Letter to the editor: Ketamine-only versus isoflurane effects on murine cardiac function: comparison at similar depths of anesthesia?

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TO THE EDITOR: In a recent issue of the American Journal of Physiology-Heart and Circulatory Physiology, we have read with much interest the article by Pachon and coworkers (4), where the authors report that a high dose of ketamine alone demonstrated the least deviations from the conscious state in echocardiographic determination of left ventricular (LV) function, while at the same time providing an equal, surgical, depth of anesthesia as compared with the other tested anesthetic regimens. Such finding is surprising when one takes into account that almost all studies examining echocardiographic LV function analysis in mice employ the volatile isoflurane, because it can be easily titrated to the requested depth of anesthesia and its effect on cardiac output and hemodynamics is relatively mild (3, 5). With the consideration that murine LV function is one of the most frequently reported measurements in the field of cardiovascular (patho)physiology, the present recommendation to switch to the high-dose ketamine-only regimen may have a rather large impact.

The absence of the pedal withdrawal reflex is commonly used in animal experimentation as an index of depth of anesthesia (1). Pachon et al. (4) reported that all anesthetic regimens resulted in the absence of this pedal withdrawal reflex and that the 150 mg/kg ketamine induced a surgical level of anesthesia with optimal hemodynamics for LV echocardiography. In previous work we also observed that ketamine, although in combination with an α2-agonist (medetomidine), was indeed superior in relation to hemodynamic parameters as compared with other anesthetic regimens at a similar depth of anesthesia but that this came at the cost of medetomidine-induced metabolic disturbances (6). Medetomidine causes hyperglycemia and hypoinsulinemia (6). However, we had not tried ketamine alone in that work. We were therefore very much intrigued by the findings of Pachon et al. (4) that ketamine could also be used without an α2-agonist and still produce surgical anesthesia in the mice. Were that the case, high-dose ketamine could indeed become the anesthetic choice for mice. Therefore, to further explore the applicability of high-dose ketamine alone in obtaining surgical anesthesia, we also subjected male C57Bl/6J mice (n = 4) to ketamine (Nimatek, Eurovet Animal Health, Bathel, The Netherlands). We were unable to reach a surgical plane of anesthesia with 150-250 mg/kg ketamine 5–10 min after induction; also, additional boluses of 50 mg/kg did not result in the disappearance of the pedal withdrawal reflex. This finding is commensurate with much older literature (2) reporting that ketamine alone is insufficient to produce analgesia in mice. From this we conclude that, at least in our hands, high-dosage ketamine only was insufficient to obtain a similar depth of anesthesia as we previously observed with 1.5–2% isoflurane. Overall, we would like to warn against a general consensus that high-dose ketamine alone provides a surgical plane of anesthesia in mice.

DISCLOSURES
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AUTHOR CONTRIBUTIONS
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REFERENCES