An article by Bellomo and colleagues [1] in the previous issue of Critical Care challenges the current view that hyperoxia in the immediate post-resuscitation period increases cerebral damage in cardiac arrest victims. These findings are at least remarkable and apparently contradict recent post-resuscitation guidelines.

Patients who initially survive an out-of-hospital cardiac arrest and are admitted to the ICU have a dismal prognosis. Despite the recent introduction of moderate therapeutic hypothermia, mortality is still approximately 65% to 70% [2]. The beneficial effects of moderate hypothermia are partly explained by the mitigating effects on ischemia-reperfusion injury. Consequently, other measures that may attenuate ischemia-reperfusion injury have been suggested. This includes the prevention of post-resuscitation hyperoxia as the current evidence suggests that hyperoxia may worsen cerebral injury [3]. Animal experiments apparently confirm the detrimental effects of post-resuscitation hyperoxia on outcome. Hyperoxic reperfusion increases hippocampal neuronal death and induces behavioral deficits in a rat global cerebral ischemia model [4]. In a canine ventricular fibrillation cardiac arrest model, hyperoxic reperfusion decreased the activity of the hippocampal pyruvate dehydrogenase complex, possibly due to an increase in peroxynitrite levels [5] and impaired oxidative energy metabolism [6]. Finally, a clinically applicable protocol designed to reduce post-resuscitative hyperoxia in dogs by using oximetry and aiming for an oxygen saturation as measured by pulse oximetry (SpO2) of 95% significantly reduced the number of injured CA1 neurons and improved the neurological deficit score [7]. The British Thoracic Society recently recommended that the inspired oxygen concentration be targeted to an arterial oxygen saturation of 94% to 98% [8]. This is also advocated in the most recent guidelines from the European Resuscitation Council [9].

Why then did Bellomo and colleagues arrive at a different conclusion? In an elegant retrospective analysis, they included 12,108 patients resuscitated from non-traumatic cardiac arrest. Hyperoxia was defined as an arterial partial pressure of oxygen (PaO₂) of greater than 300 mm Hg in the first 24 hours after admission. Isolated hypoxemia was defined as a PaO₂ of less than 60 mm Hg. A total of 1,285 (10.6%) patients had hyperoxia and 1,168 (9.7%) had isolated hypoxemia. Mortality was higher in the hyperoxia group compared with the normoxia group (59% versus 47%) but not compared with hypoxemia patients. Patients with isolated hypoxemia had the lowest discharge home rate (19%). In a multivariate model, hyperoxia still had an odds ratio for hospital death of 1.2 (95% confidence interval of 1.1 to 1.6), but a Cox proportional hazards model combined with sensitivity analyses and time period matching showed no independent association between hyperoxia and in-hospital mortality. In
contrast, in most of the models, isolated hypoxemia remained an independent risk factor for hospital mortality.

So where does this information leave us? Clearly, post-resuscitation care is more than moderate hypothermia alone. Uncertainty still exists over the optimal blood pressure, the amount of cerebral blood flow, the hemoglobin level, the blood glucose regulation, and the partial pressure of arterial carbon dioxide (PaCO₂) and now also over the PaO₂. Although the evidence up to now clearly suggested a detrimental effect of post-resuscitation hyperoxia, the weight of the present study raises serious doubts. Clearly, fear of hyperoxia should not lead to an indiscriminate decrease in inspired oxygen level, as hypoxemia is certainly bad for the damaged brain. On the other hand, hyperoxia had no proven beneficial effects either. Therefore, there is no reason to revise the current guidelines targeting a post-resuscitation arterial oxygen saturation of 94% to 98%.

Abbreviations
ICU, intensive care unit; PaO₂, arterial partial pressure of oxygen.

Competing interests
The authors declare that they have no competing interests.

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