International Journal of Innovative Studies in Medical Sciences (IJISMS)

ISSN 2457-063X (Online) www.ijisms.com Volume: 2 Issue: 6 | 2018

Early warning score for biological simulation (EWS-BioHazMat)

Francisco Martín-Rodríguez, MSc, PhD

Advanced Clinical Simulation Center. Department of Medicine, Dermatology and Toxicology.Faculty of Medicine. Valladolid University.Prehospital Emergency Medical Services, Advanced Medical Life Support, Valladolid. Spain.

Avda. Ramón y Cajal, 7, 47005-Valladolid. Spain. Mobile (+34) 686452313

ID ORCID: https://orcid.org/0000-0002-1773-2860

Abstract:- *The main objective of this study is to find a predictive model that a priori tells us which professionals will tolerate metabolically poorly perform a simulated resuscitation with a facility against biological risks.*

An uncontrolled quasi-experimental study was performed on 47 volunteers. The initial vital signs, and the initial and final lactic acid value (metabolic tolerance) were analyzed. This activity involves volunteers performing a simulated resuscitation in a controlled environment while wearing personal protective suits in a biohazard situation.

The median age was 41 years (interquartile range: 33-47 years). After 10 minutes of rest, the poor metabolic tolerance was 31.9 % (15 volunteers). The area under the curve for EWS-BioHazMat to predict the poor metabolic tolerance was 0.828 (95% CI: 0.68-0.96, p <0.001). The EWS-BioHazMat with the best sensitivity and specificity was 10 points with a sensitivity of 80% (95% CI: 59-100) and specificity of 71% (95% CI: 56-87).

Keywords:*Evidence-based medicine, Pre-hospital setting, Early warning score,Exposure to biological agents, Physiological stress, Personal protection*

1. INTRODUCTION

The Prehospital Emergency Medical Services (PhEMS) must be prepared to attend incidents with biological risk as an ordinary part of its portfolio of services, although it is true that conducting specific training on these complicated procedures is complex and expensive for health systems[1][2].

PhEMS professionals must attend to all kinds of situations and complex emergencies, both medical and other, so it can be very useful to know a priori, with a simple scale, which subjects will not metabolically tolerate well resuscitation with a personal protection equipment (PPE).

The world of teaching in the branch of knowledge of Health Sciences, is experiencing a real revolution, with a virtualization in the way of teaching and training future professionals in techniques, procedures and skills, representing advanced clinical simulation , a powerful and essential tool.

Clinical simulation is a learning tool, which through the use of simulators and anatomical models allows the recreation of clinical scenarios with great accuracy[3], from difficult to reproduce critical situations, to simpler scenarios where the evaluation of the situation is the fundamental competence to develop. In this way, clinical simulation promotes decision-making quickly, teamwork, self-learning and self-criticism[4].

A tool that can help identify professionals who are not going to tolerate the proposed simulation metabolically well is lactic acid, a value that is easy to obtain, cheap and highly reliable[5][6][7]. This parameter is a very reliable indicator of anaerobic metabolism as a marker of tissue hypoperfusion, used in multiple contexts in the prehospital setting[8][9]. In exercises of great intensity and short duration (even more the less trained person is), the body does not have enough immediately available oxygen, and must get energy by less efficient routes and generate more metabolic waste. Lactic acid is generated as a metabolic by-product, recycling this metabolite to the body as it originates, to a point where the body is unable to recycle lactic acid and it begins to accumulate above 4 mmol/L [10][11], surpassing the so-called anaerobic threshold. In untrained people, this accumulation of lactic acid causes a selective inhibition of the enzymes responsible for degrading glucose to obtain energy, decreasing the production of energy. Consequently, in high levels of lactic acid, the capacity to generate energy decreases and the muscular capacity decreases, fatigue appearing early [12][13].

Considering the above, the objective of this study was to evaluate the ability of the EWS-BioHazMat scale to predict poor metabolic tolerance (final lactic acid > 4 mmol/L).

