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EDITORIAL VIEWS

Perianesthetic Ischemic Episodes Cause Myocardial Infarction in Humans—A Hypothesis Confirmed

SINCE THE VERY EARLY DAYS of coronary artery surgery, many anesthetists have taken pains to attempt to avoid episodes of myocardial ischemia because of the fear that they would lead to myocardial necrosis. Dalton proposed the use of a precordial ECG lead to detect ST segment changes suggestive of ischemia for this purpose.[1] The popularity of the pulmonary artery catheter is based partially on the premise that it will help detect early ischemia. Despite widespread adoption of such measures, however, proof of a causal relationship between intraoperative ischemia and postoperative myocardial infarction (PMI) was not available.

Blood analyzed for CK-MB isoenzyme in the laboratory of C. R. Roe, M.D., provided the first highly suggestive data that anesthetic management might be an important determinant of myocardial injury in patients undergoing coronary artery bypass graft (CABG). Prebypass liberation of this enzyme, which occurs largely in cardiac muscle, ranged from 1 to 36% in three different institutions.[2-4] After changes in preoperative and intraoperative prebypass anesthetic management, the incidence of prebypass liberation decreased from 11 of 30 to 0 of 12 patients in one of those centers.*

Remarkably (to some), however, many individuals remained convinced that intraoperative ischemia was unrelated to myocardial infarction, arguing both that patients with coronary artery disease (CAD) frequently suffered episodes of angina pectoris (or silent ischemic episodes) but only rarely sustained a myocardial infarction and that the highest incidence of PMI in patients undergoing noncardiac surgery was on the third or fourth postoperative day and therefore unrelated to intraoperative events.

The present issue contains an important article by Slogoff and Keats addressing the question of whether myocardial ischemia prior to and during anesthesia causes PMI in patients undergoing coronary artery surgery.[5] Their findings inevitably will be applied to patients with CAD undergoing noncardiac surgery. The investigators followed 1,023 patients scheduled for elective myocardial revascularization from the time of arrival in the operating suite until discharge from the hospital or death occurred. Observers recorded the ECG, blood pressure, and heart rate every 2 min from arrival in the operating suite until cardiopulmonary bypass (CPB). Demographic predictive indicators of death derived from the collaborative Coronary Artery Surgery Study (CASS) were collected and an estimate of the technical efficacy of the operation obtained from the surgeon.

The data are striking: a threefold increase in PMI when ischemia was documented prior to bypass; an 11-fold difference in PMI among the patients managed by the nine anesthesiologists in the study; a high incidence of preanesthetic ischemia and of ischemia without "hemodynamic aberrations"; lack of correlation of PMI with CASS predictors but a predictive value of the surgeon's estimate of technical efficacy.

The study was methodologically impeccable in a number of ways. Unbiased observers collected the data. The statistical analysis of the data was correct. Criteria of PMI, ischemia, hypertension, hypotension, and tachycardia were determined prior to the study. The data

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* Roe CR: Personal communication.

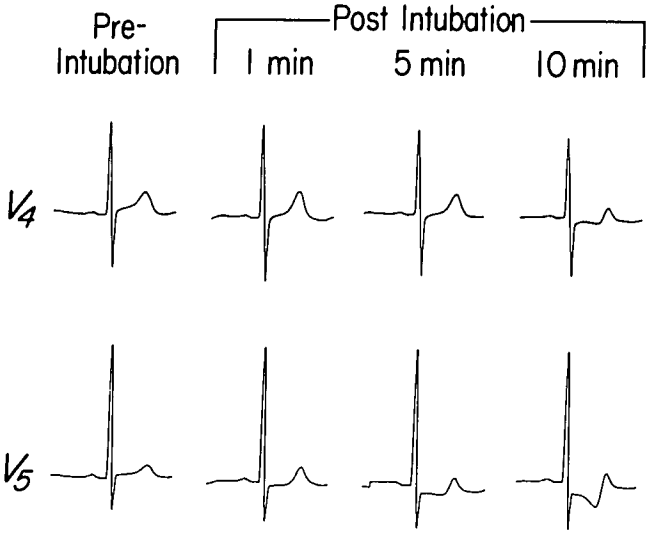

FIG. 1. Serial ECGs before and following endotracheal intubation in a patient who had undergone a thiopental, morphine–nitrous oxide anesthetic induction. During the entire period in which the ECGs indicated progressively worsening ischemia, the patient sustained only very minor changes in heart rate, systemic arterial pressure, cardiac output, pulmonary artery, pulmonary capillary wedge, and right atrial pressure, suggesting that the ischemia was due to a decreased coronary blood flow.

were collected in a single institution in a relatively short period of time, probably leading to reasonable uniformity of procedures.

