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Reply:

We thank Tonelli et al. for their interest in our study showing improved renal recovery among patients treated with continuous renal replacement therapy (CRRT).[1]

As we described, ours was a non-randomized observational study. The 'issue of crossover' should not affect interpretation, even adopting a 'worst case scenario'. Crossovers were very few and occurred only among patients who had stabilized on CRRT from the indications precluding intermittent hemodialysis (IHD). Crossovers would be a concern in a randomized trial, among patients assigned to IHD but who required CRRT due to hemodynamic instability, and who would probably die without renal replacement.

Second, the risks of dialysis-dependence and death might be an appropriate composite outcome measure in a prospective randomized analysis. In our study, as we pointed out in the methods and discussion, CRRT was applied to patients who had sufficient hemodynamic instability, intracranial hypertension, or liver failure that made use of IHD impossible. The finding of any survivors among these CRRT patients supports the use of CRRT, making randomized evaluation unethical.

Third, most studies comparing CRRT and IHD have used mortality and renal recovery as separate outcome measures, rather than composites. Tonelli et al. have suggested that studies comparing modes of RRT should concentrate on renal recovery.[2] *No study has found hospital mortality 'due' to CRRT as implied by Tonelli.*

Fourth, although serum creatinine was higher at intensive care unit admission among IHD patients, careful examination of our tables shows that at the time of institution of RRT, and as we pointed out in our discussion, serum creatinine was similar between groups.

Fifth, we agree that meta-analysis has limitations. Although Tonelli failed to find a benefit from CRRT, Kellum showed lower mortality with CRRT when patients were stratified according to severity of illness.[2,3]

Sixth, CRRT has been shown to have specific advantages over IHD. CRRT minimizes hemodynamic fluctuation in unstable patients and prevents further elevation of intracranial pressure in patients with fulminant liver failure.[4] *CRRT is superior in correcting azotemia and acidosis and is recommended for patients with severe sepsis.*[5,6]

While we support Tonelli et al. in their advocacy of the least costly alternative, insistence on minimizing cost in the face of evidence of benefit represents an inappropriately regimented approach. Finally, we thank Tonelli et al. for helping us to stimulate and inform debate on the issue of renal replacement among the critically ill, along with our descriptive study.

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Sulfadiazine-induced methemoglobinemia in a boy with thalassemia

To the Editor:

Drug-induced methemoglobinemia has been well documented,[1–3] but an acute episode of sulfadiazine-induced arterial desaturation during emergence from anesthesia has never been reported. A three-year-old boy (14 kg, 90 cm) suffered scalding injury (55% of body surface area) and was scheduled for debridement. Family history was positive for a dominant ß-thalassemia trait. Physical examination revealed no

cardiac murmurs, abnormal breath sounds or cyanosis. Preoperative hemoglobin and hematocrit were 79 $g \cdot L^{-1}$ and 25%, respectively. Acetaminophen had been prescribed for analgesia. Routine induction and maintenance of anesthesia were performed with atropine, thiamylal, atracurium, sevoflurane and oxygen. At the end of surgery, silver sulfadiazine ointment (1%) was applied for wound dressing. During emergence from anesthesia, an acute onset of arterial desaturation was documented by pulse oximetry (SpO_2: 92%–96%). After excluding sputum impaction, lung collapse and malposition of endotracheal tube as possible causes, the patient was extubated. Upon arrival in the postanesthesia care unit, SpO_2 decreased to 63% and severe cyanosis was observed. The patient was re-intubated and SpO_2 increased to 86% in the presence of pure oxygen. An emergency chest x-ray revealed no remarkable findings, although the patient remained cyanotic. The blood gas analysis revealed a PaO_2 of 428 mmHg with an estimated saturation of 99.6%. However, the blood was dark chocolate in colour, and desaturated (SpO_2: 85%) as measured by the pulse oximeter. Both hypothermia and acidosis were excluded. An emergency co-oximetry analysis revealed a high methemoglobin concentration of 27.7%. After being treated with methylene blue (1.0 $mg \cdot kg^{-1}$, *iv*), the patient became acyanotic with SpO_2 of 99%. The fraction of methemoglobin decreased to 1% within an hour, and the patient was extubated the next morning.

Both congenital (e.g., sickle cell trait, α-thalassemia) and acquired (e.g., acetaminophen, sulfamethoxazole, nitrate, benzocaine) methemoglobinemias have been well documented.[1–3] However, it has not previously been reported that silver sulfadiazine ointment may cause methemoglobinemia. In this pediatric patient with an extensive burn injury, a large area of skin debridement might have provided a route for sulfadiazine into systemic circulation. In addition, ß-thalassemia trait or disease might have predisposed to methemoglobinemia due to less resistance to oxidative stress. The dramatic therapeutic effect of methylene blue excluded sulfhemoglobenemia in this patient.[4] In conclusion, anesthesiologists should be aware that silver sulfadiazine ointment may cause methemoglobinemia in association with coexisting burn injury and thalassemia.

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