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Does Anesthetic Technique Make a Difference? Augmentation of Systolic Blood Pressure during Carotid Endarterectomy: Effects of Phenylephrine Versus *Light Anesthesia and of Isoflurane* Versus *Halothane on the Incidence of Myocardial Ischemia*

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Whether anesthetic technique affected the incidence of myocardial ischemia in 60 patients undergoing carotid endarterectomy was investigated. The patients were randomly assigned to receive halothane or isoflurane (with nitrous oxide) either at a low concentration alone or at a higher concentration with phenylephrine added to support blood pressure. Blood pressure was maintained within 20% of each patient's average ward systolic pressure. Seven leads of electrocardiograms (ECG) and echocardiograms were analyzed for segmental wall motion. The echocardiograms were analyzed using standard formulae for end-systolic meridional wall stress (SWS) and rate-corrected velocity of fiber shortening (Vcfc). Because of the nature of these calculations, only echocardiograms with normal regional wall motion could be accurately analyzed. The patients had postoperative ECG and creatinine phosphokinase (CPK) isoenzyme determinations and regularly scheduled clinical examinations to detect perioperative myocardial infarction and neurologic deficits. Although blood pressures were similar, the patients who received a higher concentration of anesthetic plus phenylephrine had a higher wall stress, regardless of the choice of anesthetic agent. All four techniques allowed provision of the same stump pressures (the marker surgeons used for adequacy of collateral carotid flow). No difference could be found in wall stress or incidence of myocardial ischemia between isoflurane and halothane. The patients who received phenylephrine had a threefold greater incidence of myocardial ischemia than did the patients who had light anesthesia to maintain similar systolic blood pressures and stump pressures. The groups were demographically and hemodynamically similar; in particular, the heart rates were not different. Increased wall stress in anesthetized patients is associated with an increased incidence of myocardial ischemia as evidenced by new segmental wall motion and wall thickening abnormalities (SWMA). (Key words: Anesthetics, volatile: halothane; isoflurane. Heart: ischemia. Monitoring: echocardiography. Surgery, vascular: carotid thromboendarterectomy. Sympathetic nervous system: phenylephrine.)

BECAUSE atherosclerosis is a systemic disorder, most patients requiring carotid endarterectomy also have coronary artery disease.[1–3] Myocardial ischemia and infarction are the most frequent causes of perioperative morbidity during or following peripheral vascular surgery.[4–7] These patients challenge the anesthesiologist to maintain adequate cerebral perfusion without causing myocardial ischemia during carotid endarterectomy. Many techniques have been advocated to determine adequacy of cerebral perfusion during temporary carotid artery occlusion, but none has been shown to affect outcome.[8–11] Measurement of the arterial pressure distal to the occluded common carotid artery (stump pressure) is believed to provide one measure of cerebral perfusion.[12] Because the stump pressure can be increased by elevating systemic blood pressure, our surgeons prefer that systemic pressure be maintained at the upper limits of the patient's normal range. This can be achieved either by administering phenylephrine or by deliberately maintaining light levels of general anesthesia.[13] Although both techniques were commonly used in our practice, we could not reach a consensus on the one more effective in maintaining stump pressure or resulting in a lower incidence of myocardial ischemia. The effects on myocardial oxygen supply and demand of the two techniques were unknown. With the development of transesophageal echocardiography, we can better detect myocardial ischemia and analyze the determinants of myocardial oxygen demand.[14–21] Therefore, we con-

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ducted this prospective randomized trial to determine if choice of anesthetic technique (deep anesthesia and phenylephrine *vs.* light anesthesia) or anesthetic agent (isoflurane *vs.* halothane) affects the incidence of myocardial ischemia.

