Author Reply

W.Y. Teoh;[1] K.T. Ng[2]

1. Year 4 Medical Student, University of Liverpool, School of Medicine, Liverpool, United Kingdom
2. Medical Officer (Doctor), Department of Anaesthesiology, Faculty of Medicine, University of Malaya, Jalan Universiti, Kuala Lumpur, Malaysia

Correspondence:
W.Y. Teoh, Medical Student
University of Liverpool, School of Medicine
Cedar House, Ashton Street
Liverpool, L69 3GE, United Kingdom
E-mail: twy1063@hotmail.com

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To the Editor,
We thank Kumar and colleagues for their interests and comments on our article titled "The Effect of Prehospital Epinephrine in Out-of-Hospital Cardiac Arrest: A Systematic Review and Meta-Analysis."[1] They pointed out that three randomized controlled trials (RCTs)[2–4] were not included in our meta-analysis. Our meta-analysis examined prehospital use of epinephrine versus placebo in out-of-hospital cardiac arrest, regardless of different types of cardiac arrest rhythms, namely ventricular tachycardia, ventricular fibrillation, asystole, and pulseless electrical activity. Nordseth and colleagues[2] investigated the administration of epinephrine in patients with initial pulseless electrical activity only. This study was assessed as high-risk of bias due to significant heterogeneity in patient inclusion and protocol violation. Olasveengen and colleagues' trial[3] was not included as their study design and methodology were fundamentally different to our included trials, where the randomization method was based on international standard Advanced Cardiac Life Support with intravenous access and drug administration (epinephrine), or according to same guideline but without intravenous access or drug administration (epinephrine) after the decision of cardiopulmonary resuscitation was done. In addition, ambulance personnel were not blinded to randomization in this trial. We did not include the RCT performed by Woodhouse and colleagues[4] because it included in-hospital (56%) and out-of-hospital (44%) cardiac arrests in their randomization. No detail data were available for analysis among the in-hospital and out-of-hospital cardiac arrest groups. Furthermore, the etiology of cardiac arrest, duration of epinephrine administration, and access to specialized emergency care were different between in-hospital and out-of-hospital cardiac arrest. Thus, their findings cannot be generalized to patients with out-of-hospital cardiac arrest, which potentially skew the findings in our final meta-analysis. Due to different methodology and high-risk of bias among these three RCTs, we came to a consensus that including only the two high-quality, large RCTs of low-risk bias would provide the best certainty on the use of epinephrine in out-of-hospital cardiac arrest. The inclusion of the aforementioned three RCTs would introduce significant heterogeneity to our findings.

Yours sincerely,
Wan Yi Teoh
(On behalf of all authors)

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