Author’s response to reviews

Title: Prognostic Value of Point-of-Care Ultrasound during Cardiac Arrest: A Systematic Review

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To the editors of Cardiovascular Ultrasound,

Thank you for the opportunity to submit our paper for peer-review and hopeful publication in your journal. We are grateful for the reviewers’ comments and have attempted to address each point that each of the reviewers have made in the letter below.

Reviewer 1:
Background: Page 4, paragraph 2. While POCUS in cardiac arrest is certainly important for diagnosis of etiology and guiding intervention, the current evaluation focuses on prognosis. You could include results that pertain POCUS guiding resuscitation and procedures in order to support this as an aim of the study as you additionally mention this aspect in your discussion. Alternatively, you could reshape your background to focus on the prognostic applications of POCUS in cardiac arrest, which better fits the current analysis.

Excellent point and this is addressed with the addition of the following sentence to the end of paragraph 2 in the Background section: “By better understanding the pathophysiology and natural history of cardiac arrest, POCUS may allow for better insights into the prognosis of patients receiving CRP following OHCA.”

Methods: 1. How many authors performed the literature search?
   We would like to thank the reviewer for noting this question. The author contributions are included in the Author Contributions section.
   2. How did you evaluate validity of study design? i.e. randomization, blinding, and follow up rate.
   All studies that were included were assessed from peer-reviewed publications that are searchable in PubMed. The following sentence from the manuscript we believe addresses this question: “Only clinical studies with adult populations that pertained to our objective and were published in English prior to June 23, 2019 were included in our review.” We believe that Figure 3 graphically depicts the
flow. Additionally we included an additional sentence in the Methods section: “Excluded from review were studies with outcomes unrelated to cardiac arrest, pediatric and fetal populations, and reviews, case reports and letters.”

Results: Table 2 - I do not see Blaivas et al, kim et al, Breithkreutz et al, or Schuster et al. in the table. Is this intentional?
Excellent observation. Thank you for noticing this. These studies were left out in error. We have rewritten the table and added these 4 studies in the table in the paper. See below:

<table>
<thead>
<tr>
<th>Study</th>
<th>Outcome</th>
<th>Outcome P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bolvardi et al.(4)</td>
<td>ROSC</td>
<td>0</td>
</tr>
<tr>
<td>Gaspari et al.(5)</td>
<td>ROSC</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>-- Survival to Hospital Admission</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>-- Survival to Hospital Discharge</td>
<td>0.04</td>
</tr>
<tr>
<td>Salen et al. (2001)(6)</td>
<td>Survival to Hospital Admission</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Ozen et al. (7)</td>
<td>ROSC</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>-- Survival to Hospital Admission</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Cebicci et al. (8)</td>
<td>24 hour survival</td>
<td>0</td>
</tr>
<tr>
<td>Chardoli et al. (9)</td>
<td>ROSC</td>
<td>N/S</td>
</tr>
<tr>
<td>Tomruk et al. (10)</td>
<td>ROSC</td>
<td>0.02</td>
</tr>
<tr>
<td>Aichinger et al. (11)</td>
<td>Survival to Hospital Admission</td>
<td>0.01</td>
</tr>
<tr>
<td>Salen et al. (2005)(12)</td>
<td>ROSC</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>-- Survival to Hospital Admission</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Hayhurst et al. (1)</td>
<td>ROSC</td>
<td>N/S</td>
</tr>
<tr>
<td>Kim et al. (15)</td>
<td>ROSC</td>
<td>0</td>
</tr>
<tr>
<td>Blaivis et al. (14)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Survival to Hospital Admission | N/S  
---|---  
Schuster et al. (17) |  
ROSC | 0.01  
Brieithkruetz et al. (16) |  
Survival to Hospital Admission | N/S  

Tables 7 and 8 are slightly redundant. I like that you stratified results based on outcomes, but most of this data is in Table 3. Rates of intervention, or stratification based on etiology of arrest, traumatic vs non-traumatic may make a more interesting evaluation.

We agree with the reviewer on this point. We included Tables 7 and 8 to further demonstrate the observations of outcomes seen with and without cardiac motion seen in the different studies. Although we agree that it may be repetitive, we believe that since the study designs are all somewhat unique, the additional tables helps to convey the tabulated data more clearly.

Discussion: Page 10, line 29 - This sentence needs a conjunction.

Excellent point by the reviewer. We are grateful for this recommendation. The first paragraph of the discussion was rewritten with more grammatically sound structure:

“Our review of the data demonstrates a consistent relationship between the presence of cardiac motion on point-of-care ultrasound during cardiac arrest and “positive” outcomes of cardiac resuscitation. As cardiac motion is required for any positive survival outcome, it is not surprising that the presence of cardiac motion is associated with survival during resuscitation efforts. With current guideline directed clinical practice recommendations, the presence of cardiac or absence of cardiac motion seen with ultrasound is not an indication to alter management decisions. The negative predictive value of cardiac motion on positive outcomes may impact clinical practice. Across all studies, the absence of cardiac motion on ultrasound results in non-ROSC in 82% of patients. Furthermore, 94% of patients with absent cardiac motion did not survive to hospital admission. This suggests the potential for clinical utility in assessing cardiac motion at the initiation of or during pauses in cardiac resuscitation as a screening measure for patients presenting to the ED in cardiac arrest.”

