preoperative PH cases using iMil prior to CPB would facilitate separation from CPB. A total of 124 adult patients were studied, and all selected patients were undergoing elective high-risk cardiac surgery with baseline mean pulmonary artery (PA) pressure of greater than 30 mm Hg or a PA systolic pressure of greater than 40 mm Hg. The cases were randomized either to receive a single dose of 5 mg iMil or to receive a placebo. Data collection included detailed hemodynamic measurements and echocardiographic data.

The results showed that nebulized iMil resulted in a modest increase in cardiac output and reductions in PA systolic pressure; there was no difference in the incidence of their primary outcome (difficult or complex separation from CPB, probability of developing RV failure, or mortality); and administration of iMil increased stroke volume and atrial contractility, yet no change was observed in heart rate and systemic blood pressure. Logistic regression was used for analyzing data, and it was noted that a higher EuroSCORE (European System for Cardiac Operative Risk Evaluation) II and RV end-systolic area were predictive of developing RV failure (22% mortality). The authors of the study identified several reasons the hemodynamic improvements occurred without statistically significant improvements in outcomes. These included the small study size and the timing of iMil administration.

It was concluded that a single dose of pre-CPB iMil is not likely to influence downstream patient outcomes. Optimizing RV function requires a comprehensive approach, and medical management of pulmonary vascular resistance with inhaled PA vasodilators is only 1 such step. Optimizing RV preload, rate and rhythm, RV contractility, and nonpharmacologic maneuvers for reducing pulmonary vascular resistance are other related measures. Although the trial involves a cardiac surgery population with PH, the principles of appropriate fluid management, optimization of systemic hemodynamics and pulmonary function, and use of pulmonary vasodilators apply to other patients as well. From this study, it is clear that perioperative management of patients with PH and RV dysfunction depends on careful management of complex physiologic variables with multiple targets for therapeutic intervention. Use of prophylactic iMil showed the required changes in hemodynamics, but it did not impact the clinically important outcomes. The study is an important step in understanding the potential role of iMil in the management of patients with RV failure. Further studies are required in related areas such as timing of iMil administration, dose adjustment, and combination therapy.

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Comparison of Isoflurane and Sevoflurane in Cardiac Surgery: A Randomized Non-inferiority Comparative Effectiveness Trial

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Clinical studies, especially on anesthetic drugs, are generally focused on new kinds of drugs, expanding the indications of existing drugs, or devices that are newly introduced. One area that was ignored was comparative studies of same class or kind of drugs. Comparative effectiveness research is a recently developed field having the objective of comparing within-class drugs and devices that are commonly utilized. Volatile anesthetics were tested in animals and found to have cardioprotective properties. This class of anesthetics, when administered throughout cardiac surgery at a level of 0.5 to 2.0 minimum alveolar concentration, gave encouraging results in human beings. This technique resulted in less dependency on inotropic support, reduced damage to the myocardium, and lower mortality compared with total intravenous anesthesia. However, it was unknown whether the use of other volatile anesthetic agents would result in similar benefits. Isoflurane has been in use since 1979, whereas sevoflurane has been in use only since 1995. Sevoflurane is less soluble than isoflurane, which results in a faster induction and recovery. It is also less irritating to the airways and easier to breathe than isoflurane (less pungent). The authors note that it is often preferred by cardiac anesthesiologists, but that this may have to do with its frequent use in cardiac anesthesia research rather than any specific characteristics of the drug.

This RISCCS (Randomized Isoflurane and Sevoflurane Comparison in Cardiac Surgery) was aimed at determining whether these 2 inhalational agents are clinically similar in their effects on outcomes for patients undergoing cardiac surgery. This was a single-center, prospective, randomized clinical effectiveness trial looking at a group of heterogeneous adults undergoing cardiac surgery. A total 464 patients having coronary artery bypass graft and/or single-valve surgery between November 2011 and March 2014 were included in the trial. Barring the anesthesiologist and perfusionist, the entire medical team was blinded to group selection of patients. Sevoflurane was administered to 231 patients, and isoflurane to the remaining 233. Throughout the surgery, a minimum alveolar concentration of 0.5 to 2.0 of volatile anesthetic was maintained. The primary outcomes captured were composite intensive care unit (ICU) stay (2484 hours) and mortality (from any cause) within 30 days of the surgery. Secondary outcomes included cardiac troponin T measured 6 hours after ICU admission, hospital and ICU lengths of stay, duration of tracheal intubation, the onset of hemodialysis or atrial fibrillation, use of an inotrope or vasopressor for more than 12 hours, use of an intra-atrial balloon pump, peak postoperative serum creatinine, perioperative stroke, and readmission to the ICU. There was a pretrial assumption that sevoflurane would not be inferior (noninferiority margin = 10% based on an expected event rate of 25%).

On comparison, the primary outcome, a composite of prolonged ICU stay and 30-day all-cause mortality, was 30% for isoflurane and 25% for the sevoflurane group (absolute difference, −5.4%; 1-sided 95% confidence interval, 1.4). Thus, it was concluded that sevoflurane was neither inferior nor superior to isoflurane for the primary outcome ($P = 0.21$). These findings are of special significance for cardiac anesthesiologists, and they may choose either of the 2 anesthetics based on these clinical findings.

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