In some other respects, however, we must question the methods and data. The first is the definition of myocardial infarction. This is a thorny problem because there is much controversy in the literature. One recent study, for instance, accepted *either* ECG changes or a maximum CK-MB of 40 U/l as sufficient to diagnose PMI.[6] In contrast, Slogoff and Keats required standard ECG criteria *plus* a CK-MB serum level of 80 U/l in a single blood sample drawn 10 h after CPB. Forty-two patients (4.1%) met these criteria and were considered to have sustained a myocardial infarction. Another four of 981 patients attained this level of CK-MB but were not considered to have PMI because they did not demonstrate characteristic ECG changes. We are not informed how many, if any, patients had a diagnostic ECG but did not attain a sufficiently high CK-MB to be included. Three patients who had persistent low output postoperatively leading to a central nervous system death, and an additional patient who died of prolonged postoperative circulatory failure, were not considered to have had an infarction. Many would question this conclusion, as they would the arbitrary choice of a level of 80 U/l CK-MB to indicate presence or absence of MI. While Slogoff and Keats contend that their criteria increase specificity and decrease false positives, this may, in fact, be misleading. An alternate interpretation is that use of such strict criteria leads to underestimation of the incidence of PMI and therefore minimizes the importance of the issue. It is likely that more individuals suffered myocardial necrosis than is apparent when the criteria of Slogoff and Keats are used.

A second major issue concerns the criteria employed to define "hemodynamic aberration." Approximately 60% of the ischemia was considered by Slogoff and Keats to have occurred in the absence of hemodynamic abnormality. The greatest drawback of the definitions used by the authors is that they lead to the conclusion that ischemia occurred very often in the absence of hemodynamic abnormalities. However, major adverse hemodynamic changes may occur within the range they specified as normal. It is thus likely that the proportion of ischemia secondary to adverse hemodynamic change was greater than the incidence reported in this study and that ischemia occurred in the absence of such changes less frequently. The reference cited (Deanfield *et al.*[7]) is one of many by Maseri's group, which unequivocally establishes the importance of decrease in coronary blood supply on the basis of coronary artery spasm as a factor in the causation of myocardial ischemia. These authors continuously monitored heart rate and noted that many episodes of angina pectoris and silent myocardial ischemia were associated with heart rate changes of less than 10 beats/min. Certainly this does indeed happen (fig. 1). However, the information presented by Slogoff and Keats does not allow us to derive a true incidence in this setting.

The necessity of achieving a heart rate of 100 beats/min to be classified as having a hemodynamic aberration seems particularly severe. Small increases in heart rate during anesthesia predictably are associated with characteristic ECG changes of ischemia in many patients with CAD. Using the classic definition of tachycardia to define a "hemodynamic aberration" in this population seems inappropriate at worst and less than optimal at best. Particularly in beta-adrenergically blocked patients, even an increase of 40–50 beats/min often will fail to achieve a rate of 100 beats/min. The data of Slogoff and Keats certainly should not be interpreted to consider such changes benign.

In a similar manner, a systolic pressure of 90 mmHg may well be too high a value to be used correctly as the threshold for hypotension. In a previous study[8] employing ECG mapping, we noted ischemic changes only when systolic pressure declined below 70 mmHg during the periinduction phase of a thiopental, halothane–nitrous oxide, pancuronium anesthetic similar to that utilized by Slogoff and Keats. Experimental work in the dog with a narrowed coronary artery indicates that perfusion pressure lower than that necessary to maintain

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blood flow across a coronary stenosis leads to ischemia.[9] However, the absolute pressure necessary to cause this is quite unpredictable. It may be higher or lower, depending upon the geometric characteristics of the constriction.[10] Thus, it seems premature to dismiss hypotension as a potential cause of ischemia on the basis of the present study. Indeed, it seems worthwhile to recall that hypotension was associated with recurrent PMI as early as 1970.[11] By arbitrarily defining hypotension as 90 mmHg, it appears inevitable that many individuals not at great risk for sustaining ischemia *at that pressure* (when heart rate is maintained at a low rate) will be included and that this will weaken or hide any relationship that exists.