Materials and Methods

With approval from our committee on human experimentation and informed consent from each patient, we studied 60 patients scheduled for elective carotid endarterectomy. All patients were treated so as to maintain systolic blood pressure within 20% of their mean systolic pressure (MSABP) defined as the mean of the values obtained by nurses during the first 24 h after hospital admission. Inhalation agents were administered in a 50% nitrous oxide and oxygen mixture. The patients were randomly assigned (by random numbers table) to one of four groups: sufficient isoflurane to maintain anesthesia yet just enough to maintain MSABP (group 1); approximately 1.4 MAC¶¶ isoflurane and an infusion of phenylephrine to maintain MSABP (group 2); sufficient halothane to maintain anesthesia yet just enough to maintain MSABP (group 3); and approximately 1.4 MAC halothane plus phenylephrine to maintain MSABP (group 4). (MAC values include the 0.55 MAC contribution of 50% N_2O assumed for this age group of patients.)

All patients were given their usual cardiac medications the morning of surgery. Prior to arrival in the operating room, a radial arterial catheter was inserted in each patient using local anesthesia. After the patient was positioned on the operating table, a conventional electrocardiographic system using leads I, II, III, avR, avL, avF, and V5 was attached (Marquette), standardized to 10 mm/mV, and a baseline ECG was recorded. Following preoxygenation and iv administration of 3 mg of *d*-tubocurare, anesthesia was induced with thiopental (1–2 mg/kg) and increasing inspired concentrations of the inhalational agent. Five to ten minutes after the start of induction, following administration of succinylcholine, the trachea was sprayed with 4 ml of 4% lidocaine solution and then intubated. Electrocardiograms were recorded at three minute intervals throughout the period of anesthetic induction and endotracheal intubation. The patients' lungs were mechanically ventilated with a rate (8–10 breaths/min) and tidal volume (10–12 ml/kg) adjusted to maintain normocapnia. End-tidal concentrations of isoflurane, halothane, nitrous oxide, and carbon dioxide were determined by mass spectrometry. Once the endotracheal tube was secured in place, a 9-mm (diameter) gastroscope tipped with a 3.5 MHz phased array ultrasonic transducer (Diasonics Inc., Milpitas, California) was inserted into the esophagus and positioned behind the heart to obtain a cross-sectional view of the left ventricle at the level of the papillary muscles. The transducer was connected to an ultrasonograph (Diasonics 3400R or CV-60) focused to 10 or 15 cm. After transducer insertion (routinely requiring 15–30 s), we recorded the echocardiographic images for 60 s on ½ inch VHS videotape while hemodynamic measurements and electrocardiographic recordings were obtained. All measurements were repeated immediately prior to cross-clamping the carotid artery, after the cross clamp was applied, after unclamping, and at skin closure. Carotid artery stump pressure (the mean, or if a phasic pressure is present, the diastolic pressure, distal to common and external carotid occlusion[12]) was measured after occlusion of the carotid artery using a 22-G needle connected to a Gould Statham transducer referenced to the base of the skull. The systolic blood pressure of all patients was maintained within 20% of mean systolic pressure at all times. However, such pressures were kept as close to their mean value as possible during carotid occlusion but allowed to drift toward the bottom of the 20% range at all other times.

Echocardiographic and electrocardiographic data were not analyzed until after surgery was completed. The anesthesiologist managing the patient's anesthetic course used only standard techniques including pressure and electrocardiographic leads MCL5 (modified chest lead V5) and II to guide therapy.

Data Analysis

The ECG were analyzed by an observer who was unaware of any patient's treatment group or clinical course. Conventional criteria were used to diagnose ischemia: 1 mm or more of horizontal or downsloping ST segment depression or greater than 1 mm of ST segment elevation, 80 ms after the J point, as compared with the preoperative electrocardiogram.[22–24] The echocardiograms were analyzed for the development of new systolic wall motion and thickening abnormalities (SWMA) using our previously described system.[14] Briefly, the cross-sectional image was divided into quadrants using the papillary muscles as guides. This floating reference system keyed to the papillary muscles compensated for translational and rotational movements of the heart. The first recorded echocardiogram was used as a baseline. Subsequent changes in SWM were determined by two independent observers unaware of the patient's clinical course or the treatment group. Any discrepancy between observers was arbitrated by a third, the director of our echocardiographic laboratory (NBS). The echocardiograms were also analyzed using a semi-automated light pen system (Diasonics Inc.) by a

¶¶ MAC is the age adjusted concentration of anesthetic agent. A one MAC dose is that end-tidal concentration preventing movement in 50% of patients at time of skin incision.

