RAMPEN
MANAGEMENT

ACADEMIEJAAR 2023-2024

Prehospital lactate for mortality prediction and triage in trauma patients: a narrative review

STUDENT: Dr. Garip Levin

PROMOTOR: Dr. Helsloot Dries

Abstract

Introduction:
In the context of mass casualty incidents, the reliance of emergency response personnel on clinical assessment limits both the timeliness and the accuracy of triage. Prehospital lactate measurements could enhance trauma triage accuracy and speed. We investigate the diagnostic performance of prehospital lactate in mortality prediction models as an adjunct to prehospital hemodynamic parameters in trauma patients and discuss its implications during mass casualty incidents. Our research questions were whether the addition of prehospital lactate to currently used prehospital scoring systems including clinical variables improved the prediction of mortality, need for resuscitative care and transfusion in terms of the area under the receiver operating characteristic curve (AUC-ROC) in trauma patients.

Methods:
A search strategy incorporating relevant terms was developed, followed by electronic searches of PubMed, Cochrane, and Embase databases. The Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool was used to critically appraise the methodological quality and risk of bias in the included studies.

Results:
Electronic searches resulted in 399 records. Twenty three records were retained for further analysis. The prognostic value of prehospital lactate regarding mortality, need for resuscitative care and transfusion in trauma patients was promising in most of the included studies. Quantitative analysis showed that prehospital lactate measurement increased the accuracy of prediction of early 2-day mortality and the need for resuscitative care (AUC increase of 0.273; $p < 0.001$ and 0.042; $p = 0.003$ respectively).

Conclusion:
Although simpler tools are preferred for rapid assessment during MCEs, more advanced triage systems including prehospital lactate may offer value in guiding more accurate triage decisions. In conclusion, prehospital lactate measurement in trauma patients offers promising prognostic value, especially when combined with vital signs. However, further research specifically addressing its role in MCEs is essential to establish definitive conclusions.

Abstract

Introductie:
Hulpverleners zijn vaak beperkt tot de klinische beoordeling van slachtoffers in de context van grootschalige incidenten. Dit limiteert de snelheid en de nauwkeurigheid van triage. Prehospitaal lactaatmetingen zouden de nauwkeurigheid en snelheid van de triage kunnen verbeteren. Wij onderzoeken de diagnostische performantie van prehospitaal lactaat in mortaliteitsvoorspellingsmodellen als aanvulling op prehospitale hemodynamische parameters bij traumapatiënten en bespreken de implicaties ervan tijdens rampen. Onze onderzoeksvragen zijn of de toevoeging van prehospitaal lactaat aan momenteel gebruikte prehospitale scoringsystemen op basis van klinische variabelen de voorspelling van mortaliteit verbetert in termen van de ‘area under the receiver operating characteristic curve’ (AUC-ROC) bij traumapatiënten.

Methodes:
Er werd een zoekstrategie ontwikkeld met relevante termen, gevolgd door elektronische zoekacties in de databases PubMed, Cochrane en Embase. De QUADAS-2 (Quality Assessment of Diagnostic Accuracy Studies-2) tool werd gebruikt om de methodologische kwaliteit en het risico op bias in de geïncludeerde studies kritisch te beoordelen.

Resultaten:
Elektronische zoekopdrachten leverden 399 resultaten op. Drieëntwintig studies werden geselecteerd voor verdere analyse. De prognostische waarde van prehospitaal lactaat met betrekking tot mortaliteit, nood aan levensreddende handelingen en transfusie bij traumapatiënten was veelbelovend in de meeste geïncludeerde studies. Kwantitatieve analyse toonde aan dat prehospitaal lactaatmeting de nauwkeurigheid van de predictie van vroege mortaliteit op dag 2 en de nood aan levensreddende handelingen verhoogde (toename in AUC-waarde van respectievelijk 0,273; $p < 0,001$ en 0,042; $p = 0,003$).

Conclusie:
Hoewel eenvoudigere tools de voorkeur hebben voor een snelle beoordeling tijdens rampen, kunnen meer geavanceerde triagesystemen met prehospitaal lactaat, waardevol zijn bij het nemen van meer accurate triagebeslissingen. Concluderend biedt prehospitaal lactaatmeting bij traumapatiënten veelbelovende prognostische waarde, vooral in combinatie met vitale functies. Verder onderzoek dat specifiek gericht is op de rol ervan bij rampen is echter essentieel om definitieve conclusies te kunnen trekken.

Introduction

During mass casualty events (MCEs), efficient triage is paramount to ensure that limited resources are allocated effectively and patients receive appropriate care based on the severity of their injuries (1). Traditional triage methods rely mostly on clinical assessment, which may be challenging in situations where large numbers of casualties overwhelm healthcare systems. To address these challenges, healthcare providers are increasingly turning to novel tools and technologies to enhance the speed and accuracy of triage processes (2). One such tool gaining prominence is the use of prehospital lactate measurements in the triage of trauma patients during mass casualty events . Lactate, a byproduct of anaerobic metabolism, is a biomarker that reflects tissue hypoperfusion and tissue hypoxia, both of which are indicators of shock and tissue injury (3). By measuring lactate levels in the prehospital setting, emergency medical services (EMS) personnel can rapidly assess the severity of a patient's condition and prioritize treatment accordingly.

Diagnostic performance evaluation of trauma triage scoring systems is crucial in ensuring their effectiveness in accurately identifying and prioritizing patients with severe injuries. These scoring systems, such as the Revised Trauma Score (RTS), Shock Index (SI) and Glasgow Coma Scale (GCS), among others, are designed to provide healthcare providers with objective measures of injury severity and physiological status, aiding in timely and appropriate triage decisions (1). The diagnostic performance of trauma triage scoring systems is typically assessed through various metrics, including the area under the receiver operating characteristic curve (AUC-ROC). The AUC-ROC provides an overall measure of the scoring system's ability to discriminate between patients with and without severe injuries (4). Continuous refinement and validation of trauma triage scoring systems are essential to address their limitations and enhance their diagnostic performance across diverse patient populations and clinical settings. Incorporating novel biomarkers, such as lactate, into existing scoring systems may further improve their accuracy and predictive value (5), enabling more precise patient triage and resource allocation during mass casualty incidents.

Point-of-care (POC) testing has revolutionized medical practice by providing rapid diagnostic information directly on scene, facilitating prompt decision-making and improving patient outcomes (2). Furthermore, the advent of portable and user-friendly POC lactate analyzers has streamlined the testing process, making it accessible even in challenging environments such as prehospital settings and mass casualty incidents. With minimal training required, frontline healthcare personnel can perform lactate measurements with ease, circumventing the delays associated with traditional laboratory testing and expediting patient care.

A systematic review in 2016 by Christopher et al. (6) about prehospital POC lactate in trauma patients included seven articles and addressed the paucity of evidence at that time. In our review, the current relevant literature is reviewed. We investigate the diagnostic performance of prehospital lactate in mortality prediction models as an adjunct to prehospital hemodynamic parameters in trauma patients and discuss its implications during mass casualty incidents.

Methods

Research question

The primary research question was whether the addition of prehospital lactate to currently used prehospital scoring systems including clinical variables improved the prediction of mortality in terms of the area under the receiver operating characteristic curve (AUC-ROC) in trauma patients. Secondary research questions were whether the addition of prehospital lactate to currently used prehospital scoring systems including clinical variables improved the prediction of the need for resuscitative care and the need for transfusion in terms of the AUC-ROC in trauma patients.

Outcome measures

The outcome measures that were relevant in this review are mortality, need for resuscitative care and need for transfusion. Mortality was defined as death at any time after admission. Need for resuscitative care was defined as any prehospital or in-hospital intervention necessary to improve patient care. These interventions included the administration of vasoactive medication, airway management, surgical procedures, transfusion or other interventions. Transfusion was defined as any administration of blood products at any time after admission.

Eligibility criteria

The eligibility criteria were defined before the literature search. All studies were considered eligible when at least a subgroup of the study population included trauma patients. Studies including lactate measurement and any prehospital data were eligible. Studies were required to discuss at least one of the three outcome measures in this review, i.e. mortality, need for resuscitative care or need for transfusion. There were no restrictions regarding the date of publication or the study type. However, only publications in English were included.

Search strategy

After a scoping search, a search strategy was conducted using relevant search terms (appendix 1). Electronic searches of the PubMed, Cochrane, and Embase databases were performed. Search results were screened by abstract using the predefined eligibility criteria. The eligibility of the articles was determined by analyzing the full text when necessary. Citation searches were also carried out in order to identify additional records. The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram was used to summarize the screening process (7).

Risk of bias analysis

The Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool was used to critically appraise the methodological quality and risk of bias in the included studies (8). This quality assessment tool was considered most suitable in this review evaluating the diagnostic accuracy of prehospital lactate. A template describing the study type, study population, index test, reference standard, target condition and test performance was used to summarize each study.

Synthesis of data

Due to the heterogeneity of the patient population and the outcome measures, the majority of results were reported in a narrative review. Studies were grouped according to the outcome measures that were investigated. A significance level of 0.05 was considered significant in this review. A quantitative analysis was conducted on early outcome measures, defined as those occurring within two days. These were considered the most likely to reflect the prognostic value of prehospital lactate. However, raw data from the included trials were not obtained. Therefore, mean differences, the power of outcome results and related p-values were used instead. Standard deviations were estimated according to the Cochrane Handbook (9). A confidence level of 95% was used. Outcomes for which the significance values were not known, were excluded from the analysis. The analyses were conducted using an open-source software tool from the Center for Evidence Synthesis, employing the DerSimonian-Laird continuous random-effects method (10). Mean differences were calculated instead of standardized mean differences, as all outcomes were readily interpretable.

Results

Search results

Electronic searches of the PubMed, Cochrane, and Embase databases resulted in 399 records. Eighteen records were considered eligible. Twelve records lacked prehospital data, eight records contained no relevant outcome measures and 340 records were considered irrelevant to this review. Full reports were not available from seven articles while the abstract contained insufficient data. Fourteen duplicate records were removed and five additional records were identified from citation searching. Finally, 23 studies remained for further analysis. The screening process is summarized in Figure 1.

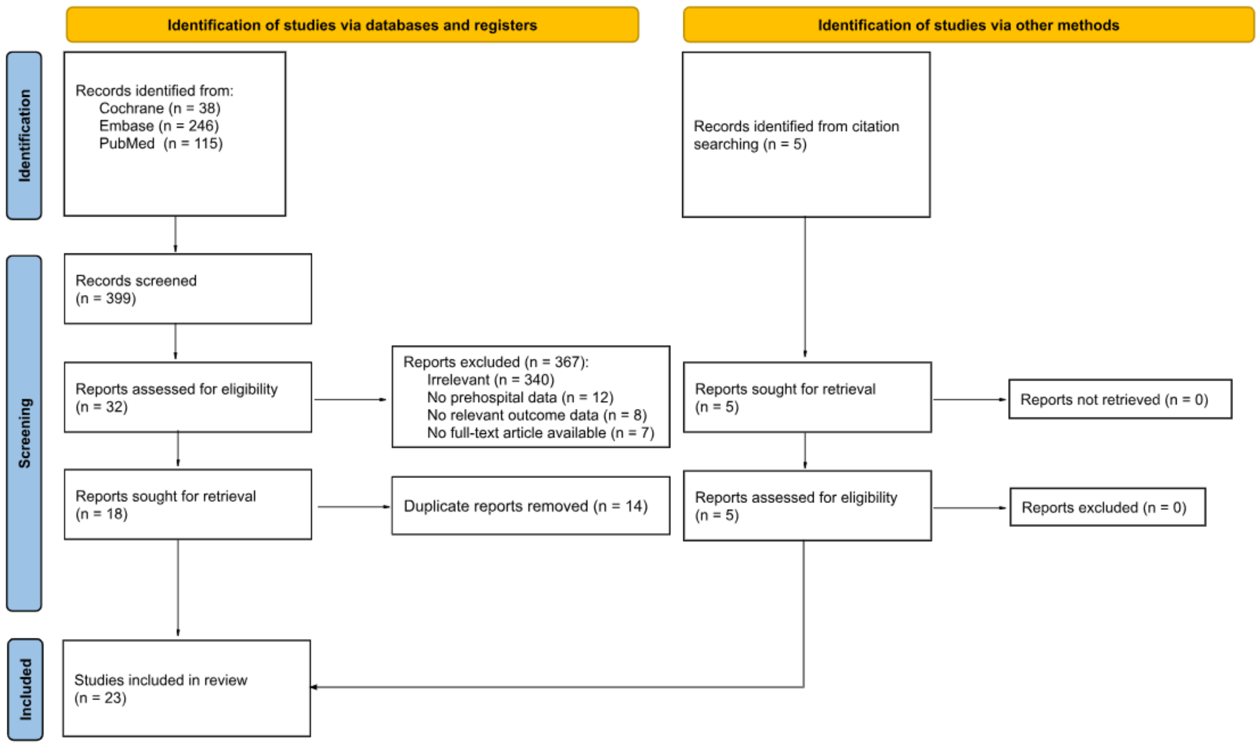

Figure 1. PRISMA 2020 flow diagram for new systematic reviews which included searches of databases, registers and other sources

Study characteristics

The total population of the studies included 20,114 patients. One study by Brio-Ibañez et al. (11) investigated the general emergency department population. In five studies (12–16), only a small subgroup of trauma patients was included. No subgroup analysis of trauma patients was performed in these studies. Shah et al. (17) focused on the pediatric trauma population. Some studies investigated patients in specific clinical conditions (16,18–22). Frequent exclusion criteria were other medical causes of increased lactate, traumatic cardiac arrest, death before hospital arrival, absence of prehospital lactate measurement or isolated traumatic brain injury. Thirteen studies were monocentric (15–21,23–28), while ten studies were multicentric (11–14,22,29–33). Two studies evaluated emergency department lactate instead of prehospital lactate (19,20). All other studies either evaluated prehospital lactate or a model or scoring system including prehospital lactate.