I would like to see more regarding limits of your study design and limitations of the studies reviewed. We are grateful for this recommendation and we have elaborated on some additional limitations:

“Additionally, there may be relevant or similar studies that fell outside of the search criteria. The studies included do not specify or include the use of pocket-sized POCUS devices that are gaining popularity in clinical practice.” We also have included an additional reference: 24. Seraphim A, Paschou SA, Grapsa J, Nihoyannopoulos P. Pocket-Sized Echocardiography Devices: One Stop Shop Service? Journal of Cardiovascular Ultrasound. 2016;24(1):1-6.

Conclusion: Page 10, line 58 - How is this statement supported by your findings or cited literature? I would recommend citing literature in your discussion or intro regarding this or removing this statement.

Page 11, line 3 - I don't believe that your study really evaluates using POCUS to diagnose pathology. It may be best to limit this conclusion to prognostic value unless you include a subanalysis of the studies that demonstrate use of POCUS to diagnosis arrest etiology.

We would like to thank the reviewer for suggesting further clarification in the conclusion. We addressed this by further qualifying our statements and conclusions reach from our review of the data.

Conclusions
“With the increasing availability of affordable handheld POCUS devices, we believe there will likely be increased physician comfort and skill with the use of ultrasound in the ED and critical care setting. While these results suggest POCUS provides additional diagnostic and prognostic information in the management of cardiac arrest, with the current body of knowledge regarding POCUS in the setting of cardiac arrest, we believe it remains vitally important that point-of-care imaging does not interfere with standard advanced cardiac life support efforts. With further study and perhaps a randomized multicenter trial using POCUS during treatment of cardiac arrest, perhaps standardized POCUS data can be incorporated in the evidence-based treatment of patients suffering from cardiac arrest. Point-of-care assessment of cardiac motion has the potential to be informative as an additive clinical data point in the clinical assessment of patients suffering from cardiac arrest.”

Reviewer 2:
The report is complete, but some minor questions need to be addressed:
The is no uniform definition of "cardiac movement" and even though it is a binary and simple assessment it could be of use to define this condition (e.g. as reported in some of the studies showed as: any detected motion within the heart including the atria, ventricles or valves).
The reviewer brings up an important point. Unfortunately, there was not a universally defined definition of “cardiac movement” or “cardiac motion”. Six of the studies did not actually define how they interpreted “cardiac movement”. In future studies, this may be useful to clarify. We added a sentence to the Results section addressing this point: “The definition of presence of cardiac motion was not standardized.”

The only case-control randomized trial where the effective impact on outcome of cardiac movement during resuscitation (Chardoli M, Heidari F, Rabiee H, Sharif-Alhoseini M, Shokoohi H, Rahimi-Movaghar V. Echocardiography integrated ACLS protocol versus conventional cardiopulmonary resuscitation in patients with pulseless electrical activity cardiac arrest. Chin J Traumatol. 2012;15(5):284-7) showed no significant differences in resuscitation results between the observed groups (whether the point-of care echo was used or not). Thus, despite the evident negative predictive values of the technique there might be several inclusion biases that need to be considered in the discussion/limitations, that could impact in the effective practical use of the technique in daily practice. Please comment.
This is an excellent point that the reviewer brings up and it is addressed in the conclusion by bringing up with possibility of more systematically reviewing POCUS in cardiac arrest patients with a randomized multicenter trial. We have added a sentence to the Discussion to reflect this point: “Also, a survivor bias effect may be present for patients that were included in the reviewed studies as this cohort of patients may have possessed characteristics that favored more prolonged survival to inclusion in these research studies.”
To increase awareness on the practical use of this approach the need of multicentric randomized case-control studies should be stressed in the conclusions.

The reviewer makes an excellent point which is addressed in the rewritten conclusion:
“With the increasing availability of affordable handheld POCUS devices, we believe there will likely be increased physician comfort and skill with the use of ultrasound in the ED and critical care setting. While these results suggest POCUS provides additional diagnostic and prognostic information in the management of cardiac arrest, with the current body of knowledge regarding POCUS in the setting of cardiac arrest, we believe it remains vitally important that point-of-care imaging does not interfere with standard advanced cardiac life support efforts. With further study and perhaps a randomized multicenter trial using POCUS during treatment of cardiac arrest, perhaps standardized POCUS data can be incorporated in the evidence-based treatment of patients suffering from cardiac arrest. Point-of-care assessment of cardiac motion has the potential to be informative as an additive clinical data point
in the clinical assessment of patients suffering from cardiac arrest.”
We would like to again thank the editors and reviewers of our submission titled: Prognostic Value of Point-of-Care Ultrasound during Cardiac Arrest: A Systematic Review. We humbly resubmit our review with edits that have addressed each point of made by each reviewer for hopeful publication in Cardiovascular Ultrasound.

Sincerely,

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