Author’s response to reviews

Title: Gender and age disparity in the initiation of life-supporting treatments: a population-based cohort study

Authors:

Peng-Sheng Ting (ting.pengsheng@gmail.com)
Likwang Chen (likwang.chen@gmail.com)
Wei-Chih Yang (weichih@nhri.org.tw)
Tien-Shang Huang (huangts@ntu.edu.tw)
Chau-Chung Wu (chauchungwu@ntu.edu.tw)
Yen-Yuan Chen (chen.yenyuan@gmail.com)

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Author’s response to reviews:

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Dear Editor, BMC Medical Ethics

We are pleased to submit this revised manuscript entitled: “Gender and age disparity in the initiation of life-supporting treatments: a population-based cohort study”, for consideration as a research article. We followed the two reviewers’ suggestions to revise the manuscript, and attached a point-to-point response to the two reviewers’ comments following this cover letter.

This manuscript has not been previously published and is not under consideration in the same or substantially similar form in any other journals. To the best of our knowledge, no conflict of interests exists. This study was supported by research grants from Taiwan Ministry of Science and Technology (MOST 103-2511-S-002-008-MY5), National Taiwan University Hospital (NTUH 106-3553) and by Taiwan National Health Research Institutes (PH-100-PP-19 and PH-101-PP-16). The funding agencies did not have any involvement in data collection, data analysis,
and data interpretation. This study was approved by the Research Ethics Committee in National Taiwan University Hospital (201212043W).

Best Regards,

Corresponding Author
Yen-Yuan Chen, M.D., M.P.H., Ph.D.

Associate Professor
Graduate Institute of Medical Education & Bioethics
National Taiwan University College of Medicine
Attending Physician
Department of Medical Education
National Taiwan University Hospital
Address: No.1, Rd. Ren-Ai sec. 1, Chong-Cheng District, Taipei, 10051, Taiwan
Telephone: 886-2-23123456 ext 63911
Fax: 886-2-23710615

To Reviewer 1

Dear Dr. Aslihan Akpinar,

Thank you for your thoughtful comments on our work. Our point-to-point responses to your comments are as follows:
“In introduction You should explain why the extra-corporeal membrane oxygenation data was used. (1st page, 2nd paragraph) you should give short information about Extracorporeal Life Support Registry Report including who prepared this report with which patients' data?” and “In addition this paragraph is very difficult to understand because of using too many numbers and the last sentence (in summary…) do not represent the paragraph. You should consider rewriting this paragraph. (2nd page, 1st paragraph)”

1. We followed your suggestion to rewrite the second paragraph: we deleted all the numbers and summarized the information using brief sentences (highlighted by yellow): “According to Extracorporeal Life Support Registry Report, a collection of ECMO cases reported to Extracorporeal Life Support Organization by hundreds of medical institutions worldwide which operated ECMO, the annual number of ECMO patients gradually rose since 1990. ECMO is mostly used to support neonates who, compared to adults and pediatric patients, not only have the highest rates of surviving ECMO use, but also surviving to hospital discharge.” We also followed your suggestions to provide short information about the Extracorporeal Life Support Registry Report (highlighted by yellow in the first sentence of the second paragraph), as well as to explain why ECMO was used as the example of LSTs in this study (highlighted by yellow in the first sentence of the third paragraph). Please let us know if you still have concerns about our revisions.

“Objectives in this paragraph only include showing statistical results however in summary your 3rd objective is different. Please review and rewrite your objectives with ethical relevance.”

2. According to your comments, we carefully reviewed Results and Discussion, with a particular focus on the objectives at the end of Background. We found that both Results and Discussion followed a gender-age order. That is, we presented gender-related results ahead of age-related results, and gender-related discussions ahead of age-related discussions. Therefore, we decided to rewrite the objectives in a gender-age order. Additionally, we also added an objective (6) for pointing out the discussion of ethical, cultural, and societal implications based on the empirical study results (highlighted by yellow): “The objectives of this study were as follows: (1) to examine the gender disparities in ECMO use; (2) to examine the age disparities in ECMO use; (3) to estimate the trend of ECMO use as stratified by gender; (4) to estimate the trend of ECMO use as stratified by age; (5) to examine the trend change of ECMO use for each gender and age group; and (6) to deliberate the ethical, cultural, and societal implications of the study results.”

“In findings Is there a data about survival rates of patients receiving ECMO?”
3. This study completely focused on the initiation of life-supporting treatments using ECMO as an important example, not the life or death of the ECMO patients. Therefore, we did not include survival/mortality rate of ECMO users. However, if you consider it as important information somewhere in this paper, please do not hesitate to let us know where to place that information. We will be very happy to follow your suggestion.

“In discussion: (8th page, Line 26) "Particularly, the trends of the male GIR, the female GIR and Adult AIR all had a joinpoint in 2006, implying a significant trend change of ECMO use following 2006". I think this is very important finding you did not discuss; you should consider discussing the meaning of this trend change (you had already discussed before #6).”