TABLE 1. Hemodynamic Data on the Ward

	Group 1 Isoflurane	Group 2 Isoflurane + Phenylephrine	Group 3 Halothane	Group 4 Halothane + Phenylephrine
N	16	14	15	15
Age	70 ± 2	70 ± 2	65 ± 3	66 ± 3
Male	10	6	12	10
Female	6	8	3	5
Heart rate (beats/min)	73 ± 2	74 ± 3	69 ± 3	74 ± 2
Systolic blood pressure (mmHg)	144 ± 6	142 ± 6	135 ± 4	141 ± 4
Diastolic blood pressure (mmHg)	79 ± 3	76 ± 3	75 ± 2	80 ± 2
Patients taking beta adrenergic blocking drugs	5	4	5	4
Patients with angina	10	7	9	8
Patients with prior myocardial infarction	7	5	4	5

The data are presented as mean ± SEM. The values for heart rate and blood pressure are the mean of at least four values recorded on the ward as described in the text. There were no significant differences between the groups in any of these variables. Patients in all groups also breathed 50% nitrous oxide.

technician unaware of the patient's treatment group. After the system had been orthogonally calibrated for each patient, tracings of the left ventricular short-axis endocardium and epicardium at end-systole were digitized to obtain the following: the total area (At) enclosed by the left ventricular epicardium and the right side of the septum; the cavitary area (Ac) with the papillary muscles included; and the endocardial circumference at end-systole (LVESC) and at end-diastole (LVEDC). The mean of three consecutive beats obtained at end-expiration was used. Using a modification of the method of St. John Sutton,[25] left ventricular end-systolic wall stress (SWS) was determined as follows:

$$SWS = (1.33 * P * Ac)/(A_t - A_c)$$

where SWS is in grams per square centimeter, P is systolic blood pressure in millimeters of mercury, Ac and At are in square centimeters, and 1.33 is a factor to convert millimeters of mercury to grams per square centimeter. Left ventricular ejection time (LVET) was determined as the number of frames (one every 33 ms) from end-diastole to end-systole. Ventricular end-diastole was identified by the peak of the R wave and end-systole by the minimal left ventricular dimension. The rate-corrected velocity of fiber shortening (Vcfc) was calculated as:

$$Vcfc = (LVEDC - LVESC)/(LVEDC * LVET) * (RR)^{1/2}$$

where RR equals the interval between cardiac cycles.[26] Patients with segmental wall motion and thickening abnormalities (SWMA) were not used in the analysis of SWS or Vcfc because of the geometrical assumptions implicit in their determinations.[27]

All patients had an ECG in the recovery room and another the morning following surgery as well as one set of CPK isoenzymes. The routine CPK isoenzymes set was drawn one hour after the patient's arrival in the recovery room. In addition, patients were questioned about symptoms of chest pain, shortness of breath, and neurologic symptoms on postoperative days 1 and 3. Any suggestion of myocardial ischemic pain or symptoms caused the additional drawing of blood for CPK isoenzyme levels; any suggestion of new neurologic symptoms called forth a full additional neurologic examination. Statistical tests included analysis of variance, followed by Fisher's progressive least squares difference test, analysis of covariance, and chi-square test with Bonferroni correction. A probability (P) less than 0.05 was considered significant.[28]

Results

The groups were demographically similar (table 1). All patients had hemodynamically significant carotid arterial disease with at least one prior transient ischemic attack (TIA). There was no difference among groups in age, sex, blood pressure, medications, or incidence of angina and myocardial infarction preoperatively.

