For answering the question of Lagier et al. we had to reexamine our dataset, as this question had not been addressed in our study protocol. To begin, it was expected that the chosen randomization strategy should have done its work and that distribution of morning versus afternoon operation timing over the 3 treatment groups should be about equal. Indeed, analyzing the time of randomization in the intention-to-treat population, randomization being done just after induction of anesthesia as time of randomization in the intention-to-treat population, a circadian rhythm in the patients undergoing this operation was observed in randomization allocation in the daytime. Furthermore, to investigate whether for on-pump, low-risk isolated coronary artery bypass graft surgery patients are not confounded by an imbalance in randomization allocation in the daytime.

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We appreciate the interest of Lagier et al. in our article. The authors highlighted in their letter the work of Montaigne et al., who have recently published on the circadian rhythm in relation to ischemia reperfusion injury in a single-center retrospective propensity-matched cohort study addressing this subject on 596 (matched-pairs) patients undergoing aortic valve replacement with or without coronary artery bypass grafting, together with a single-center randomized study in 88 patients undergoing isolated aortic valve replacement, in which the perioperative myocardial injury has been assessed with the geometric mean of perioperative cardiac troponin T release. Together with these reported studies these authors also reported in the same article on an ex vivo analysis of the human myocardium that showed an intrinsic morning afternoon variation concomitant with a circadian variation of Rev-Erbα. An accompanying comment noticed that gene-expression analysis, mainly performed in rodents, had shown in the early 2000s a rhythmic expression of clock genes in the heart; whether or not clock genes modulate cell death directly and whether they affect ischemia reperfusion injury remained to be established, even after the publication of Montaigne.

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Furthermore, to investigate whether for on-pump, low-risk isolated coronary artery bypass graft (CABG) surgery, a circadian rhythm in the patients undergoing this operation might exist, we again reexamined our intention-to-treat