4. Thank you for your careful review, and for suggestions for us to discuss these interesting findings. We followed your suggestion to add Trend Change in Extra-corporeal Membrane Oxygenation Use in Discussion (highlighted by yellow) “Prior studies have proposed the possibility that significantly increased ECMO use in Taiwan’s population might be associated with significant social events and their related overly-optimistic reports on the Internet and newspapers. We also highlighted the possibility that the media literacy of the audience, i.e. patients, family members, and health care workers, might play an important role in medical decision-making, as well as decision-making to initiate, withhold, or withdraw LSTs. By further stratifying into different sub-populations, we found that ECMO use was significantly increased following 2006 in both gender groups and in the adult population. Therefore, the decision-making of both gender groups and the adult population to initiate ECMO might be influenced by information from the media. How the media literacy of an individual associates with LSTs decision-making, as well as other medical decision-making, should be further investigated in the future.”

“In general you should enriched your discussion section with the studies about at least - status of and autonomy perception for women, infants, children and elders in Taiwan, - attitudes and opinions for life sustaining treatments and decision making process of physicians, nurses, other health care professionals, patients, public… especially in the context of Confucianism that you mostly mentioned without citation. For example are paternalistic attitudes common for health care professionals, who decide to use of LSTs, always families? - What about the legislations and national ethical guidelines or regulations about this issue?”
5. We followed your suggestions to enrich our discussions: (1) We added a paragraph in Gender Disparity in Extra-corporeal Membrane Oxygenation Use, which provided another reason to account for gender disparity (highlighted by yellow) “In addition, women’s self-perceived burden to others may explain the gender disparity in the use of LSTs as indicated by ECMO. According to a study conducted by Tang et al., women were more likely than men were to perceive themselves as a burden to others when facing end-of-life decision-making (21). Thus, women would be more likely to consent to a DNR order to relieve their sense of self-perceived burden to others”; (2) In the fourth paragraph in Age Disparity in Extra-corporeal Membrane Oxygenation Use, we added the following: “First, individual autonomy/self-determination and family autonomy/family-determination: Western societies mostly honor individual autonomy/self-determination, while Taiwan, as part of East Asian societies where Confucianism is influential, mostly values family autonomy/family-determination. Fan and Lee both proposed the theoretical foundations, based on Confucianism, in support of family autonomy/family determination in the Eastern world, and also highlighted the distinctions between individual autonomy/self-determination and family autonomy/family-determination. Although Chen et al.’s study had shown that the Western societal value of individual autonomy/self-determination has been more and more influential, the East Asian societal value of family autonomy/family determination undoubtedly still remains more influential. In addition, surrogate decision making by family members is more prevalent in the initiation of ECMO than the initiation of other LSTs, because patients, suffering from cardiac or respiratory failure refractory to conventional treatment, are usually incapable of autonomous decision-making. Therefore, a patient’s self-determination, usually influenced by his/her personal experiences with other people’s critical illnesses as proposed by Carmel et al., plays little role in determining whether to receive LSTs or not. Especially when patients are imminently dying, family members as the surrogate decision-makers tend to overestimate patient preference for the use of LSTs, and in Taiwan, family members usually have poor-to-fair consensus on LST-related issues”; and (3) Several studies which mainly focused on Taiwan’s situations have been added to references to support our arguments (21, 28, 29, 33). We do not find more recent data regarding surrogate decision-making in Taiwan. However, we already have Reference (31) in the manuscript which showed most of the DNR were consented to by family members. We did not have national ethical guidelines and regulations when this data was collected. The lawmakers did pass a law called the “Patient Self-Determination Act,” which will take effect starting in January 2019, not in effect when this data was collected.

“Your conclusion looks does not directly related your findings and discussion, therefore I think you should review you objectives, to put your findings in a proper ethical perspective and socio-cultural context in Taiwan, and re-write a conclusion based on your findings and discussion.”
6. Thank you for this reminder. For relating to the study results, discussions, and the objectives in Background, the conclusion was rewritten as the following: “Taiwan has become the country with the most prevalent ECMO use in the world. We examined the current medical practice of ECMO with a particular focus on the differences between gender and age groups, as well as the trend change of ECMO use in different groups. We identified the disparities of ECMO use in different gender and age groups, and also the increasing ECMO use following 2006 in both gender groups and the adult group. The study results suggested that patients’/family members’ medical decision-making to request LSTs is associated with the ethical, cultural, and societal values surrounding the particular context. Future studies may be focused on further examining the ethical, cultural, and societal implications related to the gender and age disparities of ECMO use in Taiwan using qualitative research methods”. The ethical relevance was also hinted in Conclusion.

We would like to thank you for your efforts in review of our study. We are grateful for how your feedback and comments have benefited and advanced our approach to the study. In summary, we hope that the revised manuscript is more suitable for being published in BMC Medical Ethics.

To Reviewer 2

Dear Dr. Bambonye,

Thank you for your comments on our work.