Risk of bias

A complete risk of bias assessment according to QUADAS-2 was conducted for each study (appendix 2). Selection bias is a large concern in a majority of the studies. Some studies requested intravenous access in order to obtain a lactate measurement, while other studies only included certain prehospital pathways by restricting air or ground EMS or by requiring prehospital attendance by a physician (14,17,18,22,24,25,27,29,32). The problem regarding these restrictions arises when the decision to obtain intravenous access or to dispatch an emergency physician to the scene is unprotocolized and based on the subjective evaluation of the patient's clinical condition. In accordance with this, Griggs et al. (30) examined the prediction of need for in-hospital blood transfusion where the decision to transfuse blood products was based on clinical gestalt. The study by Martín-Rodríguez et al. (31), in which the administration of tranexamic acid or noradrenaline was considered a lifesaving intervention, faces a similar risk.

Several studies were at risk of intervention bias due to the lack of blinding of EMS personnel. Subjects could have received more aggressive treatment when their lactate values were higher. Some studies (18,29) stated that they didn't allow any change of treatment despite the displayed lactate value. Guyette et al. (24) and Shah et al. (17) only allowed alteration of treatment in consultation with a medical command physician and blinded the receiving team. Jansen et al. (16) blinded the hospital physicians but not the prehospital team. Guyette et al. (22) and Martin-Rodriguez et al. (31) successfully blinded both the EMS providers and the receiving trauma team to the lactate values. Gaessler et al. (32) eliminated this bias altogether by processing the prehospital blood sample on arrival at the hospital.

Another possible source of bias is the inconsequent measurement of lactate. Some studies suggested that this is potentially due to inattention to the study protocol or due to patients in extremis where EMS personnel had to prioritize patient care.

Even though some studies compared prehospital lactate with prehospital scoring systems and vital signs, nine studies did not (11,14,16,17,23,25,29,30,32). In these studies, the performance of prehospital lactate was compared to chance levels (AUC = 0.5). This makes it difficult to assess their relevance to clinical practice. Finally, prehospital blood transfusion was not considered as an outcome measure in all included studies. However, Zadorozny et al. (26) controlled for this in their analysis.

Outcome measures

The mortality outcome measure was subdivided according to length of follow-up. Need for resuscitative care was not subdivided due to the heterogeneous definitions that were used. Resuscitative care was commonly defined as emergency surgery like laparotomy, thoracotomy, craniotomy, vascular repair or pelvic fixation, and interventional radiology procedures. Need for transfusion was subdivided according to the amount and the time frame of blood transfusion. Comparison of test performance with chance levels or the reference standard is summarized in table 1 and table 2 respectively.

Mortality

Emergency department mortality

Prediction of emergency department mortality by prehospital lactate was investigated by St John et al. (18) in non-hypotensive trauma patients. The AUC was calculated to be 0.863, although the study lacked sufficient statistical significance data to be considered reliable.

2-day mortality

Martín-Rodríguez et al. (12) compared the performance of prehospital lactate with Prehospital National Early Warning Score 2 (NEWS2) for the prediction of 2-day mortality. The AUC of prehospital lactate was significantly lower than the AUC of NEWS2 (0.79 vs 0.90; $p < 0.05$). Furthermore, the combination of NEWS2 and prehospital lactate did not offer any advantage compared to NEWS2 alone (AUC = 0.90 vs 0.91; $p > 0.05$) for the prediction of 2-day mortality. In another study by Martín-Rodríguez et al. (23), prehospital lactate reached an AUC of 0.813 ($p < 0.001$) for the prediction of 2-day mortality.

Table 1. Table of comparison of test performance with chance levels. If significance against chance levels was not available, but the index test was significantly different from a reference standard. Then the least significantly differing reference standard is reported. Since we assumed that this reference standard would at least have an AUC of 0.5. If the AUC of pLA and a model including pLA were both available, then the AUC of pLA is reported.

Study	Sample size	AUC of index test	Significance	Notes
Mortality				
Emergency department mortality				
St John et al., 2018	314	0.863	N/A	
2-day mortality				
Martín-Rodríguez et al., Emergencias, 2019	707	0.79	$p < 0.001$	17.5% are trauma patients
Martín-Rodríguez et al., Signa Vitae, 2019	109	0.813	$p < 0.001$	
In-hospital 2-day mortality				
Martín-Rodríguez et al., European Journal of Clinical Investigation, 2020	373	0.855	$p < 0.001$	
Brio-Ibañez et al., 2020	1341	0.800	$p < 0.001$	General ED population
Martín-Rodríguez et al., 2023	763	0.979	$p = 0.017$	
Martín-Rodríguez et al., Journal of Clinical Medicine, 2020	3081	0.913	$p < 0.001$	11.2% are trauma patients. Low-medium risk group
7-day mortality				
Martín-Rodríguez et al., Emergencias, 2019	707	0.76	$p < 0.001$	17.5% are trauma patients
Martín-Rodríguez et al., Signa Vitae, 2019	109	0.836	$p < 0.001$	
In-hospital 7-day mortality				
Brio-Ibañez et al., 2020	1341	0.736	$p < 0.001$	General ED population
30-day mortality				
Martín-Rodríguez et al., Emergencias, 2019	707	0.72	$p < 0.001$	17.5% are trauma patients
Martín-Rodríguez et al., American Journal of Emergency Medicine, 2019	279	0.82	$p < 0.05$	14.3% are trauma patients
Martín-Rodríguez et al., Signa Vitae, 2019	109	0.805	$p < 0.001$	
Corral et al., 2023	709	0.596	$p = 0.008$	
In-hospital 30-day mortality				
Brio-Ibañez et al., 2020	1341	0.691	$p < 0.001$	General ED population
Mortality (length of follow-up undefined)				
Galvagno et al., 2018	260	0.52	$p > 0.05$	
In-hospital mortality (length of follow-up undefined)				
Van Beest et al., 2009	216	0.827	$p < 0.01$	7.4% are trauma patients
Guyette et al., 2011	1168	0.89	$p < 0.001$	
Jansen et al., 2008	124	0.69	$p = 0.001$	17% are trauma patients

Need for resuscitative care				
Guyette et al., 2015	387	0.78	$p = 0.01$	
Shah et al., 2013	217	0.71	$p = 0.01$	Pediatric population
Galvagno et al., 2018	260	0.70	$p < 0.05$	
Fukuma et al., 2019	435	0.764	$p < 0.0001$	
Zadorozny et al., 2022	2170	0.823	$p = 0.07$	
St John et al., 2018	314	0.716	$p < 0.05$	
Martín-Rodríguez et al., 2023	763	0.927	$p < 0.05$	
Galvagno et al., 2020	261	0.71	$p < 0.05$	
Guyette et al., 2011	1168	0.71	$p = 0.02$	
Transfusion				
Need for any immediate in-hospital transfusion				
Griggs et al., 2022	194	0.72	N/A	
Galvagno et al., 2020	261	0.88	$p < 0.05$	
Gaessler et al., 2023	130	0.731	$p < 0.05$	
Need for at least 5 units of blood transfusion within 6 hours after admission				
St John et al., 2018	314	0.785	$p < 0.05$	
Need for any in-hospital blood transfusion within 24 hours after admission				
Zadorozny et al., 2022	2170	0.867	$p = 0.03$	
Need for at least 10 units of blood transfusion within 24 hours after admission				
Galvagno et al., 2018	260	0.85	$p < 0.05$	
Fukuma et al., 2019	435	0.764	$p < 0.0001$	

Table 2. Table of comparison of test performance with the reference standard. The best performing reference standard is reported when multiple reference standards were used. If performance of pLA and a model including pLA were both available, then pLA model performance is reported.

Study	Reference standard	Sample size	AUC of index test	AUC of reference standard	Significance	Notes
Mortality						
Emergency department mortality						
St John et al., 2018	Chance levels	314	0.863	0.5	N/A	
2-day mortality						
Martín-Rodríguez et al., Emergencias, 2019	Prehospital National Early Warning Score 2	707	0.91	0.90	p > 0.05	17.5% are trauma patients
Martín-Rodríguez et al., Signa Vitae, 2019	Chance levels	109	0.813	0.5	p < 0.001	
In-hospital 2-day mortality						
Martín-Rodríguez et al., European Journal of Clinical Investigation, 2020	Chance levels	373	0.855	0.5	p < 0.001	
Brio-Ibañez et al., 2020	Chance levels	1341	0.800	0.5	p < 0.001	General ED population
Martín-Rodríguez et al., 2023	Mechanism, GCS, age and prehospital arterial blood pressure	763	0.979	0.901	p = 0.017	
Martín-Rodríguez et al., Journal of Clinical Medicine, 2020	Prehospital National Early Warning Score 2	3081	0.913	0.5	p < 0.001	11.2% are trauma patients. Low-medium risk group
7-day mortality						
Martín-Rodríguez et al., Emergencias, 2019	Prehospital National Early Warning Score 2	707	0.86	0.85	p > 0.05	17.5% are trauma patients
Martín-Rodríguez et al., Signa Vitae, 2019	Chance levels	109	0.836	0.5	p < 0.001	
In-hospital 7-day mortality						
Brio-Ibañez et al., 2020	Chance levels	1341	0.736	0.5	p < 0.001	General ED population
30-day mortality						
Martín-Rodríguez et al., Emergencias, 2019	Prehospital National Early Warning Score 2	707	0.82	0.82	p > 0.05	17.5% are trauma patients
Martín-Rodríguez et al., American Journal of Emergency Medicine, 2019	Chance levels	279	0.82	0.5	p < 0.05	14.3% are trauma patients
Martín-Rodríguez et al., Signa Vitae, 2019	Chance levels	109	0.805	0.5	p < 0.001	
Corral et al., 2023	Glasgow Coma Scale	709	0.596	0.812	N/A	
In-hospital 30-day mortality						
Brio-Ibañez et al., 2020	Chance levels	1341	0.691	0.5	p < 0.001	General ED population
Mortality (length of follow-up undefined)						
Galvagno et al., 2018	Prehospital continuous vital signs analysis	260	0.52	0.90	p < 0.05	
In-hospital mortality (length of follow-up undefined)						
Van Beest et al., 2009	Prehospital heart rate	216	0.827	0.500	p < 0.01	7.4% are trauma patients
Guyette et al., 2011	Age, sex, initial systolic blood pressure, heart rate, respiratory rate, and GCS	1168	0.89	0.85	p < 0.001	