2. METHODOLOGY

An uncontrolled quasi-experimental study was carried out on 47 volunteers selected by means of random sampling stratified by sex and academic level (Health Sciences professionals) from an opportunity sample of 164 volunteers, between February 1 and March 30, 2017.

The sample was selected among physicians and nurses of the Emergency Services, aged between 21 and 65

ISSN 2457-063X (Online) www.ijisms.com Volume: 2 Issue: 6 | 2018

years old, and who voluntarily decided to participate. Any volunteer presenting at least one exclusion criteria was rejected (Table 1).

Table 1. Exclusion criteria to participate in the study

Body mass index greater than 40	Temperature greater than 38ºC
Capillary glucose levels less than 65 mg/dL	Systolic blood pressure greater than 160 mmHg
Baseline heart rate greater than 150 beats per minute	Baseline heart rate less than 35 beats per minute
Severe hearing or visual loss	Functional impotence

All participants underwent a baseline measurement of vital signs (heart rate, mean arterial pressure and tympanic temperature), an anthropometric evaluation using the body mass index and International Physical Activity Questionnaire - Short Form (IPAQ-SF) and an initial evaluation of your anxiety level through the Beck Anxiety Inventory (BAI). In addition, to check your metabolic profile, a determination of basal lactic acid (AL) was made and another one after 10 minutes of finishing the simulated resuscitation.

Once the evaluation of physiological, psychological, anthropometric and metabolic aspects, the volunteers were equipped with a type D PPE against biological risks, guided at all times by an instructor and under the standards of the European Center for Disease Prevention and Control [14].

With the PPE correctly placed, the volunteers in groups of 4 people agreed to a 20-m^2 laboratory with controlled temperature and humidity (average temperature of 33.66 ºC and average humidity of 51.16%), and in this place they performed a simulated resuscitation on a simulator, applying the advanced life support protocol for a time of 20 minutes. Then the volunteers left the laboratory and the PPE was removed according to the protocol. After 10 minutes of rest, a new determination of AL was made.

The main researcher was responsible for collecting the demographic variables (sex and age), and the level of training in biological hazards (basic or advanced), at this time the BAI was also performed and the anthropometric variables were collected (weight, height and IPAQ-SF). The weight study was carried out with the precision scale TANITA model BC-601 and height with the mechanical tape measuring SECA model 206. The physiological variables (heart rate, mean arterial pressure and tympanic temperature) were then collected. The temperature measurement was carried out with a thermometer tympanic brand Braun model ThermoScan® PRO 6000 with ExacTemp ™ technology, and blood pressure and heart rate measurements with the LifePAK® 15 monitor of the Physio-Control brand. The analytical variables were also collected, including the two determinations of AL in capillary blood. For the determination of lactic acid levels, the Accutrend® Plus meter of the Roche brand was used, with a measuring range of 0.8-21.7 mmol/L.

The main outcome variable is AL after resuscitation (understood as poor tolerance to end up with more AL than initial and more than 4 mmol/L of final AL).

All the data were stored in an XLSTAT® BioMED database for Microsoft Excel® (version 14.4.0.), With which the subsequent statistical analysis was carried out.

Through the Shapiro-Wilk and Anderson-Darling tests it was observed that the study variables do not follow a normal distribution, so the quantitative variables were described as median and interquartile range (IQR) and the qualitative variables were described by absolute frequencies with its 95% confidence interval (95% CI). For the comparison of means of quantitative variables the U-Mann-Whitney test was used. The Chi-square test was used for 2x2 contingency tables or / and proportional contrast to stipulate the association or dependency relationship between qualitative variables if necessary (percentage of squares with expected values less than five, greater than 20%) was used Fisher's exact test.

The area under the curve (AUC) of the receiver operating characteristic (ROC) of the EWS-BioHazMat scale was calculated in terms of AL greater than 4 mmol/L. The best score on the EWS-BioHazMat scale was determined, which offered greater sensitivity and specificity using the Youden index, calculating in each case: sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio and likelihood ratio. negative.