The observation that more than 20% of patients arrived in the operating room with new ischemic ECG changes is important. One is forced to question, however, whether this unexpectedly high incidence of ischemia upon arrival reflects some aspect of the premedication–preanesthetic regimen used in the authors' institution. The differing incidences of cardiovascular changes and myocardial ischemia in two institutions during insertion of pulmonary artery catheters are relevant here. At Utah, Lunn and associates reported significant increases in heart rate and blood pressure leading to a sufficiently high incidence of ischemia in patients not receiving propranolol to cause them to recommend insertion after induction of anesthesia.[12] At Emory, hemodynamic changes were not observed, and the opposite conclusion was reached.[13] We observed no instances of ST segment depression or elevation during insertion of pulmonary artery catheters in any of 46 well-sedated patients undergoing precordial 18 lead ECG mapping.[14] Clearly, a multitude of factors are involved in such disparate findings. Therefore, it is important that others now document the incidence of preanesthetic ischemia to confirm or refute that the Slogoff and Keats experience is typical and determine whether or not such a high incidence of ischemia is unavoidable and due to the nature of the disease. In contrast, if some aspect of preanesthetic management can avoid this, it is crucial that all physicians caring for these patients learn it, since preanesthetic ischemia appears potentially as important as intraanesthetic in the causation of PMI.

A major question raised by this study is whether the coronary artery surgical patient is an appropriate model for studying anesthesia-associated PMI. There are a number of advantages: since numerous such operations are performed, many subjects for study are available; all have severe, anatomically defined CAD; and hemodynamic, ECG, and enzyme monitoring are accepted as standards of care. However, serious disadvantages also exist. The incidence of myocardial damage probably is minimized by the short duration of the period at risk, *i.e.*, the prebypass period. It takes a finite time without blood flow to cause irreversible myocardial damage. The interval between induction of anesthesia and onset of CPB conceivably might be less than this threshold time. One wonders if this phenomenon minimized the incidence of PMI in the environment of the Texas Heart Institute, with its world-renowned efficiency. We are not informed of the duration of the interval between induction and CPB, so we cannot judge. If the incidence of patients "at risk" is minimized by this factor, however, it is quite possible that similar hemodynamic conditions maintained for a longer period of time might increase the incidence of ischemia and infarction. While this consideration presents a potential problem for anesthetists (and patients) at less expeditious cardiac surgical centers, it appears even more crucial for patients with CAD undergoing noncardiac surgery, since their hearts are not "revascularized," and they must confront the entire intraoperative and postoperative periods with their physiological and coronary vascular hydraulic status unchanged. One wonders whether the data of Rao and El Etr would have been as impressive if they had attempted only to keep the systolic BP between 90 and 180 mmHg and the heart rate below 100 beats/min![15]

On the other hand, coronary bypass may increase the incidence of myocardial infarction in several ways. One is by technical misadventure (avoidable or unavoidable). A second is by inadequate myocardial preservation during the period of interruption of coronary blood flow. It is possible that under these circumstances, when energy stores have been depleted by prebypass ischemia, maximal suppression of oxygen demand by optimal cardioplegia may determine whether or not a jeopardized area of myocardium survives. Slogoff and Keats' data indicate that ischemia time is an independent variable that partially may reflect this. Unfortunately, studying the effect of anesthesia upon patients undergoing CPB with an obligatory period of myocardial ischemia is of necessity impure and emphasizes the importance of establishing the relationship between intraoperative myocardial ischemia and PMI in the absence of this confounding variable.

In his recent Rovenstine Lecture, Dr. Keats quite correctly described the relative paucity of outcome studies in anesthesiology.[16] Slogoff and Keats have presented us with an outstanding outcome study that clearly demonstrates just how necessary such investigations are. The reservations expressed above should not be interpreted to distract from the messages that come through loud and clear. First, that myocardial ischemia is a precursor to myocardial necrosis in humans. For those (hopefully few) remaining anesthesiologists who still subscribe to the opinion that intraoperative myocardial ischemia does not entail dire consequences, the infor-

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mation provided should be more than sufficient to change their minds. Second, the study emphasizes how important detection of ischemia is and should add impetus to the search for more sensitive, specific, and easily employed methods for perioperative detection of myocardial ischemia.[17] Lastly, the study demonstrates that an anesthetist working in the same environment and using the same drugs as another can be associated with myocardial infarction more than ten times as frequently as his colleague in an adjacent operating room. This knowledge should lead every anesthetist to document the incidence of ischemia in the patients under his care and to take active measures to minimize the incidence whenever it is found to be excessive.