Jansen et al., 2008	Chance levels	124	0.69	0.5	$p = 0.001$	17% are trauma patients
Need for resuscitative care						
Guyette et al., 2015	Prehospital shock index	387	0.78	0.66	$p = 0.01$	
Shah et al., 2013	Chance levels	217	0.71	0.5	$p = 0.01$	Pediatric population
Galvagno et al., 2018	Prehospital continuous vital signs analysis	260	0.70	0.71	$p > 0.05$	
Fukuma et al., 2019	Prehospital systolic blood pressure, heart rate, respiratory rate, GCS, shock index and mechanism of penetrating injury	435	0.882	0.837	$p = 0.0073$	
Zadorozny et al., 2022	Prehospital vital signs, mission type, anatomic location of injury and prehospital administration of blood products	2170	0.823	0.819	$p = 0.07$	
St John et al., 2018	Prehospital shock index	314	0.716	0.631	$p = 0.125$	
Martín-Rodríguez et al., 2023	Mechanism, GCS, age and prehospital arterial blood pressure	763	0.927	0.900	$p = 0.061$	
Galvagno et al., 2020	Chance levels	261	0.71	0.5	$p < 0.05$	
Guyette et al., 2011	Age, sex, initial systolic blood pressure, heart rate, respiratory rate, and GCS	1168	0.71	0.68	$p = 0.02$	
Transfusion						
Need for any immediate in-hospital transfusion						
Griggs et al., 2022	Chance levels	194	0.72	0.5	N/A	
Galvagno et al., 2020	Chance levels	261	0.88	0.5	$p < 0.05$	
Gaessler et al., 2023	Chance levels	130	0.871	0.5	$p < 0.05$	
Need for at least 5 units of blood transfusion within 6 hours after admission						
St John et al., 2018	Chance levels	314	0.785	0.5	$p < 0.05$	
Need for any in-hospital blood transfusion within 24 hours after admission						
Zadorozny et al., 2022	Prehospital vital signs, mission type, anatomic location of injury and prehospital administration of blood products	2170	0.867	0.863	$p = 0.03$	
Need for at least 10 units of blood transfusion within 24 hours after admission						
Galvagno et al., 2018	Prehospital continuous vital signs analysis	260	0.85	0.96	$p > 0.05$	
Fukuma et al., 2019	Prehospital systolic blood pressure, heart rate, respiratory rate, GCS, shock index and mechanism of penetrating injury	435	0.903	0.895	$p = 0.32$	

In-hospital 2-day mortality

Four studies reported the performance of prehospital lactate for predicting in-hospital 2-day mortality (11,13,29,31). Brio-Ibañez et al. (11) and Martín-Rodríguez et al. (29) reported AUC values of 0.800 ($p < 0.001$) and 0.855 ($p < 0.001$) respectively. The study by Martín-Rodríguez et al. (31) compared the use of the prehospital mSOFA score with other scoring systems that do not include lactate measurement. The mSOFA score contains GCS, mean arterial pressure, oxygen saturation divided by fraction of inspired oxygen, creatinine and lactate. The predictive capacity of prehospital mSOFA, a scoring system including lactate, was superior to any other scoring system (AUC = 0.979). The second best scoring system was the MGAP score (mechanism of injury, GCS, age and prehospital arterial blood pressure) (AUC = 0.901; $p = 0.017$ compared to mSOFA). Another study by Martín-Rodríguez et al. (13) compared prehospital lactate with the NEWS2 after stratifying the study population according to NEWS2 risk groups. The study showed that prehospital lactate was superior to NEWS2 in predicting in-hospital 2-day mortality in the low and medium risk groups with AUC values as high as 0.913 ($p < 0.001$). However, prehospital lactate did not perform better than NEWS2 in the high risk group (AUC = 0.762 vs 0.756; $p = 0.86$). A quantitative analysis demonstrated that the implementation of prehospital lactate measurement significantly improved the prognostic value regarding 2-day mortality. A significant increase of 0.273 of the AUC value was observed ($p < 0.001$) (Figure 2).

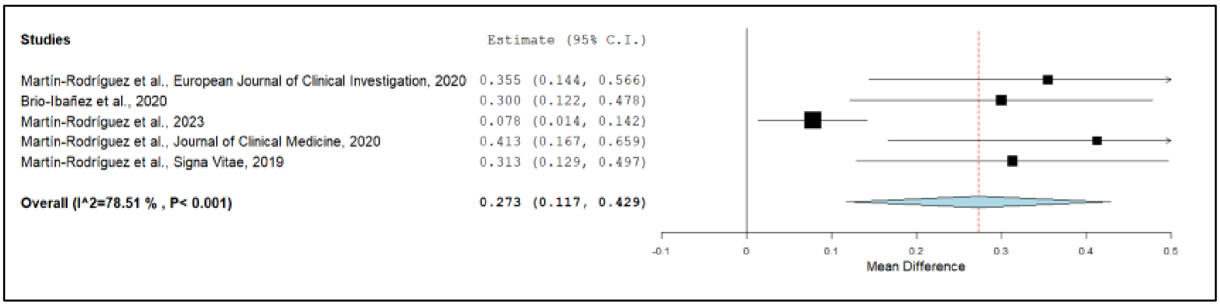

Figure 2. A forest plot of 2-day mortality is shown. Mean difference equals the difference between the AUC value of the index and reference test. A positive value favors the index test performance and thus prehospital lactate measurement. The black squares and horizontal lines represent individual studies and their confidence intervals respectively. The red dotted line and blue diamond represent the overall effect size and its confidence interval respectively. Overall mean difference is 0.273 ($p < 0.001$).

7-day mortality

Prehospital lactate performed worse than NEWS2 for the prediction of 7-day mortality (AUC = 0.76 vs 0.85; $p < 0.05$). The addition of lactate to NEWS2 did not improve performance (AUC = 0.85 vs 0.86; $p > 0.05$) (12). In another study by Martín-Rodríguez et al. (23), prehospital lactate reached an AUC of 0.836 ($p < 0.001$) for the prediction of 7-day mortality.

In-hospital 7-day mortality

Only one study (11) compared the prediction of in-hospital 7-day mortality by prehospital lactate to chance levels. An AUC of 0.736 ($p < 0.001$) was reached.

30-day mortality

In line with 2-, and 7-day mortality, the AUC of prehospital lactate for 30-day mortality was inferior to NEWS2 (AUC = 0.72 vs 0.82; $p < 0.05$). The addition of lactate to NEWS2 did not improve performance (AUC = 0.82 vs 0.82; $p > 0.05$) (12). Another study reported the predictive capacity of prehospital lactate (AUC = 0.596; $p = 0.008$), systolic blood pressure (AUC = 0.599; $p < 0.001$), heart rate (AUC = 0.538; no p-value), respiratory rate (AUC = 0.695; $p < 0.001$), oxygen saturation (AUC = 0.593; $p < 0.001$) and GCS (AUC = 0.812; $p < 0.001$) for 30-day mortality (33). Two studies by Martín-Rodríguez et al. reported AUC values of 0.805 ($p < 0.001$) (23) and 0.82 ($p < 0.05$) (14) for the prediction of 30-day mortality.

In-hospital 30-day mortality

Only one study (11) compared the prediction of in-hospital 30-day mortality by prehospital lactate to chance levels. An AUC of 0.691 ($p < 0.001$) was reached.

Mortality (length of follow-up undefined)

Galvagno et al. (28) studied the use of continuous vital signs data analysis for the prediction of mortality. A multivariate logistic regression analysis was used to analyze over 300 vital signs waveform components like heart rate variability using time-domain methods and various vital sign thresholds. Continuous vital signs data analysis outperformed prehospital lactate measurement for the prediction of mortality (AUC = 0.90 vs 0.52; $p < 0.05$).

In-hospital mortality (length of follow-up undefined)

Jansen et al. (16) reached an AUC of 0.69 ($p = 0.001$) for prehospital lactate in predicting in-hospital mortality in patients with abnormal prehospital vital signs. Guyette et al. (24) concluded that the addition of prehospital lactate improved the performance of a model including age, sex, initial systolic blood pressure, heart rate, respiratory rate, and GCS (AUC = 0.89 vs 0.85; $p < 0.001$). Van Beest et al. (15) compared the performance of prehospital lactate (AUC = 0.827) to other prehospital vital signs for the prediction of in-hospital mortality. Prehospital oxygen saturation (AUC = 0.127), mean arterial pressure (AUC = 0.350) and heart rate (AUC = 0.500) were all inferior to prehospital lactate ($p < 0.01$).

Need for resuscitative care

Prehospital lactate measurement accurately predicted the need for emergent surgery within 24 hours in combination with age, sex, initial systolic blood pressure, heart rate, respiratory rate, and GCS. The addition of prehospital lactate to the model significantly improved the prediction of emergent surgery within 24 hours (AUC = 0.71 vs 0.68; $p = 0.02$) (24). Prehospital lactate was performant in the prediction of both prehospital (AUC = 0.71; $p < 0.05$) and in-hospital lifesaving interventions (AUC = 0.72; $p < 0.05$) (25). Prehospital lactate had the greatest association with the prediction for lifesaving interventions compared to static vital signs and other laboratory parameters. Continuous vital signs data analysis performed similar to prehospital lactate for predicting need for lifesaving interventions (AUC = 0.71 vs 0.70; $p > 0.05$) (28). The mSOFA score reached the highest AUC compared to other prehospital scoring systems (AUC = 0.927). The mSOFA, a score including lactate, was significantly better at predicting need for lifesaving interventions than the BIG score (base deficit, INR and GCS) (AUC = 0.579; $p < 0.001$) and the New Trauma Score (GCS, systolic blood pressure and oxygen saturation) (AUC = 0.539; p < 0.001) (31). A comparison of shock index and prehospital lactate resulted in AUC values of 0.631 and 0.716 respectively, but these values did not differ significantly (p = 0.125) (18). However, another study (22) showed that prehospital lactate was more predictive than prehospital systolic blood pressure (AUC = 0.78 vs 0.59; p < 0.001) and prehospital shock index (AUC = 0.78 vs 0.66; p = 0.01). Zadorozny et al. (26) failed to prove the additional value of prehospital lactate in a model including vital signs, mission type, anatomic location of injury and prehospital administration of blood products for the prediction of need for lifesaving interventions (AUC = 0.823 vs 0.819; p = 0.07). In a study by Fukuma et al. (27), prehospital lactate was no different from prehospital physiological variables for the prediction of need for immediate intervention (AUC = 0.764 vs 0.837; no p-value). But the addition of prehospital lactate significantly improved prediction performance compared to physiological variables alone (AUC = 0.837 vs 0.882; p = 0.0073). In a pediatric population, an AUC value of 0.71 (p = 0.01) was reached (17). A quantitative analysis demonstrated that the implementation of prehospital lactate measurement significantly improved the prognostic value regarding the need for resuscitative care. A significant increase of 0.042 of the AUC value was observed (p = 0.003) (Figure 3).

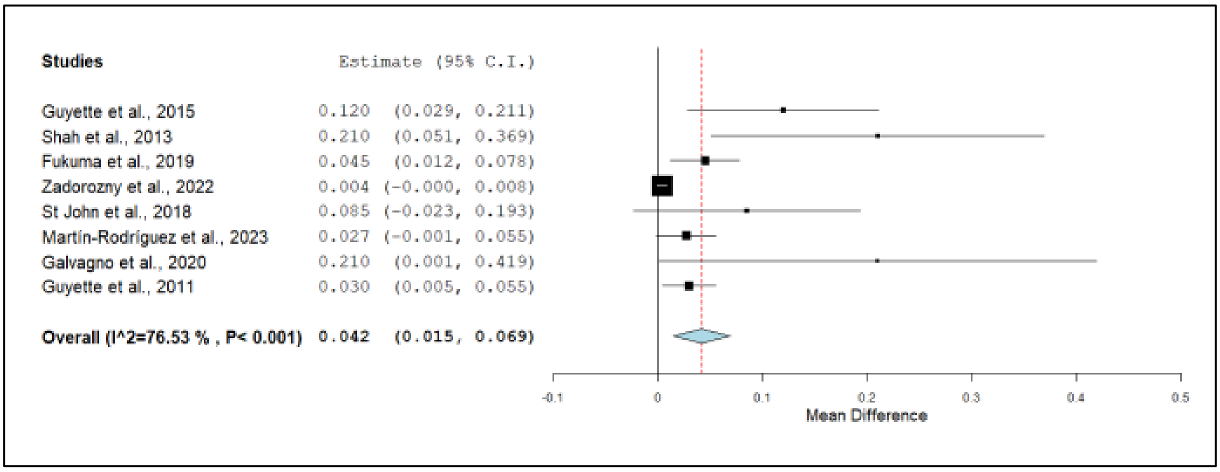

Figure 3. A forest plot of need for resuscitative care is shown. Mean difference equals the difference between the AUC value of the index and reference test. A positive value favors the index test performance and thus prehospital lactate measurement. The black squares and horizontal lines represent individual studies and their confidence intervals respectively. The red dotted line and blue diamond represent the overall effect size and its confidence interval respectively. Overall mean difference is 0.042 (p = 0.003).

