

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Critical Care Medicine

**Manuscript NO:** 44983

**Title:** Neutrophil-Lymphocyte Ratio: A Prognostic Tool in Patients with In-Hospital Cardiac Arrest

**Reviewer's code:** 03491558

**Reviewer's country:** Italy

**Science editor:** Jia-Ping Yan

**Date sent for review:** 2018-12-13

**Date reviewed:** 2018-12-13

**Review time:** 7 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

### SPECIFIC COMMENTS TO AUTHORS

This manuscript focused on a significant topic. There is a dire need to identify available, inexpensive and robust biomarkers that can clinically be helpful to determine outcomes/mortality after ROSC. The authors should mention the retrospective Weiser'



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study on Resuscitation (Resuscitation 2017, 116:49-55) conducted on patients with out of hospital cardiac arrest. Other suggestions to the authors 1. Please, add number of patients in abstract 2. The findings on figure 2 should be better discussed (significance on PEA group) 3. Please, emphasize that the study concerns in-hospital mortality in both title and abstract.

### **Response by the Authors**

We have now included the restrospective study on out of hospital cardiac arrest. Although our paper looks at in hospital cardiac arrest, it is important to acknowledge the utility and findings of Weiser et al. as we both agree that NLR may have a role in prognosticating survival after cardiac arrest. Other revision have been made as suggested.

### **INITIAL REVIEW OF THE MANUSCRIPT**

#### ***Google Search:***

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

#### ***BPG Search:***

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Critical Care Medicine

**Manuscript NO:** 44983

**Title:** Neutrophil-Lymphocyte Ratio: A Prognostic Tool in Patients with In-Hospital Cardiac Arrest

**Reviewer's code:** 00502743

**Reviewer's country:** Argentina

**Science editor:** Jia-Ping Yan

**Date sent for review:** 2018-12-29

**Date reviewed:** 2018-12-31

**Review time:** 2 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input checked="" type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

### SPECIFIC COMMENTS TO AUTHORS

It would be great to be able to consider - according to the authors - that the Neutrophil-Lymphocyte Ratio (NLR) is a reliable prognostic marker in patients with intra-hospital cardiac arrest. However, we must also remember that there are many



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other nosological conditions capable of causing changes in this marker (for example, S beta-100 has shown remarkable specificity in cases associated with trauma or cranio-encephalic damage, very much greater than 73% reported for the NLR). Anyway, it will be very useful to keep in mind this NLR marker while progressing towards greater prognostic specificity in patients with intra-hospital cardiac arrest.

#### **INITIAL REVIEW OF THE MANUSCRIPT**

##### ***Google Search:***

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##### ***BPG Search:***

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- ☐ No

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Critical Care Medicine

**Manuscript NO:** 44983

**Title:** Neutrophil-Lymphocyte Ratio: A Prognostic Tool in Patients with In-Hospital Cardiac Arrest

**Reviewer's code:** 02730715

**Reviewer's country:** China

**Science editor:** Jia-Ping Yan

**Date sent for review:** 2018-12-29

**Date reviewed:** 2019-01-01

**Review time:** 3 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

### SPECIFIC COMMENTS TO AUTHORS

This manuscript focused on finding a simple and rapid prognostic marker for the patients with IHCA, which is a significant study. I make the following recommendations: 1) references need to be updated. 2) It would be better to describe the



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results section in detail. 3) Horizontal axis ( types of cardiac rhythm) should be formatted consistently in Figure2.

#### **Response by the Authors**

We have updated the references as suggested and the results section have been described in better detail. Other revisions as suggested have been made as well.

#### **INITIAL REVIEW OF THE MANUSCRIPT**

##### ***Google Search:***

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- ☐ No

##### ***BPG Search:***

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- ☐ Plagiarism
- ☐ No

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Critical Care Medicine

**Manuscript NO:** 44983

**Title:** Neutrophil-Lymphocyte Ratio: A Prognostic Tool in Patients with In-Hospital Cardiac Arrest

**Reviewer's code:** 03106792

**Reviewer's country:** United Kingdom

**Science editor:** Jia-Ping Yan

**Date sent for review:** 2018-12-29

**Date reviewed:** 2019-01-03

**Review time:** 12 Hours, 5 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
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### SPECIFIC COMMENTS TO AUTHORS

The findings are relatively novel although tested in a very small population. The study may serve as hypothesis generating. The limitations are discussed. The article is of limited interest for such limitation. Otherwise it is well-written. How the authors



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derived the sample size should be explained.

**Answer:** To our knowledge, this is the first study looking at using NLR as a prognostic tool in patients with IHCA. We didn't have a previous study that we could use to estimate or gauge for an appropriate sample size. As a result, data was collected for all patients that have an IHCA event during a twelve month duration and analyzed.

Were the retrieved data collected electronically or on paper chart?

**Answer:** The data was collected from an electronic medical record and put in Excel. The abstract needs to be more focused in its introduction. It seems unclear the way the cut-off is derived reading the abstract. The cutoff was derived from the actual data based on the receiver operating characteristic curve analysis with the goal to identify the optimal cutoff for survival and non-survival .

Previous research? From the actual data? From the main document it seems the latter, then this part should be inserted in the abstract results rather than in the methods. Throughout the manuscript please use Target temperature management rather than therapeutic hypothermia.

**Answer:** We have made this correction now. Also some NLR are not abbreviated We have made this correction now.

In the discussion please do not report the results of univariate analysis but rather of the multivariate since these are more robust.





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**Answer:** We agree that multivariate analysis are more robust but we feel univariate analysis will provide better understanding of the characteristics of the population.

Line 6 of discussion delete “for”

**Answer:** We have made this correction now.

It would be useful for readers if the authors reports the sensitivity/specificity of other markers (i.e. NSE and S-100)

**Answer:** The range of sensitivity and specificity of neuron specific enolase with a cutoff level of 33mg/l as a biomarker for worse neurologic injury after cardiac arrest is 72-80% and 84-100% respectively. The false positive rate of this biomarker is 0-23%. Similarly the reported range of sensitivity and specificity of S-100 with a cutoff range of 0.2-1.5mg/l as a adverse marker of neurologic injury after cardiac arrest is 72-80% and 85-100% respectively with a 0-16% false positive rate. While the timing of measurement of both of these biomarkers may alter the sensitivity and specifity of both biomarkers, the effect targeted temperature management is not well known. Noteworthy, Kim et al. 2018 showed that the NLR cut off value of 6 at 72 hours after ROSC achieved in patients with out of hospital cardiac arrest and targeted temperature management had a sensitivity and specificity of 89 and 47% respectively. In our study, we found that NLR measured within 24 hours of IHCA of greater than or equal to 4.5 has a 82% sensitivity, 42% specificity and a 73% positive predictive value to be a marker of mortality.

## **INITIAL REVIEW OF THE MANUSCRIPT**

*Google Search:*



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