

## Myocardial Ischemia Revisited

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Does perioperative myocardial ischemia lead to postoperative myocardial infarction? By Stephen Slogoff and Arthur S. Keats. ANESTHESIOLOGY 1985; 62:107-14. Reprinted with permission.

To determine if a relationship exists between perioperative myocardial ischemia (ST segment depression greater than or equal to 0.1 mV) and postoperative myocardial infarction (PMI), nonparticipating observers recorded all electrocardiographic, hemodynamic, and other events between arrival of patients in the operating room and onset of cardiopulmonary bypass during 1,023 elective coronary artery bypass operations (CABG). The roles of preoperative patient characteristics, quality of the operation limited by disease as rated by the surgeon and duration of ischemic cardiac arrest as risk factors for PMI also were quantified. Electrocardiographic ischemia occurred in 36.9% of all patients, with almost half the episodes occurring before induction of anesthesia. PMI was almost three times as frequent in patients

with ischemia (6.9% vs. 2.5%) and was independent of when ischemia occurred. Ischemia was related significantly to tachycardia but not hypertension nor hypotension and was frequent in the absence of any hemodynamic abnormalities. The anesthesiologist whose patients had the highest rate of tachycardia and ischemia had the highest rate of PMI. Although neither single nor multiple preoperative patient characteristics related to PMI, suboptimal quality of operation and prolonged ischemic cardiac arrest increased the likelihood of PMI independent of the occurrence of myocardial ischemia. The authors conclude that perioperative myocardial ischemia is common in patients undergoing CABG, occurs randomly as well as in response to hemodynamic abnormalities, and is one of three independent risk factors the authors identified as related to PMI. PMI is unrelated to preoperative patient characteristics such as ejection fraction and left main coronary artery disease, and its frequency will relate primarily to perioperative management rather than patient selection.

DURING the 1970s, the explosive growth of coronary artery bypass operations (CABG) created a new subpopulation of “cardiac anesthesiologists” who rapidly relearned the basic physiology of the tectonboard depicting the determinants of myocardial oxygen supply and demand. A major responsibility in their new roles was to maintain the supply-demand balance. Their failure to do so would lead

to myocardial ischemia, presumed to be the precursor of myocardial infarction, just as angina was in the unanesthetized patient. High-dose opioid-based anesthesia was in vogue to preserve myocardial contractility and hemodynamic stability (epitomized by a “railroad track” anesthesia record). “Prevailing Wisdom” (which was then what evidence-based medicine is today) shunned the myocardial depression and hemodynamic instability of volatile anesthetics. To avoid myocardial depression,  $\beta$ -adrenergic blockers were withdrawn 2 weeks before operation. In addition to using opioid anesthesia, prevention of myocardial ischemia was accomplished by “optimizing hemodynamics” with intravenous vasodilators—usually nitroglycerine, with pressors such as dopamine and with the help of the pulmonary artery catheter, which was believed to be a more sensitive indicator of myocardial ischemia because wedge pressure often increased before electrocardiographic evidence of ischemia appeared.

Our anesthetic practices at the Texas Heart Institute (Houston, Texas) were generally contrarian to this Prevailing Wisdom. We used volatile anesthetics primarily, believing most patients requiring CABG at that time had normal or hyperdynamic ventricles. Because we were unable to demonstrate myocardial depression by propranolol in dogs<sup>1</sup> and did demonstrate the hazards of its

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Received from the Department of Anesthesiology, Stritch School of Medicine, Loyola University Chicago, Chicago, Illinois, and the Department of Cardiovascular Anesthesiology, Texas Heart Institute, Houston, Texas. Submitted for publication September 7, 2005. Accepted for publication October 25, 2005. Support was provided solely from institutional and/or departmental sources.

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preoperative withdrawal,<sup>2</sup> we did not discontinue  $\beta$ -adrenergic blockers before operation. At times, we even administered propranolol intravenously to treat intraoperative ischemia and more often to treat arrhythmias. In addition, our patients were denied the benefits, costs, and complications of pulmonary artery catheterization. Despite these contrarian practices, we believed our outcomes in terms of mortality and postoperative myocardial infarction (PMI) were as good or better than those published.

