

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Predictors of good functional outcome in counterpulsation-treated recent ischemic stroke patients
<b>AUTHORS</b>	LIN, WEN HUA; Han, Jinghao; Chen, Xiang-Yan; Xiong, Li; Leung, Ho wan; Leung, W.H.; Soo, Yannie; Wong, Lawrence

### VERSION 1 - REVIEW

<b>REVIEWER</b>	Ozlem Soran, MD, MPH, FACC, FESC Associate Professor of Medicine Associate Professor of Epidemiology/ Research Director of EECP Lab. Heart and Vascular Institution University of Pittsburgh
<b>REVIEW RETURNED</b>	12-Apr-2013

<b>THE STUDY</b>	<p>1. Is the overall study design appropriate and adequate to answer the research question:</p> <p>This is a single center observational study therefore the results are not adequate to answer the research question however, it provides valuable data to initiate a randomized clinical trial.</p> <p>2. Are the abstract/summary/key messages/limitations accurate?</p> <p>The term "ECP" has been used interchangeably with the term "EECP". Authors should cite the terminology as is used in the original papers ( such as : reference numbers 3-6; 8,9,11,12, 15)</p>
<b>RESULTS &amp; CONCLUSIONS</b>	<p>1.Do the results answer the research question?</p> <p>External countrepulsation treatment efficacy is higly dependend on the diastolic/ systolic augmentation ratio (D/S ratio) . Authors should include this in the analysis.</p> <p>There are several limitations of the study however, authors stated them clearly.</p>

<b>REVIEWER</b>	Han Hwa Hu, MD Neurological Department Taipei Veterans General Hospital Taipei Taiwan
<b>REVIEW RETURNED</b>	14-Apr-2013

<b>THE STUDY</b>	This is a retrospective study with small sample size. The ECP treatment is not randomized and the duration of ECP treatment is not randomized either. Whether or not the ECP or longer treatment
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	of ECP is associated with better functional outcome cannot be adequate to answer by this study design.
<b>RESULTS &amp; CONCLUSIONS</b>	Again, this is a retrospective study with small sample size. The ECP treatment is not randomized and the duration of ECP treatment is not randomized either.
<b>GENERAL COMMENTS</b>	As described in the manuscript, the controls were selected from the patients who fulfilled the same inclusion and exclusion criteria with ECP group but refused ECP. The followings are my questions: Did you include all the patients who fulfilled the inclusion and exclusion during the study period? Why these patients refused ECP treatment?

<b>REVIEWER</b>	Christopher Chen, Associate Professor, Department of Pharmacology National University of Singapore  I have no relevant competing interests to declare
<b>REVIEW RETURNED</b>	23-Apr-2013

<b>THE STUDY</b>	The stated aim is "to explore predictors of good functional outcome for ECP treated ischemic stroke patients". but this study is limited to only patients with large vessel stroke, only those who completed at least 10 sessions. I suggest that the aim is revised to "to explore predictors of good functional outcome for ECP treated ischemic stroke patients who completed a minimum of 10 sessions"
<b>RESULTS &amp; CONCLUSIONS</b>	The authors state that "Small sample size limited us to further analyze the effects of ECP on different subtype of ischemic stroke, such as artery-to-artery embolism, small vessel disease, and watershed strokes." This is not entirely correct as the inclusion criteria limited recruitment to patients with large artery disease which would lead to a bias towards particular stroke subtypes.

### VERSION 1 – AUTHOR RESPONSE

Reviewer 1: Ozlem Soran, MD, MPH, FACC, FESC  
Associate Professor of Medicine  
Associate Professor of Epidemiology/ Research  
Director of EECP Lab.  
Heart and Vascular Institution  
University of Pittsburgh

1. Is the overall study design appropriate and adequate to answer the research question:

This is a single center observational study therefore the results are not adequate to answer the research question however, it provides valuable data to initiate a randomized clinical trial.

Authors: Thanks for your support.

2. Are the abstract/summary/key messages/limitations accurate?

The term "ECP" has been used interchangeably with the term "EECP". Authors should cite the terminology as is used in the original papers ( such as : reference numbers 3-6; 8,9,11,12, 15)

Authors: We revised the relative statements as you suggested in the introduction and discussion. Please check in the revision.

1. Do the results answer the research question?

External countrepulsation treatment efficacy is highly dependent on the diastolic/ systolic augmentation ratio (D/S ratio) . Authors should include this in the analysis.

Authors: We really appreciate your comments. We agreed that ECP treatment efficacy is highly dependent on the diastolic/systolic augmentation ration in the application of ECP in coronary heart disease. However, cerebral circulation is different from coronary circulation with a cerebral autoregulation system. We failed to confirm the association between D/S ratio and augmentation of cerebral blood flow in our exploration of ECP used in ischemic stroke. We are looking for a more promising hemodynamic index associated to cerebral augmentation and clinical benefits. Therefore, we did not include D/S ratio in our analysis.

There are several limitations of the study however, authors stated them clearly.

Reviewer 2: Han Hwa Hu, MD  
Neurological Department  
Taipei Veterans General Hospital  
Taipei  
Taiwan

This is a retrospective study with small sample size. The ECP treatment is not randomized and the duration of ECP treatment is not randomized either. Whether or not the ECP or longer treatment of ECP is associated with better functional outcome cannot be adequate to answer by this study design.

Authors: We admitted that this was not a randomized study. But it is the first report from an ECP registry for ischemic stroke patients and it provides important data for the large sample-size randomized clinical trials in the future.

As described in the manuscript, the controls were selected from the patients who fulfilled the same inclusion and exclusion criteria with ECP group but refused ECP. The followings are my questions: Did you include all the patients who fulfilled the inclusion and exclusion during the study period? Why these patients refused ECP treatment?

Authors: Yes, in this retrospective study we included all the patients who fulfilled the inclusion and exclusion during the study period. Those patients only received medical treatment had many kinds of reasons to refuse ECP treatment. Most of them did not trust this novel treatment method which was still under investigation. They were unwilling to spend time on ECP treatment for the uncertain clinical benefits. Some patients lived in Mainland China rather than Hong Kong, and therefore preferred receiving medical treatment at home instead of frequent regular ECP treatment in hospital. Some patients refused for personal reasons, like being over-sensitive to potential leg pain or scared of being wrapped up during the treatment.

Reviewer 3: Christopher Chen,  
Associate Professor,  
Department of Pharmacology  
National University of Singapore

I have no relevant competing interests to declare

The stated aim is "to explore predictors of good functional outcome for ECP treated ischemic stroke patients". but this study is limited to only patients with large vessel stroke, only those who completed at least 10 sessions.

I suggest that the aim is revised to "to explore predictors of good functional outcome for ECP treated ischemic stroke patients who completed a minimum of 10 sessions"

Authors: Thanks. We revised the aim as you suggested.

The authors state that "Small sample size limited us to further analyze the effects of ECP on different subtype of ischemic stroke, such as artery-to-artery embolism, small vessel disease, and watershed strokes." This is not entirely correct as the inclusion criteria limited recruitment to patients with large artery disease which would lead to a bias towards particular stroke subtypes.

Authors: In the revision, we deleted relative statements in article summary and limitations.