The means of all patients' heart rates and blood pressures were similar among groups upon their arrival in the operating room, but systolic blood pressure was significantly greater than on the ward (table 2). The blood pressures measured on the ward were taken by oscillometry; those in the operating room, by transducing radial arterial pressure. Performance of oscillometry in the operating room verified that the transduced systolic blood pressure was never more than 5 mmHg different than oscillometrically measured pressure upon arrival in the operating room. At the time of temporary carotid occlusion (clamping), blood pressure was similar among groups to that recorded preoperatively. Heart rate, stump pressure, carotid occlusion time, and the number of patients who had carotid arterial shunts did not differ among the groups (table 3). When the end-tidal concentration of volatile

TABLE 2. Hemodynamic Data upon Arrival in the Operating Room

	Group 1 Isoflurane	Group 2 Isoflurane + Phenylephrine	Group 3 Halothane	Group 4 Halothane + Phenylephrine
Heart rate (beats/min)	78 ± 4	72 ± 3	73 ± 3	73 ± 3
Systolic blood pressure (mmHg)*	163 ± 5	169 ± 7	163 ± 6	158 ± 8
Diastolic blood pressure (mmHg)	78 ± 4	78 ± 5	73 ± 3	68 ± 4

The data are presented as mean ± SEM. These data were collected upon arrival in the operating room.

* $P < 0.05$ from the mean ward value.

anesthetic was converted to MAC equivalents, the patients in the light anesthesia groups, 1 and 3 (1.04 and 1.01 MAC, respectively), had significantly lower levels of anesthetic administered than those in deep anesthesia and phenylephrine groups, 2 and 4 (1.43 and 1.48 MAC). The target concentration of anesthetic was reached and maintained during the time leading up to carotid dissection, and in patients in groups 2 and 4 phenylephrine was administered by infusion to maintain blood pressure. By the time of complete insertion of the echocardiographic transducer and the first measurement period, 11 of 29 patients in groups 2 and 4 (38%) were receiving phenylephrine, 22 of 29 (76%) were receiving phenylephrine at time of skin incision, and all were receiving phenylephrine at the time of carotid occlusion.

No patient had electrocardiographic evidence of myocardial ischemia upon arrival in the operating room. Six patients had either left bundle branch block (LBBB) or a ventricularly paced rhythm, and, consequently, their ECG could not be analyzed for the presence of ischemic change. Four patients demonstrated ECG changes during surgery: one patient in groups 2 and 3, and two patients in group 4. In one patient (group 4) the ST segment depression persisted until the time of skin closure. All patients who demonstrated ECG changes had concurrent new SWMA.

The incidence of myocardial ischemia in patients did not differ between the two anesthetic agent groups. Seven of 30 patients who received isoflurane, and 11 of 30 patients who received halothane had evidence of myocardial ischemia intraoperatively ($P \geq 0.3$; table 3). It would require study of approximately 240 patients for such a difference to become significant (at the $P \leq 0.05$ level) if trends continued.

The incidence of myocardial ischemia in patients did differ depending on the technique used to maintain MSABP. Patients who received an infusion of phenylephrine had a 275% greater chance of experiencing myocardial ischemia than those in whom the same MSABP and stump pressure were maintained without phenylephrine.

Thirteen of the 29 patients who received phenylephrine and five of the 31 patients who did not developed new wall motion changes and abnormal wall thickening presumed secondary to myocardial ischemia ($P < 0.05$) (tables 3 and 4). Five of the patients receiving phenylephrine demonstrated new SWMA after skin incision, 11 by the time of initiation of temporary carotid occlusion, and two additional patients developed SWMA by the time carotid flow was restored. These wall motion and thickening abnormalities had reverted to baseline by the time of skin closure in all but three patients.

