However, chronobiology should be applied also during the perioperative period. For instance, acute coronary syndrome occurs more frequently in the early morning, so beta-blockers or other rate-control drugs as well as nitrates and anti-arrhythmia drugs should be administered between 6 AM and 12 noon.⁶

The routine practice requires us to submit patients to cardiac surgery both during the morning and during the afternoon. After the study by Montaigne and colleagues,² many patients and surgeons wondered whether it was better to wait until the afternoon to undergo or to perform a cardiac operation, especially a high-risk operation. The study by Nemeth and colleagues⁵ provides us with the opportunity to tell a patient that the outcome of his or her intervention depends on many factors, but certainly not on the time of day he or she enters the operating room.

See Article page 56.

Check for updates

Commentary: Maybe timing isn't everything!

Derrick Y. Tam, MD, and
Stephen E. Fremes, MD, MSc

Commonly, in North America, operating rooms perform 2 cases of open-heart surgery a day, resulting in a morning case and an afternoon case. Not infrequently, when our patients are told that they will be the afternoon case (ie, the second case of the day), they may have concerns regarding the potential for surgeon fatigue on performance. Although we often simply reassure our patients that their outcome would be the same regardless of whether they went in the morning or in the afternoon, the impact of the timing of surgery on patient outcomes is not entirely clear and remains controversial. Interestingly, the controversy is only partly related to the surgeon and the team's ability to perform a

Stephen E. Fremes, MD, MSc, and Derrick Y. Tam, MD

CENTRAL MESSAGE

Outcomes in coronary bypass and aortic valve replacement surgery are similar regardless of morning or afternoon case.

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safe operation in the afternoon and potentially more related to the impact of the patient's circadian rhythm on reperfusion injury after cardiopulmonary bypass. In addition, recent work published in the *Journal* by Huard and colleagues¹ also showed that 24-hour coverage of the cardiac surgery intensive care unit led to better outcomes than intensive care units that were only managed by intensivists during the day (with residents and fellows covering in the evening). Thus, there may be several factors that impact

outcomes as it relates to the timing of the start of the surgery.

In the *Lancet*, Montaigne and colleagues² from Lille, France, showed an increase in major adverse cardiac events in a propensity score–matched cohort of 298 pairs of patients undergoing aortic valve replacement (AVR) in those undergoing morning surgery compared with afternoon surgery. The same study also randomized 88 patients undergoing isolated AVR to morning or afternoon surgery and found greater levels of troponin release in the morning group and, taken together, these findings suggest that perioperative myocardial injury maybe related to circadian rhythm and that afternoon surgery may be protective in patients undergoing isolated AVR. Conversely, no evidence of harm has been demonstrated in studies involving patients undergoing coronary artery bypass grafting. Indeed, a study of more than 18,000 patients from the Cleveland Clinic found that the start time of surgery had no impact on early outcomes following surgery.³

Nonetheless, the intriguing findings from this *Lancet* publication prompted further evaluation by other groups, leading to the study by Nemeth and colleagues⁴ published in this issue of the *Journal*. Using data gathered for the Society of Thoracic Surgeons Adult Cardiac Surgery Database from 11 cardiac surgical centers in the Columbia Heart-Source program, 3:1 propensity score matching was performed to create a population of patients undergoing morning (defined as cases starting between 06:30 and 09:00 AM) and afternoon (defined as cases starting between noon and 2:30 PM) surgery. For patients undergoing coronary artery bypass grafting (5830 AM and 1961 PM patients), there was no difference in operative mortality or morbidity (stroke, prolonged postoperative ventilation, renal failure, deep sternal wound infection, and reoperation). These findings were also replicated for the 1645 morning and 613 afternoon propensity score–matched patients undergoing isolated AVR. Importantly, authors controlled for the impact of institutional effects and surgeon related effects by including hospital and surgeon as independent random effects in sensitivities analyses using hierarchical modeling.

However, the current paper by Nemeth and colleagues⁴ must be interpreted in the context of some significant limitations, several of which have been discussed in the paper. Despite the use of propensity score matching on an

extensive list of variables, there remains the concerns of treatment allocation bias and unmeasured/unknown confounders, which may bias the results. The allocation of patients to morning or afternoon slots may be prioritized for several reasons that are not captured in the dataset. For example, at our institution, longer and more complicated cases are often scheduled in the morning so that the case finishes in the afternoon rather than the late evening. While overall, the groups were fairly well balanced after the match, ethnicity, in particular, the proportions of Hispanics patients, remained different between the groups in the AVR cohort. Although a subgroup analysis of only Hispanic patients showed no difference in outcome, we note that subgroup analyses may be underpowered to detect differences when event rates are low. Furthermore, this study lacked serum measurements of biomarkers associated with circadian homeostasis—such as cortisol secretion. In contrast to the paper by the French group, markers of myocardial injury were not included and would have been informative. In addition, this paper mainly focused on patient-related factors that may be associated with timing of surgery and postoperative outcomes; the impact of surgeon-related fatigue on performance was not assessed explicitly.

Despite these limitations, the authors are to be congratulated for conducting this important study. Although these findings are at odds with those recently published by the French group, the multicenter nature of this study along with the strong statistical methods employ suggest that these findings are robust and that the assignment of patients to either morning or afternoon surgery unlikely have an effect on the outcomes of our patients.

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