In all the tests carried out, a confidence level of 95% and a p value of less than 0.05 were considered significant.

The study was approved on 6 April 2016, by the Clinical Research Ethics Committee at Río Hortega University Hospital in Valladolid (Spain), with registration code #412016. All the participants had to read and sign the informed consent, and the entire study was carried out with the highest safety standards, protecting the physical integrity and confidentiality of the participants, complying with national and international regulations for the study in human subjects included in the Helsinki Treaty.

3. EXPERIMENTAL RESULTS

Between February 1 and March 30, 2017 a total of 47 volunteers were included in our study. The median age was 41 years (IQR: 33-47), 25 (53.2%) of the patients were female. The poor metabolic tolerance after sham resuscitation was 15 participants (31.9%).

During the pre-resuscitation phase with the PPE, a systematic evaluation was made of all the participants in the study, being gender, age, BMI and IPAQ-SF statistically significant among participants who tolerated metabolically well or not resuscitation (p <0.001) (table 2, end of the paper).

Taking into account the data previously exposed, and the clinical significance of the parameters studied, an Early Warning Score was made. The EWS-BioHazMat was composed of physiological parameters (heart rate, mean arterial pressure and tympanic temperature), anthropometric parameters (BMI and IPAQ-SF), psychological parameters (BAI) and age.

The mean scores of the EWS-BioHazMat showed statistically significant differences between good and poor tolerance (p <0.001). All AUC of the EWS-BioHazMat obtained statistical significance for the prediction of poor metabolic tolerance (AL final > 4 mmol/L) (Figure 1). The EWS-BioHazMat that obtained an AUC of 0.828 (95% CI: 0.68-0.96, p <0.001).

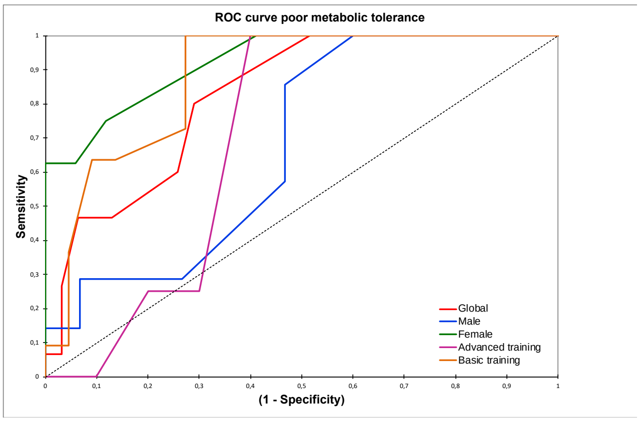

Fig -1: *Diagnostic performance curve and area under the curve with 95% confidence intervals. Analysis of poor metabolic tolerance globally, by gender and by level of training in biological risk*

In the stratification by gender, these differences were maintained in all the scales studied (p = 0.017). However, if we study both curves separately we can see how the AUC of the EWS-BioHazMat for female 0.923 (95% CI: 0.78-1, p <0.001) obtains better result than the AUC for male 0.676 (95% CI: 0.42-0.93, p = 0.176), respectively.

In the stratification by level of training in HAZMAT (specifically in biological risks), the statistical significance is maintained (p = 0.028), highlighting the good performance of the AUC of the EWS-BioHazMat for advanced training 0.876 (95% CI: 0.73- 1, p <0.001), compared to the results of the AUC for basic training 0.700 (95% CI: 0.37-1, p = 0.235) (Table 3, end of the paper).

4. DISCUSSION

We present the first study conducted in the field of a PhEMS in which the prognostic performance of an early warning scale is compared to know which participants are not going to tolerate metabolically well the proposed simulation with the PPE against biological risks.

In the analysis carried out, it can be observed that the EWS-BioHazMat scale has a high capacity to predict poor metabolic tolerance (understood as LA> 4 mmol / L at the end of the simulation and increase in the final figures over the initial ones).