TABLE 3. Hemodynamic Data at the Time of Carotid Occlusion

	Group 1 Isoflurane	Group 2 Isoflurane + Phenylephrine	Group 3 Halothane	Group 4 Halothane + Phenylephrine
Heart rate (beats/min)	76 ± 2	73 ± 3	69 ± 4	72 ± 3
Systolic blood pressure (mmHg)	142 ± 6	150 ± 6	135 ± 5	143 ± 5
Diastolic blood pressure (mmHg)	69 ± 4	75 ± 3	71 ± 2	71 ± 2
Stump pressure (mmHg)	54 ± 7	59 ± 7	56 ± 6	49 ± 6
Carotid occlusion time (min)	25 ± 2	21 ± 2	21 ± 1	24 ± 2
MAC multiple (including N_2O)	1.04 ± .03	1.43 ± .03*	1.01 ± .05	1.48 ± .05†
SWS (g/cm^2)	91.6 ± 11.1	128.8 ± 12.7*	95.9 ± 6.4	134.7 ± 14.4†
Vcfc	0.956 ± .070	0.675 ± .079*	0.722 ± .051*	0.464 ± .046‡
Patients with new SWMA	2	5	3	8

Data are presented as mean ± SEM. These data were collected immediately prior to carotid cross-clamping. The determinations of SWS and Vcfc were made only on those patients without SWMA. When the incidence of new SWMA is compared between patients who received phenylephrine and those who did not, the difference is statistically significant ($P < 0.05$ by chi-square).

SWS = left ventricular end-systolic wall stress; Vcfc = rate-corrected velocity of circumferencial fiber shortening; SWMA = segmental wall motion and wall thickening abnormalities.

* $P < 0.01$ compared with group 1.

† $P < 0.01$ compared with group 3.

‡ $P < 0.01$ compared with group 2.

TABLE 4. Incidence of Myocardial Ischemia with and Without Phenylephrine

	Deep Anesthesia and Phenylephrine	Light Anesthesia
New segmental wall motion and thickening abnormality present	13*	5*
No new segmental wall motion or thickening abnormalities present	16	26

* Significantly different at the $P \leq 0.05$.

No patient suffered a perioperative myocardial infarction. No patient had an elevation of CPK isoenzymes reflecting myocardial cell damage into an abnormal range. One patient awoke from surgery with a new neurologic deficit; no additional patients developed new neurologic dysfunction during their postoperative hospital course.

Patients with SWMA were excluded from analysis of SWS and Vcfc because such calculations assume uniformity of myocardial contractility.[26] Eighteen patients had new SWMA (including four with a SWMA at baseline) and were excluded for that reason; one additional patient each in groups 1, 2, and 3 had a SWMA at baseline, which precluded analysis, and one patient in group 1 had inadequate wall definition for analysis. The echocardiograms from the remaining 38 patients were analyzed for SWS and Vcfc according to the methods. Although they always had a lower Vcfc, those patients who received halothane (with or without phenylephrine) had a SWS similar to those who were given isoflurane at a similar MAC equivalent. At the time of carotid cross-clamping, those patients who had a higher concentration of anesthetic plus phenylephrine had a significantly higher SWS and lower Vcfc when compared with those patients who received a lower concentration of the same agent without phenylephrine (table 3).

Discussion

There is a 40% incidence of coronary artery disease in asymptomatic patients with carotid arterial disease and up to a 94% incidence in patients with a history of angina or abnormal electrocardiogram.[1-3] Consequently, myocardial infarction remains a leading cause of death in patients with cerebral ischemic attacks, and myocardial events are the leading cause of death following carotid endarterectomy.[4-7] Nevertheless, some consider it necessary to preserve or even to augment systolic blood pressure during temporary carotid occlusion to minimize the risk of cerebral ischemia.[7-11,12] Although many techniques have been advocated to diagnose intraoperative cerebral ischemia, outcome has not improved. Our surgeons have used stump pressure to guide the need for inserting a shunt with a published 1.5% stroke rate in their series dating to 1966, similar to that found in the 60 patients reported here and in the best studies in the literature for patients with prior documented transient ischemic attacks.[7-12] Although stump pressure is clearly an imperfect guide to cerebral perfusion, areas distal to a stenosis may be served by fully dilated vessels, and therefore flow into those regions may be pressure-dependent.[12] Our goal in this study was to determine which of our commonly used anesthetic techniques best preserves blood pressure and stump pressure and avoids myocardial ischemia.