Need for transfusion

Need for any immediate in-hospital blood transfusion

Two studies reported a prehospital lactate AUC value of 0.88 ($p < 0.05$) (25) and 0.72 (no p-value) (30) for the prediction of immediate in-hospital blood requirement. Gaessler et al. (32) developed a model including prehospital lactate, the presence of suspected bleeding and the presence of cardiovascular instability. This model (AUC = 0.871; $p < 0.05$) reached a higher AUC value compared to prehospital lactate (AUC = 0.731; $p < 0.05$), the presence of suspected bleeding (AUC = 0.766; p = 0.001) or the presence of cardiovascular instability alone (AUC = 0.701; $p < 0.001$).

Need for at least 5 units of blood transfusion within 6 hours after admission

One study (18) reported that prehospital lactate had an AUC value of 0.785 ($p < 0.05$) for predicting the need for at least 5 units of blood transfusion within 6 hours after admission.

Need for any in-hospital blood transfusion within 24 hours after admission

The predictive performance of a model including vital signs, mission type, anatomic location of injury and prehospital administration of blood products was significantly better in predicting blood requirement when prehospital lactate was incorporated into the model (AUC = 0.867 vs 0.863; p = 0.03) (26).

Need for at least 10 units of blood transfusion within 24 hours after admission

Massive transfusion is regarded as the need for at least 10 units of blood transfusion within 24 hours after admission. In a study by Fukuma et al. (27), prehospital lactate was no different from prehospital physiological variables for the prediction of need for massive transfusion (AUC = 0.764 vs 0.895; no p-value). The addition of prehospital lactate did not improve prediction performance compared to physiological variables alone (AUC = 0.895 vs 0.903; p = 0.32). No difference in prediction performance was observed between continuous vital signs data analysis and prehospital lactate measurement for massive transfusion (AUC = 0.96 vs 0.85; $p > 0.05$) (28).

Discussion

This is the first review to address the current literature regarding the utilization of prehospital lactate measurement in injured patients and to discuss the implications in the context of mass casualty events. In mass casualty incidents, primary and secondary triage systems play crucial roles in efficiently managing patient care and allocating resources (34). Primary triage occurs at the scene of the incident, where trained personnel quickly assess and categorize patients based on the severity of their injuries and the urgency of medical intervention needed. Primary triage is fast and simple and can be applied rapidly by first responders and healthcare providers with varying levels of training. This assessment helps prioritize treatment and transportation, ensuring that those with life-threatening injuries receive immediate attention. In situations where the number of injured individuals is significant, and logistical constraints prevent the immediate transfer of all patients to medical facilities, or when the scale of the incident overwhelms prehospital resources, the process of evacuating all casualties from the scene may be prolonged. Consequently, it is possible that some injured individuals may remain on scene for an extended period. In such cases, secondary triage systems are implemented. Secondary triage takes place at designated triage areas, where patients are reassessed upon arrival. More advanced triage systems are used in this case. This allows for further evaluation of injuries, adjustment of priorities based on evolving medical needs, and distribution of patients to appropriate facilities or treatment areas. The objective of our review was to assess the additional prognostic value of prehospital lactate measurement in these advanced triage systems used for secondary triage in MCEs.

Prehospital lactate levels serve as a valuable biomarker for assessing tissue perfusion and metabolic status in trauma patients (3). In MCEs, where resources may be limited and patient volume overwhelms healthcare systems, accurately identifying patients with occult hypoperfusion - those with inadequate tissue perfusion despite normal vital signs - is challenging but essential. In the prehospital setting, where traditional vital signs may not fully capture the severity of injury or shock, lactate measurement provides an objective assessment of tissue perfusion status. Our study revealed that the integration of prehospital lactate levels into triage protocols during MCEs can enhance the ability to prioritize patients based on their physiological status rather than relying solely on external signs of injury. Patients with elevated lactate levels are at higher risk of adverse outcomes, need for immediate intervention and expedited transport to higher-level care facilities.

Quantitative analysis showed that prehospital lactate measurement increased the accuracy of prediction of early 2-day mortality and the need for resuscitative care. An increase in AUC value of 0.273 ($p < 0.001$) and 0.042 ($p = 0.003$) was seen respectively. Prehospital lactate measurement can also improve the accuracy of prehospital criteria for designating trauma center referral. Brown et al. (35) found that incorporating prehospital lactate in an algorithm to designate trauma activation level reclassified patients to more appropriate levels of trauma activation compared to the algorithm based on clinical criteria alone. The lactate algorithm achieved this overall benefit by significantly reducing overtriage relative to a very small increase in undertriage. Overtriage was reduced by 7,2%, while undertriage only increased by 0.7%. The AUC was significantly higher for the lactate algorithm (AUC = 0.79 vs 0.76; $p < 0.01$). The study suggests that this trade-off may be acceptable in the context of trauma team activation. This may also be the case during MCEs.

While other biomarkers such as ionized calcium, base deficit, hemoglobin and pH have specific roles in trauma evaluation (36), lactate offers unique advantages in its systemic reflection of tissue perfusion and utility in guiding early resuscitation efforts during the critical initial phase of trauma care. Lactate is the biologically most plausible mediator of inadequate tissue perfusion (3). In the study by Corral et al. (33), prehospital lactate, pH, pCO_2, hemoglobin concentration, hematocrit and glycemia were significantly associated with 30-day mortality. However, Da Costa et al. (21) found that lactate was the only laboratory variable that was significantly associated with death. Lactate had the greatest association with the prediction for lifesaving interventions compared to static vital signs and other laboratory parameters (25).

When incorporating lactate values into a triage algorithm, threshold values need to be established for their clinical use. Most studies agreed on a lactate threshold value of 2, 2,5 or 4 mmol/L depending on the model that was used and the outcome measure that was investigated. In general, a lactate level of less than 2 mmol/L is considered normal, while a level greater than 4 mmol/L is considered abnormal. It is important to exercise caution when interpreting lactate levels in mass casualty victims, as they can also be elevated in crush injuries, hyperventilation or the presence of toxins (3).

During MCEs, the cost-effectiveness and ease of use of point-of-care lactate devices play a crucial role in enhancing the efficiency of patient care and resource utilization (2). POC lactate devices offer rapid on-site lactate measurement, enabling timely and easy identification of patients with tissue hypoperfusion or shock. This minimizes unnecessary interventions and maximizes the use of available resources, resulting in cost savings and improved outcomes. In resource-limited settings or during MCEs, access to laboratory-based lactate assays may be limited or delayed. POC lactate devices offer a cost-effective alternative by providing rapid results at the point of care, reducing the need for unnecessary laboratory testing and associated costs. POC lactate devices are designed for simplicity and ease of use, requiring minimal training for operation and interpretation of results. Healthcare providers can quickly learn to perform capillary blood sampling and use the device to obtain lactate measurements, even in high-stress environments characteristic of MCEs.

The two main addressed sample sites for prehospital lactate measurement were capillary and venous blood. Capillary lactate has been shown to have good correlation with arterial blood but agreement with venous blood is poorer (37). Capillary lactate values from the fingertip and earlobe were respectively 47% and 27% higher than arterial lactate indicating potential for overestimation of the lactate values in hemodynamically compromised patients. However, these inaccuracies can be overcome by calibrating future lactate thresholds with the sample site of interest.

There are several obstacles to the incorporation of prehospital lactate into triage algorithms. Integrating prehospital lactate values into triage algorithms requires standardized operating procedures, which are necessary to ensure consistency and effectiveness during MCEs. In these resource-limited settings, access to point-of-care lactate devices cannot be guaranteed. Overcoming logistical challenges to ensure widespread availability of these devices is essential. Although POC lactate devices are easy to use, effective utilization requires adequate training for emergency response workers.

Our review has some limitations. First, there was a considerable degree of heterogeneity between the study populations, the reference standards they employed and their clinical contexts. Substantial bias was evident in the majority of studies. In some studies, only a minority of the population were trauma patients. Second, no studies were identified that specifically examined the role of lactate measurement in triage systems employed during mass casualty events. However, conducting studies during MCEs is highly challenging. Therefore, trauma patients were used in this review as a surrogate population for mass casualty victims. However, mass casualty victims can face other dangers than trauma, such as exposure to hazardous materials. Third, the methodology employed in this review was not systematic, but it is conceivable that a more systematic approach could be implemented in the future. It is imperative that rigorous studies be conducted to validate intuitive and practical models in the context of mass casualty incidents.

Conclusion

In conclusion, the use of prehospital lactate measurement in trauma patients shows promising prognostic value, particularly when used alongside vital signs. Its integration into triage protocols during mass casualty events might enhance patient prioritization based on physiological status, which may improve outcomes and resource use. However, further studies focusing on the use of prehospital lactate during mass casualty events are warranted to draw definitive conclusions.

References

1. Bazyar J, Farrokhi M, Khankeh H. Triage Systems in Mass Casualty Incidents and Disasters: A Review Study with A Worldwide Approach. Open Access Maced J Med Sci. 2019;7(3):482-494. Published 2019 Feb 12. doi:10.3889/oamjms.2019.119

2. Stojek L, Bieler D, Neubert A, Ahnert T, Imach S. The potential of point-of-care diagnostics to optimise prehospital trauma triage: a systematic review of literature. Eur J Trauma Emerg Surg. 2023;49(4):1727-1739. doi:10.1007/s00068-023-02226-8

3. Andersen LW, Mackenhauer J, Roberts JC, Berg KM, Cocchi MN, Donnino MW. Etiology and therapeutic approach to elevated lactate levels. Mayo Clin Proc. 2013;88(10):1127-1140. doi:10.1016/j.mayocp.2013.06.012

4. Mandrekar JN. Receiver operating characteristic curve in diagnostic test assessment. J Thorac Oncol. 2010;5(9):1315-1316. doi:10.1097/JTO.0b013e3181ec173d

5. Moon J, Hwang K, Yoon D, Jung K. Inclusion of lactate level measured upon emergency room arrival in trauma outcome prediction models improves mortality prediction: a retrospective, single-center study. Acute Crit Care. 2020;35(2):102-109. doi:10.4266/acc.2019.00780

6. Lewis CT, Naumann DN, Crombie N, Midwinter MJ. Prehospital point-of-care lactate following trauma: A systematic review. J Trauma Acute Care Surg. 2016;81(4):748-755. doi:10.1097/TA.0000000000001192

7. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. Published 2021 Mar 29. doi:10.1136/bmj.n71

8. Yang B, Mallett S, Takwoingi Y, et al. QUADAS-C: A Tool for Assessing Risk of Bias in Comparative Diagnostic Accuracy Studies. Ann Intern Med. 2021;174(11):1592-1599. doi:10.7326/M21-2234

9. Cochrane Handbook. Version 6.0. [2019]. Cochrane, London, UK: Cochrane Collaboration. Available from: https://training.cochrane.org/handbook.

10. Wallace, B. C., Dahabreh, I. J., Trikalinos, T. A., Lau, J., Trow, P., & Schmid, C. H. Closing the Gap between Methodologists and End-Users: R as a Computational Back-End. Journal of Statistical Software. 2012; 49(5), 1–15. https://doi.org/10.18637/jss.v049.i05

11. Brio-Ibañez PD, López-Izquierdo R, Martín-Rodríguez F, et al. Clinical Utility of Delta Lactate for Predicting Early In-Hospital Mortality in Adult Patients: A Prospective, Multicentric, Cohort Study. Diagnostics (Basel). 2020;10(11):960. Published 2020 Nov 17. doi:10.3390/diagnostics10110960

12. Martín-Rodríguez F, López-Izquierdo R, Del Pozo Vegas C, Delgado Benito JF, Del Brio Ibáñez P, Moro Mangas I, et al. Predictive value of the prehospital NEWS2-L —National Early Warning Score 2 Lactate— for detecting early death after an emergency. Emergencias. 2019;31(3):173–9.

13. Martín-Rodríguez F, López-Izquierdo R, Benito JFD, Sanz-García A, Vegas CDP, Villamor MÁC, et al. Prehospital point-of-care lactate increases the prognostic accuracy of national early warning score 2 for early risk stratification of mortality: Results of a multicenter, observational study. J Clin Med. 2020 Apr 1;9(4).