Of all the EWS-BioHazMat evaluated by subgroups, the one that behaved better was the one that was applied in female and in personnel with advanced training, yielding an AUC significantly superior to the rest, and with a powerful predictive capacity.

The EWS-BioHazMat scale was generated, which includes physiological, anthropometric, psychological and age parameters, all based on clinical criteria (table 4), parameters that were easy to obtain technically, reliable, cheap and accessible by any health system.

Table 4. Early warning score for biological simulation (EWS-BioMED) (value chart)

Parameter	3	1	0	1	2	3
Age (years old)			≤29	30-39	40-49	≥50
Rest HR (bpm)			< 80		81-90	≥91
MBP (mmHg)	≤60		61-80			≥81
TT (ºC)	≤35		35.1-37		37.1-37.5	≥37.6
BMI (kg/m2)		≤18.4	18.5-24.9		25-29.9	≥30
IPAQ-SH			Active			Sedentary
BAI			≤15		16-25	≥26

HR: Heart rate; BMI: Body mass index; TT: Tympanic temperature; MBP: Median blood pressure; IPAQ: International Physical Activity Questionnaire - Short Form; BAI: Beck Anxiety Inventory;

The resting heart rate is a predictor of the longevity and appearance of cardiovascular diseases [15], which together with the mean arterial blood pressure indicate the baseline situation of the participant [16]. In addition to the above parameters, it is also worth noting the change in body temperature. Working with personal protection equipment against biological risks involves a thermal stress for the worker, both due to the characteristics of the equipment (absence of transpiration, impermeability, etc.), as well as the physical effort inherent in the activity itself. At the conclusion of the clinical case, and after 10 minutes of rest, the volunteers should have the same or even a slight decrease in temperature, due to normal thermoregulation mechanisms, therefore alterations of this parameter are not normal [17][18].

A simple way to perform a brief anthropometric evaluation is to know your body mass index [19], and to carry out the International Physical Activity Questionnaire - Short Form [20], which classifies the study subjects into three categories: vigorous, moderate or sedentary [21], depending on the exercise performed in the last seven days. The test has seven items with high reliability (α <.80), suitable for people aged 15 and up. The full version of the questionnaire can be found on the website: www.ipaq.ki.se.

By means of the Beck Anxiety Inventory [22] the level of anxiety of the volunteers is obtained quickly, being able to obtain a score of 0 to 63 points, dividing the level of anxiety in four grades: minimum (0-7), slight (8 -15), moderate (16-25) and severe (26-63).

Many authors value the realization of techniques with the PPE placed. Szarpak et al [23] studied the advanced management of the airway by paramedical personnel wearing protective suits. Another study by Szarpak [24] assessed the correct performance of external cardiac massage techniques on a mannequin by professionals in protective suits, assessed the correct position, depth or quality, among other aspects, but not how this physical exertion affected the patients. rescuers.

Other types of thesis analyze in a very segmented way how certain physiological parameters respond to the implementation of HAZMAT protective suits. A very significant example is the article by Richmond et al. [25], which attempts to predict the body temperature that a worker may have with different types of protective suits and with different environmental conditions; this is also the case of Adams et al. [26], whose study tries to investigate the relation of the use of ballistic protection suits in personnel with a normal weight or in obese, and to observe if there are differences in body temperature between one group and another (the sample size was 20 people).

To conclude, two articles have to be highlighted, that of Stein et al. [27], which analyzes the reaction time of workers carrying personal protective equipment and their physiological response. The authors attempt to describe and compare changes in heart rate, venous pH in pCO2, bicarbonate, lactate level, oxygen saturation and temperature. Analyze the variations of these parameters in 19 healthy subjects, in two cases of 20 minutes of exercise without protective equipment, and then the variation for 20 minutes of exercise wearing protective suits. Researchers observed how heart rate was more substantially elevated in volunteers with the protective equipment placed than in the control case, as well as temperature; however, due to the size of the sample, the results were not statistically significant.

