The Preoperative and Intraoperative Hemodynamic Predictors of Postoperative Myocardial Infarction or Ischemia in Patients Undergoing Noncardiac Surgery

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Among hypertensive and diabetic patients undergoing elective noncardiac surgery, preoperative status and intraoperative changes in mean arterial pressure (MAP) were evaluated as predictors of postoperative ischemic complications. Of 254 patients evaluated before operation and monitored during operation, 30 (12%) had postoperative cardiac death, ischemia, or infarction. Twenty-four per cent of patients with a previous myocardial infarction or cardiomegaly had an ischemic postoperative cardiac complication. Only 7% of those without either of these conditions sustained an ischemic complication. No other preoperative characteristics, including the presence of angina, predicted ischemic cardiac risk. Nineteen per cent of patients who had 20 mm Hg or more intraoperative decreases in MAP lasting 60 minutes or more had ischemic cardiac complications. Patients who had more than 20 mm Hg decreases in MAP lasting 5 to 59 minutes and more than 20 mm Hg increases lasting 15 minutes or more also had increased complications ($p < 0.03$). Changes in pulse were not independent predictors of complications and the use of the rate–pressure product did not improve prediction based on MAP alone. In conclusion patients with a previous infarction or radiographic cardiomegaly are at high risk for postoperative ischemic complications. Prolonged intraoperative increases or decreases of 20 mm or more in MAP also resulted in a significant increase in these potentially life-threatening surgical complications.

IN THE LAST 20 years there have been numerous studies of the risk of perioperative ischemia among patients undergoing noncardiac surgery.[1-5] Many of the studies relied on retrospective analysis of charts.[2,4,5] In a classic prospective study, Goldman developed an index to estimate cardiac risk in noncardiac surgery from preoperative characteristics after evaluating patients before operation and following patients after operation.[6,7] Several recent prospective studies evaluating risk for postoperative myocardial ischemia have used similar methods.[8-10] Some have relied on retrospective analysis of operative records[1-6] and some did not analyze intraoperative events.[8-10] Studies that recorded postoperative events in retrospect underestimated infarction rates because many postoperative infarctions are asymptomatic.[11] Patients were evaluated before operation, monitored during operation, and followed after operation with a standard protocol in two studies.[12,13] Neither of these prospective studies reported the combined impact of intraoperative hypertension and hypotension on postoperative cardiac complications.

The present study was designed to prospectively test, after taking into account prognostically important preoperative characteristics, the hypothesis that the duration of intraoperative changes in MAP of 20 mm Hg or more would predict patients who developed postoperative cardiac complications. In this study of a high-risk population of hypertensive and diabetic patients who were undergoing elective general surgery, patients were evaluated before operation, monitored by an independent observer during operation, and followed after operation for seven days with daily examinations electrocardiograms (ECG), creatine kinase (CK), and CK-isoenzymes. Postoperative ischemic events were evaluated by reviewers who were blind to the intraoperative course and preoperative patient status.

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Methods

Assembly of Population

All patients who had essential hypertension or diabetes who were undergoing elective general surgery were eligible for enrollment. The criteria for hypertension were (1) for patients younger than 30 years, systolic pressure must be 150 mm Hg or more, or diastolic pressure must be 90 mm Hg or more; (2) for patients 30 years or older, systolic pressure must be 160 mm Hg or more, or diastolic pressure must be 95 mm Hg or more; or (3) treatment with any medication specifically employed to reduce blood pressure (*i.e.*, patients treated with diuretics for congestive heart failure alone were not considered hypertensive). Patients with secondary hypertension were excluded. The criteria for diabetes were (1) treatment with insulin or oral hypoglycemic agents, including treatment started during hospitalization; and (2) elevated fasting glucose on more than one occasion (plasma 140 mg/dL or more; whole blood 120 mg/dL or more).

Between July 1982 and September 1985, 278 patients were enrolled. To document the proportion of eligible patients who were entered into the study, the charts of all 1398 patients undergoing several types of operation (vascular surgery or cholecystectomy) during the same secular interval were reviewed; these operations accounted for 40% of the surgery performed in the prospective study. Overall of the 1398 patients who had a cholecystectomy or vascular surgery, 26% of eligible hypertensives and 34% of eligible diabetics had been entered into the prospective study (Table 1).