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References

1. Dalton BC: A precordial ECG lead for chest operations. Anesth Analg 55:740–741, 1976
2. Lell WA, Walker DR, Blackstone EH, Kouchoukos NT, Allarde R, Roe CR: Evaluation of myocardial damage in patients undergoing coronary artery bypass procedures with halothane–N_2O anesthesia and adjuvants. Anesth Analg 56:556–563, 1977
3. Isom OW, Spencer FC, Feigenbaum H, Cunningham J, Roe C: Prebypass myocardial damage in patients undergoing coronary revascularization; an unrecognized vulnerable period. Circulation 52 (Suppl) II-119, 1975
4. Oldham HN Jr, Roe CR, Young WG Jr, Dixon SH Jr: Intraoperative detection of myocardial damage during coronary artery surgery by plasma creatine phosphokinase isoenzyme analysis. Surgery 74:917–924, 1973
5. Slogoff S, Keats AS: Does perioperative myocardial ischemia lead to postoperative myocardial infarction? ANESTHESIOLOGY 62:000–000, 1981
6. Akins CW: Noncardioplegic myocardial preservation for coronary revascularization. J Thorac Cardiovasc Surg 88:174–181, 1984
7. Deanfield JE, Selwyn AP, Chierchia S, Maseri A, Ribiero P, Krikler S, Morgan M: Myocardial ischaemia during daily life in patients with stable angina: its relation to symptoms and heart rate changes. Lancet 2:753–758, 1983
8. Thomson IR, Emerson CW, Lytle B, Ohtaka M, Levine FH, Lappas DG, Buckley MJ, Lowenstein E: Rapid serial 18 precordial lead ST-segment mapping during anesthetic induction for coronary artery surgery. Clin Res 26:275A, 1978
9. Francis CM, Foex P, Lowenstein E, Glazebrook CW, Davies WL, Ryder WA, Jones LA: The interaction between regional myocardial ischaemia and left ventricular performance under halothane anesthesia. Br J Anaesth 34:965–979, 1982
10. Feldman RL, Nichols WW, Pepine CJ, Conetta DA, Conti CR: The coronary hemodynamics of left main and branch coronary stenoses. J Thorac Cardiovasc Surg 77:377–388, 1970
11. Mauney FM, Jr, Ebert PA, Sabiston DC Jr: Postoperative myocardial infarction: A study of predisposing factors, diagnosis, and mortality in a high risk group of surgical patients. Ann Surg 172:497–503, 1970
12. Lunn JK, Stanley JH, Webster LR, Bidwai AV: Arterial blood-pressure and pulse-rate responses to pulmonary and radial arterial catheterization prior to cardiac and major vascular operations. ANESTHESIOLOGY 51:265–269, 1979
13. Waller JL, Zaidan JR, Kaplan JA, Bauman DI: Hemodynamic responses to preoperative vascular cannulation in patients with coronary artery disease. ANESTHESIOLOGY 56:219–221, 1982
14. Thomson IR, Dalton BC, Lappas DG, Lowenstein E: Right bundle-branch block and complete heart block caused by the Swan-Ganz catheter. ANESTHESIOLOGY 51:359–362, 1979
15. Rao TLK, Jacobs KH, El-Etr AA: Reinfarction following anesthesia in patients with myocardial infarction. ANESTHESIOLOGY 58:499–505, 1983
16. Keats AS: The Rovenstine Lecture, 1983: Cardiovascular anesthesia: Perceptions and perspectives. ANESTHESIOLOGY 60:467–474, 1984
17. Bellows WH, Bode RH Jr, Levy JH, Foex P, Lowenstein E: Noninvasive detection of periinduction ischemic ventricular dysfunction by cardiokymography in man: Preliminary experience. ANESTHESIOLOGY 60:155–158, 1984

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