Left ventricular SWMA are sensitive and specific indicators of myocardial ischemia in experimental animals and in humans.[14,16-21,29-34] We have demonstrated that analyzing intraoperative echocardiograms for the development of new SWMA is a more sensitive method than ST segment analysis for diagnosing myocardial ischemia.[14-16] In the present study a higher incidence of new SWMA was found in patients who were given phenylephrine plus a greater concentration of anesthetic, thus a higher incidence of myocardial ischemia. Despite the high incidence of intraoperative myocardial ischemia, none of the patients suffered perioperative myocardial infarction. Although the patients had ECG and CPK levels drawn in the recovery room, were questioned on postoperative days 1 and 3, and 30 days later for symptoms or signs of myocardial ischemia, the data on myocardial infarcts may not be accurate as most infarcts after surgery are reported to occur on postoperative days 2 and 3. Although the specific pathophysiologic factors that result in myocardial infarction are not clear, prolonged myocardial ischemia is likely to be deleterious. Perhaps because the vast majority of episodes of intraoperative ischemia were brief, the patients recovered without experiencing infarction. Perhaps the wall motion abnormalities reverted to baseline in all but three patients because their systolic blood pressure tended to be lower at the end of the procedure than during carotid occlusion or because of the contribution to myocardial ischemia of some yet undefined reflex caused by carotid occlusion. Nevertheless, Slogoff and Keats[22] have demonstrated that intraoperative myocardial ischemia in patients undergoing myocardial revascularization is associated with postoperative myocardial infarction; even brief episodes of myocardial ischemia may cause microscopic areas of cell death.[35] Thus, in patients likely to have coronary artery disease we cannot recommend the use of phenylephrine to maintain or augment blood pressure when a satisfactory alternative is available.

Given that deep anesthesia and phenylephrine or light anesthesia alone produced similar blood pressures and heart rates, why was one associated with more myocardial ischemia than the other? Left ventricular wall stress (volume * pressure/thickness), along with heart rate and contractile state of the ventricle, are the major compo-

nents of myocardial oxygen consumption.[36-38] Both wall stress and the pressure perfusing coronary arteries increase as the systemic blood pressures increase, thus making it difficult to predict the net effect of increased aortic pressure on myocardial oxygen supply and demand.[39] When blood pressure increases, the heart responds by increasing end-systolic volume, followed by an increase in end-diastolic volume in order to maintain stroke volume.[15,40] The amount of preload reserve required depends on the intrinsic contractile state of the ventricle. As contractility was depressed by increasing concentration of anesthetic, ventricular dilation and wall thinning (increased wall stress) occurred (table 3).[15,25-27] Previous studies have reported a decrease in wall stress when increasing concentrations of anesthetics were associated with decreases in systemic blood pressure.[40] In this study blood pressure was maintained with the use of phenylephrine. Because systemic blood pressure, heart rate, and presumably myocardial oxygen supply were the same in all groups, the increase in SWS probably accounts for the varying incidence of ischemia between the groups that were and were not treated with phenylephrine. Perhaps inclusion of groups treated with nitroglycerin plus phenylephrine might have prevented the ventricular distention observed. Because ventricular distention may impede subendocardial blood flow, it may have led to myocardial ischemia. An additional factor contributing to the development of myocardial ischemia in the groups of patient treated with phenylephrine may be the effect of alpha adrenergic stimulation on the coronary vasculature. Although coronary blood flow is primarily regulated by the metabolic demands of the myocardium, coronary autoregulation can be partially overridden by adrenergic vasoconstriction.[41-44] Thus, there may have been a decrease in myocardial oxygen supply in these patients, as well.

One other article implies that vasopressor use contributes to myocardial ischemia during carotid endarterectomy.[45] However, that study was a retrospective survey, which found that more patients who received vasopressors had myocardial infarctions; it may well have been that the vasopressor use resulted from myocardial infarction rather than caused it in that study. Our data thus contribute to the caution in using vasopressors to increase blood pressure beyond that usually needed for coronary artery perfusion in patients with a high likelihood of coronary artery disease.