The last study related to this research, which is of special relevance, was developed by Northington et al. [28] in 2007. In this study the physiological response during exercise performed tape is evaluated, voluntary equipped with protective equipment against chemical hazards. The sample was very small (n = 9), and exercise time was reduced (10 min), being most significant finding as the temperature rise of all volunteers.

Our study has several limitations. First, the multiplicity of PPE. In this research, a level D PPE has been chosen in the face of biological risks, as it is the most usual in this type of situation, but we are aware that it is not the only type of equipment that exists, and also that the differences between a type of protection and another are totally different.

We have used the study of physiological and anthropometric parameters cited in the methodology, but the usefulness of other parameters such as cortisol, pH or insulin levels, among others, is not discussed; however, they were discarded from the study due to the complexity required to carry out the determinations.

5. CONCLUSIONS

In the present study it has been observed that there are volunteers with final AL figures greater than the initial ones and final AL figures greater than 4 mmol / L. This predictive value is especially relevant, since it allows to make a previous screening with a high sensitivity to know who could tolerate badly the performance of a work with this equipment of individual protection against biological risks. Knowing the possible behavior of workers at a physiological level, a more efficient selection can be made, and avoiding, as much as possible, situations of unnecessary risk in the interventions.

ACKNOWLEDGEMENT

We would like to thank the collaboration of the final year students of the Faculty of Health Sciences. Without their support the field phase of this study could not have been carried out.

REFERENCES

[1] Kollek D, Wanger K, Welsford M. Chemical, biological, radiological and nuclear preparedness training for emergency medical services provider. CJEM. 2009; 11(4): p. 337-42.

[2] Jama TJ, Kuisma MJ. Preparedness of Finnish Emergency Medical Services for Chemical Emergencies. Prehosp Disaster Med. 2016; 31(4): p. 392-6.

[3] Shin S, Park JH, Kim JH. Effectiveness of patient simulation in nursing education: Meta-analysis. Nurse Educ Today. 2015; 35(1): p. 176–82.

[4] Liaw SY, Chan SWC, Chen FG, Hooi SC, Siau C. Comparison of Virtual Patient Simulation With Mannequin-Based Simulation for Improving

Clinical Performances in Assessing and Managing Clinical Deterioration: Randomized Controlled Trial. J Med Internet Res. 2014; 16(9): p. e214.

[5] Léguillier T, Jouffroy R, Boisson M, Boussaroque A, Chenevier-Gobeaux C, Chaabouni T, et al. Lactate POCT in mobile intensive care units for septic patients? A comparison of capillary blood method versus venous blood and plasma-based reference methods. Clin Biochem. 2018; 55: p. 9-14.

[6] van Horssen R, Schuurman TN, de Groot MJM, Jakobs BS. Lactate point-of-care testing for acidosis: Cross-comparison of two devices with routine laboratory results. Pract Lab Med. 2016; 4: p. 41-9.

[7] Florkowski C, Don-Wauchope A, Gimenez N, Rodriguez-Capote K, Wils J, Zemlin A. Point-of-care testing (POCT) and evidence-based laboratory medicine (EBLM) - does it leverage any advantage in clinical decision making? Crit Rev Clin Lab Sci. 2017; 54: p. 471-94.

[8] Fukumoto Y, Inoue Y, Takeuchi Y, Hoshino T, Nakamura Y, Ishikawa K, et al. Utility of blood lactate level in triage. Acute Med Surg. 2016; 3: p. 101-6.

[9] 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: p. 445-52.

[10] Morales-Alamo D, Losa-Reyna J, Torres-Peralta R, Martin-Rincon M, Perez-Valera M, Curtelin D, et al. What limits performance during whole-body incremental exercise to exhaustion in humans? J Physiol. 2015; 593(20): p. 4631–48.