Preoperative Evaluation

The protocol was reviewed and approved by the Institutional Human Rights Committee. Informed consent was obtained from all patients. Before operation basic demographic and clinical data were recorded. Physical examination was performed in a standardized fashion; abnormalities in the pulmonary, cardiac, neurologic, or vascular exam were recorded. Height and weight were also recorded. The history of comorbid conditions was obtained using standardized questions and criteria. Dyspnea on exertion was quantified according to the activity that produces dyspnea (*i.e.*, walking uphill, walking one block, dressing, or talking).[14] Angina was defined as definite or probable angina according to the Rose criteria.[14] Patients with nocturnal or rest angina, or with a crescendo pattern were designated as having unstable angina. Myocardial infarction included patients who had been hospitalized for chest pain and developed either new Q waves in at least two leads that were 0.04 seconds in duration and 1 mm in depth, new ST segment depression of 1 mm or more, or new T-wave inversion that persisted for seven days, with elevation of CK or CK-MB isoenzyme. Patients who had electrocardiographic changes alone in the absence of a clinical history were not classified as having had a myocardial infarction. Congestive heart failure included patients with a definite history of pulmonary edema, paroxysmal nocturnal dyspnea, or dyspnea on exertion,[14] not in the setting of an acute myocardial infarction, arrhythmia, sepsis, and so on, who responded to treatment with digitalis, diuretics, or afterload reduction, and who required continued pharmacologic therapy. Decompensated congestive failure included those who had either an S_3 gallop on exam, evidence of congestive failure on chest x-ray, or jugular venous distention and rales on admission to the hospital. Patients with a history of intermittent claudication,[14] or a peripheral bypass procedure, and patients with an absent femoral pulse, or bilaterally absent popliteal pulses were defined as having peripheral vascular disease. Patients with documented valvular disease of any type (aortic, mitral, prosthetic valve, and so on), except mitral valve prolapse, were defined as having valvular heart disease. Patients with hemispheral symptoms, including motor deficit, sensory deficit, or homonymous hemianopsia were classified as having a cerebrovascular accident if the symptoms persisted for more than 24 hours or transient ischemic attack if the symptoms lasted 24 hours or less. Chronic pulmonary disease included patients with chronic bronchitis[14] and patients with a definite history of asthma that occurred without upper respiratory tract infections and that required pharmacologic treatment. Liver disease includes patients with a documented cirrhosis or chronic hepatitis. End organ complications of diabetes are retinopathy (aneurysms, exudates, or hemorrhages), nephropathy (biopsy or a serum creatinine of more than 2 mg/dL and a 24-hour urine protein of more than 250 mg/dL), and neuropathy (somatic: absent reflexes, sensory deficits, or amyotrophy; or visceral: nocturnal diarrhea, impotence, or orthostatic hypotension).

The patient's right and left arm sitting blood pressure and pulse, as well as the recumbent and standing pulse and blood pressure, was obtained. Blood pressure was re-

TABLE 1. *Number of Patients Who Were Eligible for the Study and the Number Who Were Entered for Two Types of Surgery Only (Cholecystectomy or Vascular Surgery)*

	Eligible	Entered	% of Eligible Who Were Entered
Hypertension			
Systolic/diastolic	59	6	10
Treatment	358	104	29
Total	417	110	26
Diabetes			
Elevated glucose	35	8	23
Treatment	73	29	40
Total	108	37	34

corded using a standard mercury manometer. Korotkoff Phase V was recorded as the diastolic pressure. The cuff was placed so that the lower margin was 2 to 3 cm above the antecubital space, with the bladder over the medial surface of the arm.[15] The adult cuff (13 × 24 cm) was employed for patients whose mid-arm circumference was less than 32 cm; the large adult for those whose circumferences was 33 cm or more but less than 42 cm. Blood pressures were obtained every 4 hours before surgery by the nursing staff. These systolic and diastolic blood pressures were recorded to delineate the patient's usual preoperative MAP, the standard deviation of the MAP, and the minimum and maximum MAP.

Basic preoperative laboratory values were recorded, including hemoglobin, electrolytes, urinanalysis, creatinine, CK, ECG, and chest x-ray.