Against this background, reports appeared under the CASS acronym (Collaborative Study in Coronary Artery Surgery) originally designed to answer the ultimate question of the time. Did CABG actually improve cardiac morbidity and mortality compared with medical therapy or just relieve angina more effectively? Using data accumulated from 6,176 CABG patients in 15 participating institutions, an early CASS report<sup>3</sup> sought to identify predictors of mortality after CABG. They did identify six preoperative patient characteristics that significantly “predicted” mortality in their pooled patients. Mortality among the 15 institutions, however, ranged from 0.3 to 6.0%, and application of their “predictors” to single institutions poorly predicted actual mortality at each institution. Of special interest to us, CASS did not consider any aspect of intraoperative care as possibly contributing to mortality. Our bias was that much of our good results owed to the skill of our surgeons, the short perfusion time, and perhaps some as yet unidentified aspect of anesthetic care. Our study<sup>4</sup> was therefore originally created to ask whether surgical technique and anesthetic care in addition to preoperative patient characteristics contributed to outcome. Secondly, we asked whether the CASS predictors could be validated in our patients. Consequent to Prevailing Wisdom’s position on anesthesia care, we focused on hemodynamic stability and myocardial ischemia in data collection. As a single institution study, our patient numbers would be smaller than the CASS pool. We therefore selected a higher frequency event, PMI, as the surrogate for mortality. PMI accounted for almost half the mortality after CABG during those years.

In designing the study, we agonized over how to define hemodynamic abnormality. Prevailing Wisdom considered changes as small as 10–20% in blood pressure, heart rate, or both as a potential cause of myocardial ischemia. We sought, however, a more unequivocal definition. To that end, we queried a handful of well-known cardiac anesthesiologists as to extremes of heart rate and blood pressure that would define unequivocally for them “hemodynamic abnormality in CABG patients.” They concurred on “hypertension” as 180 mmHg or greater systolic, “hypotension” as 90 mmHg or less systolic, and tachycardia as 100 beats/min or greater.

During the period June 1, 1981, to May 30, 1982, data relating to the perioperative experiences of 1,023 patients undergoing elective CABG in our operating rooms were collected by two dedicated research nurses, Car-

olee Arlund and Juliette Dean. This represented 75% of all eligible patients during that period. In addition to the preoperative and postoperative data, these nurses attended all the operations from the time the patient arrived in the operating room until the onset of cardiopulmonary bypass. Every 2 min during those periods, they recorded heart rate, blood pressure, and an electrocardiographic strip of lead II and V5. They subsequently measured ST-segment displacement on every strip compared with the preoperative trace taken the day before and tabulated all data. It was a phenomenal effort by two remarkable women. On analyzing these data, we found that new myocardial ischemia, not present the day before, was apparent between arrival to the operating room and the start of cardiopulmonary bypass in 37% of all patients and was significantly related to PMI. In almost half of these patients, ischemia was present on arrival to the operating room even before induction of anesthesia. We found that tachycardia, but neither hypertension nor hypotension, was significantly associated with myocardial ischemia and that most tachycardia and ischemia were associated with tracheal intubation and surgical stimulation such as sternotomy. We found that one of the nine participating anesthesiologists (No. 7) experienced a significantly higher incidence of tachycardia, ischemia, and PMI. Further, our surgeons’ estimate of how good a technical repair they did (graded I–IV) was also a significant predictor of postoperative myocardial infarction. Finally, we found that postoperative myocardial infarction in our patients was not significantly related to any of the CASS predictors. Subsequent studies of mortality by others also could not duplicate the CASS findings.<sup>5,6</sup> It seemed to us that what went on in the operating room was more importantly predictive of PMI than the patients’ preoperative characteristics.