14. Martín-Rodríguez F, López-Izquierdo R, Castro Villamor MA, et al. Prognostic value of lactate in prehospital care as a predictor of early mortality. Am J Emerg Med. 2019;37(9):1627-1632. doi:10.1016/j.ajem.2018.11.028

15. van Beest PA, Mulder PJ, Oetomo SB, van den Broek B, Kuiper MA, Spronk PE. Measurement of lactate in a prehospital setting is related to outcome. Eur J Emerg Med. 2009;16(6):318-322. doi:10.1097/mej.0b013e32832dbe54

16. Jansen TC, van Bommel J, Mulder PG, Rommes JH, Schieveld SJ, Bakker J. The prognostic value of blood lactate levels relative to that of vital signs in the pre-hospital setting: a pilot study. Crit Care. 2008;12(6):R160. doi:10.1186/cc7159

17. Shah A, Guyette F, Suffoletto B, et al. Diagnostic accuracy of a single point-of-care prehospital serum lactate for predicting outcomes in pediatric trauma patients. Pediatr Emerg Care. 2013;29(6):715-719. doi:10.1097/PEC.0b013e318294ddb1

18. St John AE, McCoy AM, Moyes AG, Guyette FX, Bulger EM, Sayre MR. Prehospital Lactate Predicts Need for Resuscitative Care in Non-hypotensive Trauma Patients. West J Emerg Med. 2018;19(2):224-231. doi:10.5811/westjem.2017.10.34674

19. Shackelford S, Yang S, Hu P, et al. Predicting blood transfusion using automated analysis of pulse oximetry signals and laboratory values. J Trauma Acute Care Surg. 2015;79(4 Suppl 2):S175-S180. doi:10.1097/TA.0000000000000738

20. Vandromme MJ, Griffin RL, Weinberg JA, Rue LW 3rd, Kerby JD. Lactate is a better predictor than systolic blood pressure for determining blood requirement and mortality: could prehospital measures improve trauma triage?. J Am Coll Surg. 2010;210(5):861-869. doi:10.1016/j.jamcollsurg.2010.01.012

21. da Costa LGV, Carmona MJC, Malbouisson LM, et al. Independent early predictors of mortality in polytrauma patients: a prospective, observational, longitudinal study. Clinics (Sao Paulo). 2017;72(8):461-468. doi:10.6061/clinics/2017(08)02

22. Guyette FX, Meier EN, Newgard C, et al. A comparison of prehospital lactate and systolic blood pressure for predicting the need for resuscitative care in trauma transported by ground. J Trauma Acute Care Surg. 2015;78(3):600-606. doi:10.1097/TA.0000000000000549

23. Francisco Martín-rodríguez, Raúl López-izquierdo. Prognostic value of lactate in prehospital care as a predictor of mortality and high-risk patients with trauma. Signa Vitae. 2019. 15(1);59-61.

24. Guyette F, Suffoletto B, Castillo JL, Quintero J, Callaway C, Puyana JC. Prehospital serum lactate as a predictor of outcomes in trauma patients: a retrospective observational study. J Trauma. 2011;70(4):782-786. doi:10.1097/TA.0b013e318210f5c9

25. Galvagno SM Jr, Sikorski RA, Floccare DJ, et al. Prehospital Point of Care Testing for the Early Detection of Shock and Prediction of Lifesaving Interventions. Shock. 2020;54(6):710-716. doi:10.1097/SHK.0000000000001567

26. Zadorozny EV, Weigel T, Stone A, et al. Prehospital Lactate is Associated with the Need for Blood in Trauma. Prehosp Emerg Care. 2022;26(4):590-599. doi:10.1080/10903127.2021.1983096

27. Fukuma H, Nakada TA, Shimada T, et al. Prehospital lactate improves prediction of the need for immediate interventions for hemorrhage after trauma. Sci Rep. 2019;9(1):13755. Published 2019 Sep 24. doi:10.1038/s41598-019-50253-6

28. Galvagno S. Prehospital continuous vital signs data analysis outperforms lactate for the prediction of lifesaving interventions in patients with traumatic shock. Shock. 2018.

29. Martín-Rodríguez F, López-Izquierdo R, Medina-Lozano E, et al. Accuracy of prehospital point-of-care lactate in early in-hospital mortality. Eur J Clin Invest. 2020;50(12):e13341. doi:10.1111/eci.13341

30. Griggs JE, Lyon RM, Sherriff M, et al. Predictive clinical utility of pre-hospital point of care lactate for transfusion of blood product in patients with suspected traumatic haemorrhage: derivation of a decision-support tool. Scand J Trauma Resusc Emerg Med. 2022;30(1):72. Published 2022 Dec 13. doi:10.1186/s13049-022-01061-x

31. Martín-Rodríguez F, Sanz-García A, Justel AB, et al. Prehospital mSOFA Score for Quick Prediction of Life-Saving Interventions and Mortality in Trauma Patients: A Prospective, Multicenter, Ambulance-based, Cohort Study. West J Emerg Med. 2023;24(5):868-877. doi:10.5811/westjem.59048

32. Gaessler H, Helm M, Kulla M, et al. Prehospital predictors of the need for transfusion in patients with major trauma. Eur J Trauma Emerg Surg. 2023;49(2):803-812. doi:10.1007/s00068-022-02132-5

33. Corral Torres E, Hernández-Tejedor A, Millán Estañ P, et al. Prognostic value of metabolic parameters measured by first responders attending patients with severe trauma: associations with the New Injury Severity Score and mortality. Emergencias. 2023;35(2):90-96.

34. Christian MD. Triage. Crit Care Clin. 2019;35(4):575-589. doi:10.1016/j.ccc.2019.06.009

35. Brown JB, Lerner EB, Sperry JL, Billiar TR, Peitzman AB, Guyette FX. Prehospital lactate improves accuracy of prehospital criteria for designating trauma activation level. J Trauma Acute Care Surg. 2016;81(3):445-452. doi:10.1097/TA.0000000000001085

36. Connelly CR, Schreiber MA. Endpoints in resuscitation. Curr Opin Crit Care. 2015;21(6):512-519. doi:10.1097/MCC.0000000000000248

37. Raa A, Sunde GA, Bolann B, et al. Validation of a point-of-care capillary lactate measuring device (Lactate Pro 2). Scand J Trauma Resusc Emerg Med. 2020;28(1):83. Published 2020 Aug 18. doi:10.1186/s13049-020-00776-z

Appendices

Appendix 1. Search strategy used for the Cochrane, Embase and Pubmed databases.

Pubmed:

((lactate[Title/Abstract]) OR (lactic acid[Title/Abstract])) AND ((prehospital[Title/Abstract]) OR (on-site[Title/Abstract]) OR (on terrain[Title/Abstract]) OR (before admission[Title/Abstract])) AND ((trauma[Title/Abstract]) OR (injury[Title/Abstract])) AND ((mortality[Title/Abstract]) OR (survival[Title/Abstract]) OR (death[Title/Abstract]) OR (transfusion[Title/Abstract]) OR (intervention[Title/Abstract]) OR (resuscitative care[Title/Abstract]) OR (resuscitation[Title/Abstract]) OR (treatment[Title/Abstract]))

Embase:

('lactate':ab,ti OR 'lactic acid':ab,ti) AND ('prehospital':ab,ti OR 'on-site':ab,ti OR 'on terrain':ab,ti OR 'before admission':ab,ti) AND ('trauma':ab,ti OR 'injury':ab,ti) AND ('mortality':ab,ti OR 'survival':ab,ti OR 'death':ab,ti OR 'transfusion':ab,ti OR 'intervention':ab,ti OR 'resuscitative care':ab,ti OR 'resuscitation':ab,ti OR 'treatment':ab,ti)

Cochrane:

((lactic acid):ti,ab,kw OR (lactate):ti,ab,kw)) AND ((prehospital):ti,ab,kw OR (on-site):ti,ab,kw OR (on terrain):ti,ab,kw OR (before admission):ti,ab,kw)

Appendix 2. QUADAS-2 templates for all included studies.

(See following pages).

Brio-Ibañez P. Clinical Utility of Delta Lactate for Predicting Early In-Hospital Mortality in Adult Patients: A Prospective, Multicentric, Cohort Study. Diagnostics, 2020

Study type	Prospective observational multicentric cohort study.
Patients	1341 adults treated and transported by ambulance with high priority by ALS personnel from the scene to the emergency department in Spain.
Index test(s)	Prehospital venous lactate measurement (in mmol/L). Lactate clearance (100*[prehospital lactate – in-hospital lactate]/prehospital lactate) (in %).
Reference standard	No reference standard. Index test performance was tested against chance levels (AUROC = 0.5).
Target condition	In-hospital 2-, 7- and 30-day mortality.
Test performance	AUROC = 0.800 ($p < 0.001$) of pLA for in-hospital 2-day mortality. AUROC = 0.736 ($p < 0.001$) of pLA for in-hospital 7-day mortality. AUROC = 0.691 ($p < 0.001$) of pLA for in-hospital 30-day mortality. In-hospital 2-day mortality of pLA < 2 mmol/L vs pLA ≥ 2 mmol/L (0.4% vs 9,6%; $p < 0.001$). In-hospital 2-day mortality of ΔLA < 10% vs ΔLA ≥ 10% (15,6% vs 4,4%; $p < 0.001$).
Notes	Study was conducted in 5 hospitals involving 6 ALS teams.

Risk of bias assessment			
Bias		**Judgment**	**Support for judgment**
Patient selection	Risk of bias	Low risk	Patients were consecutively enrolled. Sicker patients may receive different treatment.
	Concerns regarding applicability	High risk	No data of trauma patients available.
Index test	Risk of bias	Low risk	Lactate threshold levels were prespecified.
	Concerns regarding applicability	Low risk	No concerns.
Reference standard	Risk of bias	Unclear risk	No reference standard. Index test performance was tested against chance levels (AUROC = 0.5). This is common practice.
	Concerns regarding applicability	High risk	Prehospital vital parameters or scoring systems are the preferred reference standard in this review.
Flow and timing	Risk of bias	Low risk	In-hospital lactate values were measured only in those patients who required it. No specific time interval between lactate measurements.

Corral T. Prognostic value of metabolic parameters measured by first responders attending patients with severe trauma: associations with the New Injury Severity Score and mortality. Emergencias, 2023

Study type	Prospective observational multicenter study
Patients	709 trauma patients transferred by the emergency service to 4 trauma centers in Madrid.
Index test(s)	Prehospital venous lactate measurement (in mmol/L). Prehospital clinical and laboratory data.
Reference standard	No reference standard was used.
Target condition	30-day mortality.
Test performance	Predictive capacity of pLA (AUC = 0.596; p = 0.008), systolic blood pressure (AUC = 0.599; p < 0.001), heart rate (AUC = 0.538; no p-value), respiratory rate (AUC = 0.695; p < 0.001), oxygen saturation (AUC = 0.593; p < 0.001) and Glasgow coma scale (AUC = 0.812; p < 0.001).
Notes	Patients with isolated traumatic brain injury were excluded. All patients were attended by 2 physicians and 2 nurses on the scene.

Risk of bias assessment

Bias		**Judgment**	**Support for judgment**
Patient selection	Risk of bias	Low risk	No concerns.
	Concerns regarding applicability	Low risk	Trauma patients.
Index test	Risk of bias	Low risk	No concerns.
	Concerns regarding applicability	Low risk	No concerns.
Reference standard	Risk of bias	Unclear risk	No reference standard was used.
	Concerns regarding applicability	High risk	Even though clinical data were available, prediction performance was not actively compared with prehospital lactate data.
Flow and timing	Risk of bias	Low risk	97 cases were excluded due to insufficient data.

Da Costa L. Independent early predictors of mortality in polytrauma patients: a prospective, observational, longitudinal study. Clinics, 2017.

