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Letter to the Editor: "Association between metformin and survival outcomes in in-hospital cardiac arrest patients with diabetes"

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With great interest, we read the recently published article by Jin, et al. who conclude that administration of 500–1000 mg/day metformin resulted in a better survival to discharge rate than administration of other doses of metformin [1]. In addition, as the time interval from administration of metformin before intra-hospital cardiac arrest (IHCA) increased, the rate of survival to discharge showed a decreasing trend [1]. The patients who administered metformin within 6 h, the half- life of metformin [2], before IHCA and 6–12 h before IHCA had better survival rates than those who did not [1]. Plasma metformin concentration might be an important factor [1]. Although not measured in the study, we fully agree that plasma metformin concentration play a crucial role. We beg to differ as important confounder may perhaps alter the study' results.Regarding baseline data between survivors and non-survivors after an IHCA, 36.7% of survivors had received metformin whereas non-survivors were only 9.8% to receive metformin ($P < 0.001$) [1]. When reviewing also the two cohorts, we could see that survivors had no continuous renal replacement therapy (CRRT) [1]. On the contrary, almost 18% of non-survivors were on CRRT [1]. Because of its low molecular weight (165 Da) and minimal protein binding, metformin is equally (highly) eliminated by ultrafiltration (convection) and dialysis (diffusion) [2]. Furthermore, its large volume of distribution within a two-compartment pharmacokinetic model implies that metformin may be more effectively cleared by prolonged RRT [2]. This was corroborated by Keller et al., who showed a dramatic reduction of metabolic acidosis and plasma metformin concentrations within the first 24 h after initiating CRRT in patients with metformin-induced lactic acidosis (MALA), followed by normalization on the second day in all subjects [3]. It stand to reason that non-survivors had not only received less often metformin but that plasma metformin concentration in non-survivors was severely decreased by the use of CRRT [4] and that this could lead to much larger effect upon mortality in the group on CRRT.We believe that matching CRRT between the two group could lead to different results and perhaps different conclusions.

Author's contributions

PMH designed the paper.
PMH, SB,IB, EP participated in drafting and reviewing.
PMH,SB,IB, EP read and approved the final version of the manuscript.

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Consent for publication

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Declaration of Competing Interest

The authors declare to have no competing interests.

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Abbreviations: IHCA, intra-hospital cardiac arrest; CRRT, continuous renal replacement therapy; MALA, metformin-induced lactic acidosis.

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