The depressant effect of volatile anesthetics on myocardial contractility is well recognized, but the differing effects of these agents on ventricular afterload makes comparison difficult. However, echocardiographically determined indices of contractility and afterload can be used to examine the effects of anesthetic agents on ventricular function. Several load independent indices of left ventricular contractility have been defined in terms of physiologic events occurring at end-systole and are able to separate changes in left ventricular contractility from alterations in preload (approximated by end-diastolic volume or dimensions) and afterload (force opposing left ventricular fiber shortening best measured as wall stress[25,43]). The Vcfc has been shown to be an index of myocardial contractility that is preload-independent but variable with afterload.[26] The relationship between Vcfc and SWS allows us to separate the effects of changes in afterload and contractility on myocardial performance. In this study we compared the effects of similar concentrations of anesthetics at similar afterloads. Isoflurane causes less depression of contractility than does halothane, even when isoflurane's afterload reducing effects are overcome by using phenylephrine. Thus, isoflurane may be a superior agent to maintain contractility in patients with impaired left ventricular function. Although others have questioned whether it is a better agent in patients with coronary artery disease,[46] in this randomized prospective trial in patients likely to have coronary artery disease[1-3] (table 1), we found no difference in incidence of myocardial ischemia between the patients anesthetized with isoflurane and those anesthetized with halothane (table 3). There was an opposite trend toward a reduction of myocardial ischemia associated with isoflurane relative to that associated with halothane.

There are several explanations for the similar heart rates between the groups despite the differing anesthetic agents and depths of anesthesia. First, our patients were elderly; aging attenuates the baroreceptor reflex. Second, patients with carotid arterial disease have diminished baroreceptor sensitivity. Third, one-third of the patients in each group were chronically taking β-adrenergic receptor blocking drugs. Finally, although the wall stress was different between the groups, the systemic blood pressure was the same. If our patients who were lightly anesthetized had developed a rapid heart rate, the incidence of myocardial ischemia may have differed.

There are some limitations in our methods. First, the wall motion changes we observed might be due to primary changes in loading conditions rather than to myocardial ischemia. If areas of scar were to be unmasked because of changes in loading, these areas would have diminished or absent wall thickening at baseline, which they did not. Because of the criteria of our wall motion grading system, areas that do not contract at baseline cannot subsequently develop a SWMA.[14] Thus, all areas that developed worsening of wall motion had some contraction at the control measurement, suggesting that worsening of regional function was not due to changes in loading *per se*, but rather to development of myocardial ischemia. Only four of the 18 new SWMA occurred in areas that were not graded as normal at baseline. Second, we did not attempt to measure the wall stress in those patients who developed

myocardial ischemia; we cannot say that these patients did in fact have a greater wall stress than did those who did not demonstrate SWMA. Because of the theoretical assumptions involved in its determination, wall stress can only be determined in patients with symmetrically contracting ventricles.[26] Third, although we used systolic blood pressure to determine wall stress, numerous approximations of left ventricular end-systolic pressure have been used (including systolic blood pressure) showing strong correlations.[26] Finally, we used two-dimensional echocardiography to determine the LVET. Although the temporal resolution of this technique is limited, other investigators have demonstrated good correlations with results obtained by M-mode echocardiography.[27] Thus, although there were limitations to this study, they apply evenly to all groups and should not affect the validity of the results.

In summary, both anesthetic techniques maintained systemic blood pressure and cerebral perfusion as determined by carotid artery stump pressure and, more importantly, neurologic outcome. Patients who received isoflurane and halothane had similar incidences of myocardial ischemia. However, those patients who received phenylephrine had an almost threefold greater incidence of myocardial ischemia at the same blood pressure than did those who did not receive phenylephrine. This increased incidence of myocardial ischemia presumably occurred because of an increase in myocardial oxygen demand without a concomitant increase in supply. Thus, these data do not support the routine use of phenylephrine to maintain blood pressure in patients at high risk for the development of myocardial ischemia.

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