Study type	Longitudinal prospective observational study		
Patients	200 adults submitted to high-energy trauma with an injury severity score > 16 who were treated and transported by rescue system medical teams to the hospital by land or helicopter.		
Index test(s)	Prehospital venous lactate measurement (in mmol/L). Clinical data and laboratory data at 4 time points (on scene, in the emergency room, 3 and 24 hours after admission).		
Reference standard	No reference standard was used.		
Target condition	30-day mortality.		
Test performance	Generalized estimating equation model across 4 time points shows significant association of oxygen saturation (OR = 0.988; p < 0.001), diastolic blood pressure (OR = 0.997; p < 0.001), lactate level (OR = 1,060; p < 0.001), Glasgow coma score (OR = 0.980; p < 0.001), crystalloid infusion (OR = 1,001; p = 0.015) and presence of traumatic brain injury (OR = 6,087; p < 0.001) with 30 day mortality.		
Notes	Study population with a male predominance and a high incidence of traumatic brain injury.		
Risk of bias assessment			
Bias		**Judgment**	**Support for judgment**
Patient selection	Risk of bias	Low risk	High incidence of traumatic brain injury. Based on a single trauma center.
	Concerns regarding applicability	Low risk	No concerns.
Index test	Risk of bias	Low risk	No concerns.
	Concerns regarding applicability	High risk	No specific focus on prehospital lactate.
Reference standard	Risk of bias	Unclear risk	No reference standard was used.
	Concerns regarding applicability	High risk	Even though clinical data were available, prediction performance was not actively compared with prehospital lactate data.
Flow and timing	Risk of bias	Low risk	22 patients were removed from the analysis due to incomplete data.

Fukuma H. Prehospital lactate improves prediction of the need for immediate interventions for hemorrhage after trauma. Scientific reports, 2019

Study type	Retrospective observational study.
Patients	435 trauma patients transferred by trauma physician-staffed ambulance to a level 1 trauma center in Osaka (Japan).
Index test(s)	Prehospital venous lactate measurement (pLA) (in mmol/L). Prehospital physiological variables plus prehospital venous lactate measurement (VAR + pLA).
Reference standard	Prehospital physiological variables (systolic blood pressure, heart rate, respiratory rate, GCS, shock index score at the scene and mechanism of penetrating injury) (VAR).
Target condition	Immediate intervention for hemorrhage. Massive transfusion (≥ 10 units of blood products within 24 hours).
Test performance	AUC for immediate intervention of pLA vs VAR vs VAR + pLA (0.764 vs 0.837 vs 0.882). P-value of VAR vs VAR + pLA ($p = 0.0073$). AUC for massive transfusion of pLA vs VAR vs VAR + pLA (0.764 vs 0.895 vs 0.903). P-value of VAR vs VAR + pLA ($p = 0.32$). All AUC values were significantly different from chance levels ($p < 0.0001$).
Notes	Immediate intervention for hemorrhage is defined as immediate surgical/radiological intervention for hemostasis and/or blood transfusion within 24 hours after emergency room arrival. Ambulance was staffed with 2 trauma physicians, 1 nurse, 1 EMS technician and a driver.

Risk of bias assessment			
Bias		**Judgment**	**Support for judgment**
Patient selection	Risk of bias	Low risk	Only patients attended by a trauma physician were included. Single-center study.
	Concerns regarding applicability	Low risk	No concerns.
Index test	Risk of bias	Low risk	No concerns.
	Concerns regarding applicability	Low risk	No concerns.
Reference standard	Risk of bias	Low risk	No concerns.
	Concerns regarding applicability	Low risk	Prehospital vital parameters were used.
Flow and timing	Risk of bias	Low risk	No lactate measurement in 72 patients.

Gaessler H. Prehospital predictors of the need for transfusion in patients with major trauma. European journal of trauma and emergency surgery, 2023

Study type	Prospective multicentric observational study.
Patients	130 adult trauma patients treated by a helicopter medical emergency service and transported by ground or air to 2 level 1 trauma centers in Ulm (Germany).
Index test(s)	Prehospital venous lactate measurement (in mmol/L). Model containing pLA, suspected bleeding (in chest, abdomen or pelvis) and cardiovascular instability (prehospital systolic blood pressure < 100 mmHg).
Reference standard	Presence of suspected bleeding (in chest, abdomen or pelvis). Presence of cardiovascular instability (prehospital systolic blood pressure < 100 mmHg).
Target condition	Early transfusion (transfusion of blood or coagulation products in the resuscitation room or during immediate surgery).
Test performance	AUC of model vs pLA vs suspected bleeding vs cardiovascular instability (AUC = 0.871; p < 0.05 vs 0.731; p < 0.05 vs 0.766; p = 0.001 vs 0.701; p < 0.001).
Notes	Patients with pre-existing coagulation disorders or who had already received tranexamic acid were excluded. The EMS was staffed by a physician and a paramedic. Significance levels are compared to chance levels.

Risk of bias assessment

Bias		**Judgment**	**Support for judgment**
Patient selection	Risk of bias	Low risk	Only patients treated by helicopter EMS were included.
	Concerns regarding applicability	Low risk	No concerns.
Index test	Risk of bias	Low risk	No prehospital blood transfusion.
	Concerns regarding applicability	Low risk	No concerns.
Reference standard	Risk of bias	Unclear risk	Variables were selected based on a stepwise selection procedure.
	Concerns regarding applicability	Low risk	Prehospital vital signs were used.
Flow and timing	Risk of bias	Low risk	Prehospital lactate was measured after hospital admission. The decision for transfusion was based on predefined triggers and was made by a senior trauma team leader.

Galvagno S. Prehospital continuous vital signs data analysis outperforms lactate for the prediction of lifesaving interventions in patients with traumatic shock. Shock, 2018

Study type	Prospective observational study.
Patients	260 adult trauma patients transported by helicopter emergency medical services in Baltimore.
Index test(s)	Prehospital venous lactate measurement (in mmol/L).
Reference standard	Prehospital continuous vital signs data analysis (CVS).
Target condition	Mortality. Lifesaving intervention (need for uncrossmatched or massive blood transfusion, emergency surgery, etc.) Massive transfusion.
Test performance	AUC for mortality of pLA vs CVS (0.52 vs 0.90; $p < 0.05$). AUC for massive transfusion of pLA vs CVS (0.85 vs 0.96; $p > 0.05$). AUC for lifesaving intervention of pLA vs CVS (0.70 vs 0.71; $p > 0.05$).
Notes	Information based on abstract only. No full-text article available. 21 different prehospital laboratory results were obtained using a portable lab analyser.

Risk of bias assessment			
Bias		**Judgment**	**Support for judgment**
Patient selection	Risk of bias	Unclear risk	Method for enrolling patients unknown.
	Concerns regarding applicability	Low risk	Trauma patients.
Index test	Risk of bias	Low risk	No concerns.
	Concerns regarding applicability	Low risk	No concerns.
Reference standard	Risk of bias	Unclear risk	Multivariate logistic regression analysis was used to analyze over 300 vital signs waveform components.
	Concerns regarding applicability	Low risk	Prehospital vital parameters were used as a reference standard.
Flow and timing	Risk of bias	Unclear risk	40 patients were excluded due to insufficient data.

Galvagno S. Prehospital Point of Care Testing for the Early Detection of Shock and Prediction of Lifesaving Interventions. Shock, 2020

Study type	Prospective observational study		
Patients	261 adult trauma patients flown by helicopter EMS to a level 1 trauma center in Baltimore.		
Index test(s)	Prehospital venous lactate measurement (in mmol/L). 16 different prehospital laboratory values.		
Reference standard	Prehospital shock index, mean shock index, revised trauma score (RTS), injury severity score and Charlson comorbidity score.		
Target condition	Need for prehospital lifesaving interventions (preLSI). Need for in-hospital lifesaving interventions (inLSI). Requirement of uncrossmatched blood after admission.		
Test performance	AUC of pLA for preLSI (AUC = 0.71; p < 0.05). AUC of RTS for preLSI (AUC = 0.61; p-value unknown). AUC of pLA for inLSI (AUC = 0.72; p < 0.05). AUC of pLA for blood requirement (AUC = 0.88; p < 0.05). Lactate has the greatest association with the prediction for LSI compared with static vital signs and other laboratory parameters.		
Notes	Prehospital lifesaving interventions included endotracheal intubation, placement of a surgical airway, needle chest decompression, fluid bolus for severe hypotension (systolic blood pressure < 90 mmHg), tourniquet or pelvic binder application, and CPR. In-hospital lifesaving interventions included transfusion requirements and the need for immediate use of uncrossmatched blood or massive transfusion (> 6 units of packed RBC of within 6 h or > 10 units of packed RBC within 24 h), exploratory laparotomy for control of intra-abdominal bleeding, endotracheal intubation, tourniquet application, chest tube thoracostomy, or emergent resuscitative thoracotomy.		
Risk of bias assessment			
Bias		**Judgment**	**Support for judgment**
Patient selection	Risk of bias	Low risk	Single-center study.
	Concerns regarding applicability	Low risk	No inclusion of ground EMS.
Index test	Risk of bias	Low risk	No concerns.
	Concerns regarding applicability	Low risk	No concerns.
Reference standard	Risk of bias	Unclear risk	Data not available.
	Concerns regarding applicability	Low risk	Different scoring systems based on prehospital vital parameters were used.
Flow and timing	Risk of bias	Low risk	No concerns.

Griggs J. Predictive clinical utility of pre-hospital point of care lactate for transfusion of blood product in patients with suspected traumatic haemorrhage: derivation of a decision-support tool. Scandinavian journal of trauma, resuscitation and emergency medicine, 2022

Study type	Retrospective observational study.
Patients	194 trauma patients (> 16 years of age) with suspected major hemorrhage transported to 3 major trauma centers in southeast England.
Index test(s)	Prehospital venous lactate measurement (in mmol/L).
Reference standard	No reference standard was used.
Target condition	In-hospital blood transfusion.
Test performance	AUC = 0.72 (no p-value).
Notes	Prehospital transfusion was not accounted for. AUC was calculated with available sensitivity and specificity data.

Risk of bias assessment			
Bias		**Judgment**	**Support for judgment**
Patient selection	Risk of bias	High risk	No lactate measurement in 85 patients. These were possibly patients in extremis.
	Concerns regarding applicability	Low risk	No concerns.
Index test	Risk of bias	High risk	No AUC value reported. AUC value was calculated based on available data. Prehospital transfusion was not accounted for.
	Concerns regarding applicability	Low risk	No concerns.
Reference standard	Risk of bias	Unclear risk	No reference standard was used.
	Concerns regarding applicability	High risk	Prehospital vital parameters or scoring systems are the preferred reference standard in this review.
Flow and timing	Risk of bias	High risk	Possible indication bias. The decision to transfuse blood products was based on clinical gestalt.

Guyette F. Prehospital serum lactate as a predictor of outcomes in trauma patients: a retrospective observational study. The Journal of trauma, 2011

Study type	Retrospective observational cohort study.
Patients	1168 adult trauma patients transported by air medical service to a level 1 trauma center in Pittsburgh.
Index test(s)	Model of reference standard including prehospital venous or capillary lactate measurement.
Reference standard	Model containing age, sex, initial systolic blood pressure, heart rate, respiratory rate, and GCS.
Target condition	In-hospital mortality. Emergent surgery in the first 24 hours of hospitalization.
Test performance	Performance of lactate model vs reference model to predict in-hospital mortality (AUC = 0.89 vs 0.85; $p < 0.001$) and need for emergent surgery (AUC 0.71 vs 0.68; $p = 0.02$). Odds ratio of pLA for mortality (OR = 1,23; $p < 0.0001$) and need for emergent surgery (OR = 1,13; $p < 0.001$).
Notes	Emergent surgery is defined as any of the following procedures for hemorrhage control: thoracotomy, laparotomy, pelvic fixation, and embolization.

Risk of bias assessment

Bias		**Judgment**	**Support for judgment**
Patient selection	Risk of bias	High risk	Retrospective, single-center study. Predominantly blunt trauma victims of higher acuity as minor trauma patients would be sent by ground. No lactate measurement in cases of short flight time or patients in extremis.
	Concerns regarding applicability	Low risk	No concerns.
Index test	Risk of bias	Low risk	The contribution of lactate to total model fit was investigated.
	Concerns regarding applicability	Low risk	No concerns.
Reference standard	Risk of bias	Low risk	Variables were selected based on biologic plausibility and availability to clinicians in the prehospital environment.
	Concerns regarding applicability	Low risk	No concerns.
Flow and timing	Risk of bias	Low risk	Prehospital providers were not blinded to pLA but could only alter treatment after consultation with medical command physicians. The receiving trauma team was blinded to the results of pLA.