[11] Ražanskas P, Verikas A, Olsson C, Viberg PA. Predicting Blood Lactate Concentration and Oxygen Uptake from sEMG Data during Fatiguing Cycling Exercise. Sensors (Basel). 2015; 15(8): p. 20480–500.

[12] Vikmoen O, Raastad T, Seynnes O, Bergstrøm K, Ellefsen S, Rønnestad BR. Effects of Heavy Strength Training on Running Performance and Determinants of Running Performance in Female Endurance Athletes. PLoS One. 2016; 11(3): p. e0150.

[13] Hall MM. Lactate: Friend or Foe. PM&R. 2016; 8(3): p. S8-15.

[14] Velasco-Muñoz C , de-Boer J, van-Kranendonk L, Varela-Santos C, Bartels C. Safe use of personal protective equipment in the treatment of infectious diseases of high consequence. Thecnical document. Stockholm: European Centre for Disease Prevention and Control (ECDC), ECDC; 2014. Report No.: Version 2.

[15] Böhm M, Reil JC, Deedwania P, Kim JB, Borer JS. Resting heart rate: risk indicator and emerging risk factor in cardiovascular disease. Am J Med. 2015; 128(3): p. 219-28.

[16] Garg R, Malhotra V, Kumar A, Dhar U, Tripathi Y. Effect of isometric handgrip exercise training on resting blood pressure in normal healthy adults. J Clin Diagn Res. 2014; 8(9): p. BC08-10.

[17] Reidy P, Fletcher T, Shieber C, Shallcross J, Towler H, Ping M, et al. Personal protective equipment solution for UK military medical personnel working in an Ebola virus disease treatment unit in Sierra Leone. J Hosp Infect. 2017; 96(1): p. 42–8.

[18] Verbeek JH. Personal protective equipment for preventing highly infectious diseases due to exposure to contaminated body fluids in healthcare staff. Cochrane Database Syst Rev. 2016; 19(4): p. CD011621.

[19] Morais SS, Ide M, Morgan AM, Surita FG. A novel body mass index reference range - an observational study. Clinics (Sao Paulo). 2017; 72(11): p. 698-707.

[20] Nicaise V. Agreement between the IPAQ and Accelerometer for Detecting Intervention-Related Changes in Physical Activity in a Sample of Latina Women. J Phys Act Health. 2014; 11(4): p. 846-52.

[21] Lee PH, Macfarlane DJ, Lam TH, Stewart SM. Validity of the international physical activity questionnaire short form (IPAQ-SF): A systematic review. Int J Behav Nutr Phys Act. 2011; 8: p. 115.

[22] Vázquez Morejón AJ, Vázquez-Morejón Jiménez R, Zanin GB. Beck Anxiety Inventory: psychometric characteristics in a sample from the clinical Spanish population. Span J Psychol. 2014; 17: p. E76.

[23] Szarpak L, Madziała M, Smereka J. Comparison of endotracheal intubation performed with 3 devices by paramedics wearing chemical, biological, radiological, and nuclear personal protective equipment. Am J Emerg Med. 2016; 34(9): p. 1902-3.

[24] Szarpak L, Truszewski Z, Gałązkowski R, Czyzewski L. Comparison of two chest

ISSN 2457-063X (Online) **www.ijisms.com** *Volume: 2 Issue: 6 | 2018*

compression techniques when using CBRN-PPE: a randomized crossover manikin trial. Am J Emerg Med. 2016; 34(5): p. 913-5.

[25] Richmond VL, Davey S, Griggs K, Havenith G. Prediction of Core Body Temperature from Multiple Variables. Ann Occup Hyg. 2015; 59(9): p. 1168-78.

[26] Adams JD, Mcdermott BP, Ridings CB, Mainer LL, Ganio MS, Kavouras SA. Effect of Air-Filled Vest on Exercise-Heat Strain When Wearing Ballistic Protection. Ann Occup Hyg. 2014; 58(8): p. 1057-64.

