prehospital patients.

No attempt was made to adjust for severity of illness which is a clear limitation. Lactate clearance is primarily hepatic (50%) and renal (20%).^{44,45} Impaired hepatic or renal function can decrease clearance, as can metabolic acidosis or alkalosis.^{44,46} No

attempt was made to adjust for these factors either. Lastly, our study failed to consider any medical treatment such as intravenous fluids or antibiotics provided to the patients by ACTAS or hospital medical staff. These factors limit the interpretation of the results.

4.6. Future research

This study should be corroborated by multicentre research with longer study durations and larger samples. This is especially important for outcomes such as length of hospital stay and ICU admission rates, given they are influenced by bed availability and practice variation. Disagreement still exists regarding the use of pLA, including whether it can be used as a reliable surrogate marker for in-hospital serum lactate. Additional research is needed to address this discrepancy. Furthermore, a prospective study on serial pLA measurements would be an important avenue of further research. The optimal pLA hyperlactataemia cut-off is also yet to be firmly established.

4.7. Recommendations

It is recommended that paramedics collect and report the lactate measurement to staff on handover in the ED. Considering the many limitations of this study, the findings do not necessarily support the view that all patients with an elevated lactate are to be given a more critical triage score or fast tracking to ICU. They do highlight that health professionals need to be more vigilant in monitoring patients with elevated pLA measurements to detect and respond to clinical deterioration quickly.

Given the number of patients who had a pLA taken was extremely low as a proportion of total patients, this suggests pLA is being underutilised by ACTAS. Because the results of this study support pLA testing as an early warning sign for patient deterioration, it is recommended that paramedics test for pLA as part of their normal assessment or screening of critically ill patients, regardless of the suspected diagnosis.

5. Conclusion

This retrospective research review compared pLA with mortality, ICU admission rates, and duration of stay in hospital. There is no statistically significant relationship between pLA and mortality or length of hospital stay, but there were significant relationships between elevated pLA and admission. Elevated prehospital lactate should be considered a potential marker for clinical deterioration. Further research is recommended to determine the impact of treatment following prehospital lactate measurements and the use of serial lactate measurements.

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Supplementary information

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.aucc.2018.02.006>.

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