Guyette F. A comparison of prehospital lactate and systolic blood pressure for predicting the need for resuscitative care in trauma transported by ground. The journal of trauma and acute care surgery, 2015

Study type	Prospective observational multicentric cohort study.
Patients	387 trauma patients (> 15 years of age) with initial systolic blood pressure between 70-100 mmHg and venous access transported by ground EMS to a level 1 or 2 trauma center across 9 geographic regions in North America.
Index test(s)	Prehospital venous lactate measurement (in mmol/L).
Reference standard	Initial systolic blood pressure (in mmHg). Shock index (in bpm/mmHg).
Target condition	Need for resuscitative care.
Test performance	AUC of pLA vs systolic blood pressure (0.78 vs 0.59; $p < 0.001$). AUC of pLA vs shock index (0.78 vs 0.66; $p = 0.01$). All AUC values were significantly different from chance levels.
Notes	Resuscitative care is defined as any of the following within 6 hours of ED arrival: blood transfusion ≥ 5 units, intervention for hemorrhage including thoracotomy, laparotomy, pelvic fixation or interventional radiology embolization, or death. Patients with isolated penetrating head injury were excluded.

Risk of bias assessment

Bias		**Judgment**	**Support for judgment**
Patient selection	Risk of bias	High risk	Many patients were excluded due to the inability to obtain a venous sample or because EMS forgot to measure lactate.
	Concerns regarding applicability	Low risk	Trauma patients. No data from patients outside blood pressure range.
Index test	Risk of bias	Low risk	No concerns.
	Concerns regarding applicability	Low risk	No concerns.
Reference standard	Risk of bias	Low risk	No concerns.
	Concerns regarding applicability	Low risk	Prehospital vital parameters were used as a reference standard.
Flow and timing	Risk of bias	Low risk	EMS providers and the receiving care team were blinded to the initial lactate.

Jansen T. The prognostic value of blood lactate levels relative to that of vital signs in the pre-hospital setting: a pilot study. Critical Care, 2008

Study type	Prospective observational cohort study.
Patients	124 patients requiring urgent ambulance dispatching with a systolic blood pressure below 100 mmHg, a respiratory rate less than 10 or more than 29 breaths/minute, or a Glasgow Coma Scale (GCS) below 14 in the Netherlands.
Index test(s)	Prehospital venous or capillary lactate measurement (in mmol/L). Emergency department venous or capillary lactate measurement (in mmol/L).
Reference standard	No reference standard was used.
Target condition	In-hospital mortality
Test performance	AUC of pLA (AUC = 0.69; p = 0.001). AUC of emergency department lactate (AUC = 0.72; p = 0.001).
Notes	Dispatched ambulances were staffed by certified EMS nurses. Only lactate and GCS were independently associated with mortality in a multivariable Cox model containing change in lactate level, systolic blood pressure, heart rate and GCS.

Risk of bias assessment

Bias		**Judgment**	**Support for judgment**
Patient selection	Risk of bias	High risk	Only patients with abnormal vital signs were included.
	Concerns regarding applicability	High risk	Only 17% of the study population are trauma patients.
Index test	Risk of bias	Low risk	No concerns.
	Concerns regarding applicability	Low risk	No concerns.
Reference standard	Risk of bias	Unclear risk	No reference standard was used.
	Concerns regarding applicability	High risk	Even though clinical data were available, prediction performance was not actively compared with prehospital lactate data.
Flow and timing	Risk of bias	Low risk	Hospital physicians were blinded to lactate levels.

Martín-Rodríguez F. Predictive value of the prehospital NEWS2-L - National Early Warning Score 2 Lactate - for detecting early death after an emergency. Emergencias, 2019

Study type	Prospective observational study.
Patients	707 adults treated and transported by mobile emergency units from the scene to the emergency department in Valladolid (Spain).
Index test(s)	Prehospital venous or capillary lactate measurement (in mmol/L). Prehospital National Early Warning Score lactate (NEWS2-L).
Reference standard	Prehospital National Early Warning Score 2 (NEWS2).
Target condition	2- , 7- and 30-day mortality.
Test performance	AUC for 2-day mortality of pLA vs NEWS2 vs NEWS2-L (0.79 vs 0.90 vs 0.91). AUC for 7-day mortality of pLA vs NEWS2 vs NEWS2-L (0.76 vs 0.85 vs 0.86). AUC for 30-day mortality of pLA vs NEWS2 vs NEWS2-L (0.72 vs 0.82 vs 0.82). All AUC values were significantly different from chance levels ($p < 0.001$). Significant difference for all analyses between AUC of pLA and NEWS2/NEWS2-L, not between AUC of NEWS2 and NEWS2-L.
Notes	

Risk of bias assessment			
Bias		**Judgment**	**Support for judgment**
Patient selection	Risk of bias	Low risk	Patients were consecutively enrolled. Only patients transferred by ALS personnel were included.
	Concerns regarding applicability	High risk	Only 17.5% of the study population are trauma patients.
Index test	Risk of bias	Low risk	No concerns.
	Concerns regarding applicability	Low risk	No concerns.
Reference standard	Risk of bias	Low risk	No concerns.
	Concerns regarding applicability	Low risk	A scoring system based on prehospital vital parameters (NEWS2) was used.
Flow and timing	Risk of bias	Low risk	Loss of data in 10 patients.

Martín-Rodríguez F. Prognostic value of lactate in prehospital care as a predictor of early mortality. The American journal of emergency medicine, 2019

Study type	Longitudinal prospective observational study		
Patients	279 adults requiring intravenous line placement treated and transported by ALS personnel from the scene to the two public hospitals in Valladolid (Spain).		
Index test(s)	Prehospital venous lactate measurement (in mmol/L).		
Reference standard	No reference standard. Index test performance was tested against chance levels (AUROC = 0.5).		
Target condition	30-day mortality.		
Test performance	AUROC = 0.82 ($p < 0.05$).		
Notes	The diagnostic model of the trauma subpopulation did not reach statistical significance, although the AUC remained very high.		
Risk of bias assessment			
Bias		**Judgment**	**Support for judgment**
Patient selection	Risk of bias	High risk	Patients were consecutively enrolled. Only patients transferred by ALS personnel and requiring a venous line were included.
	Concerns regarding applicability	High risk	Only 14,3% of the study population are trauma patients.
Index test	Risk of bias	Low risk	The sample size was sufficient to obtain results overall.
	Concerns regarding applicability	High risk	The sample size was insufficient to obtain statistically significant results by study subgroups according to pathologies.
Reference standard	Risk of bias	Unclear risk	No reference standard. Index test performance was tested against chance levels (AUROC = 0.5). This is common practice.
	Concerns regarding applicability	High risk	Prehospital vital parameters or scoring systems are the preferred reference standard in this review.
Flow and timing	Risk of bias	Low risk	No concerns.

Martín-Rodríguez F. Prognostic value of lactate in prehospital care as a predictor of mortality and high-risk patients with trauma. Signa Vitae, 2019

Study type	Prospective observational study
Patients	109 adult trauma patients treated by ALS personnel and transferred to the emergency department in Valladolid (Spain).
Index test(s)	Prehospital venous lactate measurement (in mmol/L).
Reference standard	No reference standard. Index test performance was tested against chance levels (AUC = 0.5).
Target condition	2-, 7- and 30-day mortality.
Test performance	AUC of pLA for 2-day mortality (0.813; $p < 0.001$). AUC of pLA for 7-day mortality (0.836; $p < 0.001$). AUC of pLA for 30-day mortality (0.805; $p < 0.001$).
Notes	

Risk of bias assessment			
Bias		**Judgment**	**Support for judgment**
Patient selection	Risk of bias	High risk	861 patients were excluded due to transfer by BLS- instead of ALS personnel.
	Concerns regarding applicability	Low risk	Trauma patients.
Index test	Risk of bias	Low risk	No concerns.
	Concerns regarding applicability	Low risk	No concerns.
Reference standard	Risk of bias	Unclear risk	No reference standard. Index test performance was tested against chance levels (AUROC = 0.5). This is common practice.
	Concerns regarding applicability	High risk	Prehospital vital parameters or scoring systems are the preferred reference standard in this review.
Flow and timing	Risk of bias	Low risk	No concerns.

Martín-Rodríguez F. Accuracy of prehospital point-of-care lactate in early in-hospital mortality. European journal of clinical investigation, 2020.

Study type	Prospective multicentric controlled observational study.
Patients	2997 adults (373 trauma patients) treated and transported by ambulance with high priority by ALS personnel from the scene to the emergency department requiring intravenous line placement in 4 provinces in Spain.
Index test(s)	Prehospital venous lactate measurement (in mmol/L).
Reference standard	No reference standard. Index test performance was tested against chance levels (AUC = 0.5).
Target condition	In-hospital 2-day mortality.
Test performance	AUROC = 0.867 (p < 0.001). For discharge category "trauma and injury", AUROC was 0.855 (p < 0.001).
Notes	Discrimination level for neurologic pathology was lower (AUROC = 0.661; p = 0.017). Study was conducted in 5 hospitals involving 6 ALS teams.

Risk of bias assessment

Bias		**Judgment**	**Support for judgment**
Patient selection	Risk of bias	High risk	Only patients transferred by ALS personnel and requiring a venous line were included.
	Concerns regarding applicability	Low risk	AUROC was also calculated for each discharge category.
Index test	Risk of bias	Low risk	Lactate threshold levels were prespecified.
	Concerns regarding applicability	Low risk	No concerns.
Reference standard	Risk of bias	Unclear risk	No reference standard. Index test performance was tested against chance levels (AUROC = 0.5). This is common practice.
	Concerns regarding applicability	High risk	Prehospital vital parameters or scoring systems are the preferred reference standard in this review.
Flow and timing	Risk of bias	Low risk	Lactate values were displayed on scene but were not used in any type of intervention on the ambulance.

Martín-Rodríguez F. Prehospital Point-Of-Care Lactate Increases the Prognostic Accuracy of National Early Warning Score 2 for Early Risk Stratification of Mortality: Results of a Multicenter, Observational Study. Journal of clinical medicine, 2020

Study type	Prospective multicentric observational study.
Patients	3081 adults treated by EMS and transported by ALS personnel to referral hospitals in Spain.
Index test(s)	Prehospital venous lactate measurement (in mmol/L).
Reference standard	Prehospital National Early Warning Score 2 (NEWS2).
Target condition	In-hospital 2-day mortality.
Test performance	AUC in low-risk group of pLA vs NEWS2 (0.911 vs 0.568; p < 0.001). AUC in low-medium-risk group of pLA vs NEWS2 (0.913 vs 0.5; p < 0.001). AUC in medium-risk group of pLA vs NEWS2 (0.820 vs 0.525; p < 0.001). AUC in high-risk group of pLA vs NEWS2 (0.762 vs 0.756; p = 0.86). AUC of pLA was significantly different from chance levels in all analyses (p < 0.001) except in the low-medium-risk group (p = 0.07).
Notes	Study was conducted in 5 hospitals involving 6 ALS teams. The cohort was split into four NEWS2 risk groups (low, low-medium, medium, and high) before analysis.

Risk of bias assessment

Bias		**Judgment**	**Support for judgment**
Patient selection	Risk of bias	Low risk	Patients were consecutively enrolled. Only patients transferred by ALS personnel were included.
	Concerns regarding applicability	High risk	Medical pathologies (2736 cases, 88,8%) far exceeded trauma cases (345 cases, 11.2%).
Index test	Risk of bias	Unclear risk	The cohort was split into four NEWS2 risk groups before analysis.
	Concerns regarding applicability	Low risk	No concerns.
Reference standard	Risk of bias	Low risk	No concerns.
	Concerns regarding applicability	Low risk	A scoring system based on prehospital vital parameters (NEWS2) was used.
Flow and timing	Risk of bias	Low risk	the value of pLA, although unblinded, was not taken into account for clinical decision-making.

Martín-Rodríguez F. Prehospital mSOFA Score for Quick Prediction of Life-Saving Interventions and Mortality in Trauma Patients: A Prospective, Multicenter, Ambulance-based, Cohort Study. The western journal of emergency medicine, 2023

Study type	Prospective multicentric cohort study.
Patients	763 adult trauma patients with venous access screened by an ALS physician and evacuated by ALS or BLS units to 4 emergency departments in Castilla y Léon (Spain).
Index test(s)	Prehospital mSOFA score (includes GCS, mean arterial pressure, oxygen saturation divided by fraction of inspired oxygen, creatinine and lactate).
Reference standard	Revised trauma score (RTS). New trauma score (NTS). Combination of mechanism, GCS, age and arterial pressure (MGAP). Combination of base deficit, INR and GCS (BIG).
Target condition	Need for lifesaving intervention. 2-day in-hospital mortality.
Test performance	AUC for need for lifesaving intervention of mSOFA vs RTS vs MGAP vs BIG vs NTS (0.927 vs 0.889; $p = 0.078$ vs 0.900; $p = 0.061$ vs 0.579; $p < 0.001$ vs 0.539; $p < 0.001$). AUC for mortality of mSOFA vs RTS vs MGAP vs BIG vs NTS (0.979 vs 0.867; $p = 0.013$ vs 0.901; $p = 0.017$ vs 0.593; $p < 0.001$ vs 0.643; $p < 0.001$).
Notes	Lifesaving intervention is defined as invasive mechanical ventilation or administration of tranexamic acid or noradrenaline at the scene or en route. All p-values refer to comparison with mSOFA. All AUC values were significantly different from chance levels except for those of BIG and NTS.