[27] Stein C. The effect of physical exertion in chemical and biological personal protective equipment on physiological function and reaction time. Prehosp Emerg Care. 2010; 14(1): p. 36-44.

[28] Northington WE, Suyama J, Goss FL, Randall C, Gallagher M, Hostler D. Physiological responses during graded treadmill exercise in chemical-resistant personal protective equipment. Prehosp Emerg Care. 2007; 11(4): p. 394-8.

AUTHORS' BIOGRAPHIES

Francisco Martín-Rodríguez, MSc, PhD
Advanced Clinical Simulation Center. Faculty of Medicine. Valladolid University. Spain.

Table 2. General characteristics of the participants.

	Total	Good tolerance	Poor tolerance	p value
Number [n (%)]	47 (100)	32 (68.1)	15 (31.9)	< 0.001
Gender				
Male [n (%)]	22 (46.8)	15 (68.2)	7 (31.8)	0.001
Female [n (%)]	25 (53.2)	17 (68.0)	8 (32.0)	0.001
Age (years old) [Median (IQR)]	41 (33-47)	38 (28-45)	46 (41-49)	<0.001
Physiological evaluation [Median (IQR)]				
Heart rate (bpm)	78 (71-86)	75 (69-85)	83 (76-95)	0.280
MBP (mmHg)	100 (92-107)	99 (87-107)	100 (94-108)	0.308
Tympanic temperature (ºC)	36.4 (36.1-36.8)	36.4 (36.1-36.8)	36.4 (36.0-36.8)	0.582
BAI (points) [Median (IQR)]	3 (1-6)	3 (1-6)	3 (1-7)	0.950
BMI [Median (IQR)]	25 (22-28)	24 (21-26)	28 (23-30)	0.007
IPAQ-SF [n (%)]				
Sedentary	25 (53.2)	11 (34.4)	14 (93.3)	<0.001
Active	14 (29.8)	13 (40.6)	0 (0)	a
Sport	8 (17.0)	8 (25.0)	1 (6.7)	<0.001
Lactate (mmol/L) [Median (IQR)]				
Basal	1.8 (1.2-2.8)	2.0 (1.3-2.8)	1.4 (1.1-2.7)	0.905
Final	2.9 (2.1-4.1)	2.5 (1.3-3.1)	4.5 (2.9-5.1)	<0.001
EWS-BioHazMat (points) [Median (IQR)]	9 (7-11)	8 (7-11)	11 (10-14)	<0.001

IQR: Interquartile range; MBP: Median blood pressure; BAI: Beck Anxiety Inventory; BMI: Body mass index; IPAQ: International Physical Activity Questionnaire - Short Form

a The p-value can not be calculated because the standard deviation is zero

Table 3. Comparison of the different AUROC of the EWS-BioHazMat with statistical significance (p-value). Sensitivity and specificity cut-off points combined with the best score (Youden test) for the different parameters analyzed.

Test	Global	Male	Female	AT	BT
Global	1	0.100	0.135	0.308	0.388
Male	0.100	1	0.012	0.860	
Female	0.135	0.012	1		
AT	0.308	0.860			
BT	0.388				

Cut-offs (points)		Se % [IC 95%]	Sp % [IC 95%]	PPV	NPV	LR (+)	LR (-)
Global	10	0.80 (0.59-1)	0.71 (0.56-0.97)	0.57	0.88	2.84	0.27
Male	9	1 (1-1)	0.40 (0.15-0.64)	0.43	1	1.66	0
Female	10	0.75 (0.45-1)	0.88 (0.72-1)	0.75	0.88	6.37	0.28
AT	10	1 (1-1)	0.72 (0.54-0.91)	0.64	1	3.66	0
BT	9	1 (1-1)	0.60 (0.29-0.90)	0.50	1	2.50	0

CI: confidence interval; Se: Sensitivity; Sp: Specificity; PPV: positive predictive value: NPV: negative predictive value; LR: Likelihood ratio;

Bold values are different from 0 with a significance level of alpha = 0.05