We were so struck by the newfound importance of surgical and anesthetic skills in outcome compared with the CASS predictors in our single institution data, we thought that it might be one explanation for the large variability in mortality among the CASS institutions and an explanation for the failure of their predictors when applied to individual institutions. We believed this was a first demonstration of the role of physician expertise in outcome. We therefore prepared a manuscript to say just that. Surgeons were divided into two groups, senior attending and cardiovascular surgical residents, and clear differences in outcome existed. The case for anesthesiologist No. 7 was self-evident. We submitted it to the *New England Journal of Medicine*. After almost 1 yr in review, the manuscript was rejected without critique. A phone inquiry to the editor netted “. . . [it] was common knowledge that good surgeons and anesthesiologists got good results and bad ones got bad results.” There was nothing new to publish! The subsequent report of Williams *et al.*<sup>7</sup> in 1991 did describe the role of the surgeon in the outcome of CABG.

Our manuscript was then recast with a different message but with no alteration in the data other than in their presentation and submitted to *ANESTHESIOLOGY* in the present form. The recasting of how the data were presented allowed us to speculate on the pervasiveness of myocardial ischemia and to discover silent myocardial ischemia in the operative setting, described a few years earlier by observant cardiologists who subsequently demonstrated the poor prognostic implications for acute coronary syndromes among their patients with silent ischemia.<sup>8</sup> It also explains in part the high frequency of myocardial ischemia among our patients.

This article was accompanied by an editorial entitled "Perianesthetic Ischemic Episodes Cause Myocardial Infarction in Humans: A Hypothesis Confirmed."<sup>9</sup> The editorialist could not have missed it more by claiming we had demonstrated a cause-effect relation between ischemia and infarction. We took great pains to avoid such a claim by emphasizing the randomness and high frequency of silent myocardial ischemia. We further emphasized the frequency of nonhemodynamically related ischemia, whereas the editorialist complained that had we looked harder, noted smaller changes, and correlated them with ischemia, we would have found many more relationships. There is no doubt that this is true and no doubt it would have obscured the real importance of tachycardia.

Now, 20 yr later, most of our observations remain true. Intraoperative electrocardiographic ischemia remains relatively common but rarely leads to PMI (at least Q-wave PMI). It is most frequent at the times we identified. Ischemia remains more related to tachycardia than hypertension or hypotension and occurs commonly in the absence of any hemodynamic change. PMI continues to be relatively unpredictable based on preoperative patient and disease characteristics. Bypass ischemia time and surgical quality directly relate to mortality, and "Surgeon Scorecards" are in vogue. The role of the anesthesiologist remains unclear, but physician selection and perioperative management continue to play a greater role in outcome than patient selection. This is implicit from the numerous studies confirming that greater procedure volume either by institution or by surgeon leads to lower postoperative mortality.<sup>10,11</sup> Finally, the value of  $\beta$ -adrenergic blockers in decreasing morbidity and mortality in surgical patients with coronary artery disease, independent of type of surgery, has become firmly established.<sup>12,13</sup>

That these observations remain largely true today is remarkable considering what has happened during these 20 yr. Most notable has been the dramatic change in the population undergoing CABG. Not only are patients older, but also many have had one or more previous stents, more have multivessel disease, and more have serious comorbid conditions such as diabetes, renal failure, or vascular disease. As the population has changed, the identity and weighting of perioperative risk factors

have changed. New, powerful drugs such as angiotensin-converting enzyme inhibitors, angiotensin II receptor antagonists, statins, and nonaspirin platelet inhibitors are now often maintenance therapy preoperatively.

Variations of the CABG operation have been devised. Transesophageal echocardiography has become commonly available in the operating room for diagnosis and monitoring. The contribution of transesophageal echocardiography as a monitor for myocardial ischemia during CABG operations has not yet been sufficiently defined. Despite all this progress, PMI and central nervous system injury remain the leading causes of postoperative mortality.

The portion of this manuscript that evoked the greatest interest was, Who was anesthesiologist No. 7? His identity, of course, is concealed even in the raw data. He was an American Board of Anesthesiology-certified anesthesiologist with a preference for succinylcholine to facilitate tracheal intubation. He therefore feared bradycardia on induction more than heart rates greater than 100 beats/min. Not all of his patients were sufficiently obtunded at the time of intubation, and these developed hypertension and tachycardia. Anesthesiologist No. 7 dramatically demonstrated the importance of preventing and treating tachycardia in the population with coronary artery disease. This fact was and still is the major contribution of the study to the practice of anesthesiology.

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