Risk of bias assessment

Bias		**Judgment**	**Support for judgment**
Patient selection	Risk of bias	Low risk	Patients were consecutively enrolled.
	Concerns regarding applicability	Low risk	No concerns.
Index test	Risk of bias	Low risk	No concerns.
	Concerns regarding applicability	Unclear risk	The prehospital mSOFA score is a scoring system including prehospital lactate.
Reference standard	Risk of bias	Low risk	No concerns.
	Concerns regarding applicability	Low risk	Prehospital vital parameters or scoring systems were used as reference standard.
Flow and timing	Risk of bias	Unclear risk	EMS personnel and hospital investigators were blinded. No well-defined indications for administering noradrenaline or tranexamic acid.

Shackelford S. Predicting blood transfusion using automated analysis of pulse oximetry signals and laboratory values. The journal of trauma and acute care surgery, 2015

Study type	Retrospective observational study
Patients	852 adult trauma patients with shock index ≥ 0.62, critical injury requiring immediate attention or instability with a life-threatening injury without available prehospital vital signs directly admitted to a level 1 trauma center in Baltimore.
Index test(s)	Emergency department venous lactate measurement (edLA) (in mmol/L). Combination of edLA and both reference standards (edLA + VS + PWA).
Reference standard	Prehospital heart rate and systolic blood pressure (VS). Emergency department pulse oximetry waveform analysis (PWA).
Target condition	Blood transfusion within 3 hours of admission. Rapid transfusion (5 units of packed RBC within 4 hours of admission). Massive transfusion (10 units of packed RBC within 24 hours of admission).
Test performance	AUC for blood transfusion of edLA+VS+PWA vs edLA vs VS vs PWA (0.79 vs 0.77 vs 0.59 vs 0.74). AUC for rapid transfusion of edLA+VS+PWA vs edLA vs VS vs PWA (0.86 vs 0.80 vs 0.71 vs 0.82). AUC for massive transfusion of edLA+VS+PWA vs edLA vs VS vs PWA (0.93 vs 0.80 vs 0.70 vs 0.88).
Notes	Neurologically impaired cervical spine injury patients were excluded. No p-values were reported.

Risk of bias assessment

Bias		**Judgment**	**Support for judgment**
Patient selection	Risk of bias	Low risk	Single-center study.
	Concerns regarding applicability	Low risk	No concerns.
Index test	Risk of bias	Low risk	No concerns.
	Concerns regarding applicability	High risk	Lactate measurements were not obtained in the prehospital setting.
Reference standard	Risk of bias	Unclear risk	No statistical comparison was reported.
	Concerns regarding applicability	Low risk	Prehospital vital signs were used as a reference standard.
Flow and timing	Risk of bias	Unclear risk	To avoid ''prediction'' of transfusions that had already occurred, blood transfused within the first 15 minutes was excluded.

Shah A. Diagnostic accuracy of a single point-of-care prehospital serum lactate for predicting outcomes in pediatric trauma patients. Pediatric emergency care, 2013

Study type	Prospective observational cohort study		
Patients	217 pediatric trauma patients transported by helicopter to a level 1 pediatric trauma center in Pittsburgh.		
Index test(s)	Prehospital venous or capillary lactate measurement (in mmol/L).		
Reference standard	No reference standard was used.		
Target condition	Need for critical care.		
Test performance	AUC of pLA = 0.71; p = 0.01.		
Notes	Need for critical care is defined as vasopressor support, endotracheal intubation or transfusion within 24 hours, emergent surgery, admission to the pediatric ICU or death.		
Risk of bias assessment			
Bias		**Judgment**	**Support for judgment**
Patient selection	Risk of bias	High risk	Lactate was not obtained in 269 patients. Based on a single trauma center.
	Concerns regarding applicability	High risk	Pediatric population. Only patients transported by air were included.
Index test	Risk of bias	Low risk	No concerns.
	Concerns regarding applicability	Low risk	No concerns.
Reference standard	Risk of bias	Unclear risk	No reference standard was used.
	Concerns regarding applicability	High risk	Prehospital vital parameters or scoring systems are the preferred reference standard in this review.
Flow and timing	Risk of bias	Low risk	Prehospital providers were not blinded to pLA but could alter treatment only after consultation with medical command physicians. The receiving trauma team was blinded to the pLA result.

St John A. Prehospital Lactate Predicts Need for Resuscitative Care in Non-hypotensive Trauma Patients. The western journal of emergency medicine, 2018

Study type	Retrospective observational cross-sectional study
Patients	314 trauma patients (> 15 years of age) with initial systolic blood pressure > 100 mmHg and venous access transported by ground ALS units to a level 1 trauma center in Seattle.
Index test(s)	Prehospital venous lactate measurement (in mmol/L).
Reference standard	Shock index (in bpm/mmHg).
Target condition	Need for resuscitative care. Death in the emergency department. Surgical intervention within 6 hours of ED arrival. Transfusion (5 units of blood products within 6 hours).
Test performance	AUC for need for resuscitative care of pLA vs shock index (0.716 vs 0.631; p = 0.125). Values were significantly different from chance levels. AUC of pLA for death in the ED (AUC = 0.863; no p-value). AUC of pLA for surgical intervention (AUC = 0.721; p < 0.05). AUC of pLA for transfusion (AUC = 0.785; p < 0.05).
Notes	Need for resuscitative care was defined as either death in the emergency department, disposition to surgical intervention within 6 hours of ED arrival, or receipt of 5 units of blood within 6 hours. Patients with isolated penetrating head injury were excluded.

Risk of bias assessment

Bias		**Judgment**	**Support for judgment**
Patient selection	Risk of bias	Low risk	Only patients transferred by ALS personnel were included. Single-center study.
	Concerns regarding applicability	Low risk	Trauma patients. No patients outside blood pressure range.
Index test	Risk of bias	Low risk	No concerns.
	Concerns regarding applicability	Low risk	No concerns.
Reference standard	Risk of bias	Low risk	No concerns.
	Concerns regarding applicability	Low risk	A scoring system based on prehospital vital parameters (shock index) was used.
Flow and timing	Risk of bias	Low risk	EMS were instructed not to change care based on lactate value. Missing lactate in 50 patients.

Van Beest P. Measurement of lactate in a prehospital setting is related to outcome. European journal of emergency medicine, 2009

Study type	Prospective observational case-control study.
Patients	216 adults attended by ambulance personnel that arrived in a nonacademic medical center in the Netherlands.
Index test(s)	Prehospital venous or capillary lactate measurement (in mmol/L).
Reference standard	Prehospital oxygen saturation (SAT), mean arterial pressure (MAP) and heart rate (HR).
Target condition	In-hospital mortality
Test performance	AUC for in-hospital mortality of pLA vs SAT vs MAP vs HR (0.827 vs 0.127 vs 0.350 vs 0.500; $p < 0.01$).
Notes	P-value refers to difference between pLA vs vital signs. In about 50% of possible cases, lactate was measured in the prehospital setting. ROC curves were constructed with prehospital data only.

Risk of bias assessment			
Bias		**Judgment**	**Support for judgment**
Patient selection	Risk of bias	High risk	Patients were not consecutively enrolled. Single-center study.
	Concerns regarding applicability	High risk	Only 7.4% of the study population are trauma patients.
Index test	Risk of bias	High risk	Study underpowered. Ambulance personnel were trained to use lactate measurement device.
	Concerns regarding applicability	Low risk	No concerns.
Reference standard	Risk of bias	Low risk	No concerns.
	Concerns regarding applicability	Low risk	Prehospital vital parameters were used as a reference standard.
Flow and timing	Risk of bias	High risk	Lactate measurements were taken only when deemed possible by ambulance personnel.

Vandromme M. Lactate is a better predictor than systolic blood pressure for determining blood requirement and mortality: could prehospital measures improve trauma triage?. Journal of the American College of Surgeons, 2010.

Study type	Retrospective observational study.
Patients	Adult trauma patients admitted to a level 1 trauma center in Alabama with emergency department (n = 2413) or prehospital (n = 787) systolic blood pressure between 90 and 110mmHg.
Index test(s)	Emergency department venous blood lactate measurement (in mmol/L).
Reference standard	Emergency department systolic blood pressure. Prehospital systolic blood pressure.
Target condition	Need for ≥ 6 units of packed red blood cells within 24 hours postinjury. In-hospital mortality.
Test performance	Performance of lactate vs emergency department systolic blood pressure to predict need for massive transfusion (AUC = 0.76 vs 0.60; $p < 0.0001$) and mortality (AUC 0.76 vs 0.61; $p < 0.0001$). Performance of lactate vs prehospital systolic blood pressure to predict need for massive transfusion (AUC = 0.72 vs 0.61; $p = 0.0025$) and mortality (AUC 0.74 vs 0.60; $p = 0.0235$).
Notes	Patients with systolic blood pressure ranging between 90 and 110 mmHg on arrival at the trauma center were selected for inclusion. An a priori-determined subgroup was identified from this cohort to have prehospital systolic blood pressure ranging between 90 and 110 mmHg.

Risk of bias assessment

Bias		**Judgment**	**Support for judgment**
Patient selection	Risk of bias	High risk	Retrospective study. Inclusion based on data from trauma registry.
	Concerns regarding applicability	Low risk	Trauma patients. No data from patients outside blood pressure range.
Index test	Risk of bias	Low risk	No concerns.
	Concerns regarding applicability	High risk	Lactate measurements were not obtained in the prehospital setting.
Reference standard	Risk of bias	Low risk	Systolic blood pressure is commonly used clinically to classify patients with shock. Data obtained retrospectively from trauma registry.
	Concerns regarding applicability	Low risk	A prehospital vital parameter was used as a reference standard.
Flow and timing	Risk of bias	High risk	Only patients in whom lactate values and blood pressures were known were included.

Zadorozny E. Prehospital Lactate is Associated with the Need for Blood in Trauma. Prehospital emergency care, 2022

Study type	Retrospective observational study.
Patients	2170 adult trauma patients with recorded prehospital venous lactate transported by a critical care transport service to a Level 1 trauma center in Pittsburgh.
Index test(s)	Model of reference standard including prehospital venous lactate measurement.
Reference standard	Model containing vital signs, mission type, anatomic location of injury and prehospital administration of blood products.
Target condition	In-hospital blood transfusion within 24 hours of admission. Life-saving interventions (LSI) within 24 hours of admission. In-hospital 1-day mortality.
Test performance	Performance of lactate model vs reference model to predict need for blood transfusion (AUC = 0.867 vs 0.863; p = 0.03) and LSI (AUC 0.823 vs 0.819; p = 0.07). Odds ratio of pLA for blood transfusion (OR = 1,13; p < 0.01), LSI (OR = 1,09; p < 0.01) and mortality (OR = 1,32; p < 0.01).
Notes	A critical care transport service was staffed by a minimum of a critical care paramedic and nurse. Subjects with isolated traumatic brain injury were excluded. Life-saving interventions include laparotomy, thoracotomy, craniotomy, vascular repair, pelvic fixation, and interventional radiology procedures.

Risk of bias assessment

Bias		**Judgment**	**Support for judgment**
Patient selection	Risk of bias	High risk	Retrospective, single-center study. No consecutive enrollment of patients.
	Concerns regarding applicability	Low risk	No concerns.
Index test	Risk of bias	High risk	Although controlled for, prehospital blood transfusion was not part of the target condition. The contribution of lactate to total model fit was investigated.
	Concerns regarding applicability	Low risk	No concerns.
Reference standard	Risk of bias	Low risk	Variables were selected based on biologic plausibility and availability to clinicians in the prehospital environment.
	Concerns regarding applicability	Low risk	No concerns.
Flow and timing	Risk of bias	High risk	No blinding of personnel. Lactate measurements were taken only when deemed possible.