Intraoperative Monitoring

On the day of surgery, a research assistant, blinded to the hypotheses of the study, accompanied the patient to the operating room and recorded pulse and blood pressure during induction and intubation and every five minutes thereafter, using either an intra-arterial catheter (at the discretion of the anesthesiologist), a mercury manometer, or an indirect automatic device. In 52 patients intra-arterial measurements were made using a 20-gauge teflon catheter in the radial artery that was connected to a Marquette 7000 dual-pressure monitor calibrated before each use (accuracy of ± 1 mm Hg). In 76 patients the Omega 1000, an indirect oscillometric blood pressure recorder, was used (accuracy of ± 2 mm Hg); the large adult cuff (15 × 33 cm) was used if the arm circumference was 30 cm or more. The oscillometric device has been shown to produce reproducible and valid measurements of blood pressure while used in the operating room.[16] In 150 patients the anesthesiologist decided to use standard mercury manometer instead of the Omega 1000. In these cases the research assistant obtained and recorded the blood pressures according to the procedures described previously. To standardize the definition of the MAP with the different techniques, MAPs were calculated as the diastolic pressure + 1/3 (systolic–diastolic.)

The primary analysis of intraoperative blood pressures was based on the differences between the intraoperative MAPs and the preoperative MAPs, after adjusting for differences between arms. Hypotension was defined as an intraoperative MAP that was 20 mm Hg or more below the patient's preoperative MAP. Similarly hypertension was defined as an intraoperative pressure that was 20 mm Hg or more above the patient's preoperative baseline.

The research assistant recorded all pharmacologic agents used during each five-minute interval of the operation. The use of anesthetic agents and adjuvants such as thiopental, nitrous oxide, fentanyl, droperidol, d-tubocurarine, pancuronium, succinylcholine, and atracurium were recorded. The use of pressors (*e.g.*, phenylephrine, dopamine, ephedrine, norepinephrine, and so on), antihypertensive agents (*e.g.*, hydralazine, nitroprusside, beta blockers, nitropaste) and other agents such as mannitol, lasix, or lidocaine were also noted. Major intraoperative events, such as skin incision, reversal of anesthesia, aortic cross-clamping, drainage of ascites, and changes in position were also recorded. All input and output was recorded at 60-minute intervals; net intake was calculated on an hourly basis. The specific fluids used and the total output during the operation (*e.g.*, suction, sponges, nasogastric drainage, urine output, or placement of a foley catheter) were also recorded. Ringers lactate, 0.9% saline, D_5 Ringers lactate, and Normosol (Abbott Laboratories, North Chicago, IL) were considered isotonic saline; D_5W, D_5 1/4 normal saline and D_5 1/2 normal saline were not. Hourly rates of infusion were calculated on the amount of time required for surgery.

Postoperative Follow-up

All patients were followed daily for seven days after operation or until death, discharge, or reoperation with clinical examinations, serum creatinines, ECGs, CK, and CK isoenzymes. Patients who underwent reoperation were considered censored in terms of follow-up at the time of reoperation.

The CKs were immediately frozen and assayed in batch using a technique based on the methods of Rosalki[17] when 100 samples were available. Isoenzymes were measured if the CK was more than 100 U/L. The initial 20% of the specimens were assayed using anion exchange beads.[18] The laboratory then switched to agarose electrophoresis.[19] The two techniques appeared reasonably comparable within the cut-offs used for the 76 samples used to compare the methods (kappa = 0.51).

All postoperative ECGs were read by two reviewers who were blinded to all aspects of the preoperative status of the patient except for their preoperative ECG; they were also blinded to the intraoperative course and all aspects of the postoperative course except for the ECGs. Disagreements were resolved by a third blinded reviewer. All postoperative ECGs were read in relation to the preoperative baseline ECG. Changes in the ST segment or T waves must all have occurred in at least two leads in the absence of new electrolyte abnormalities or the new use of digitalis. Details of the ECG classification have been published;[7] in brief patients were classified as having (1) new Q waves that were 0.03 seconds or longer in duration and more than 1 mm in depth in two leads; (2) unequivocal ST elevation 2 mm or more in comparison to the baseline ECG; (3) new ST depression of 2 mm or more. If there was pre-existing ST depression, the new depression must have added an additional 2 mm with or without T-wave inversion; and (4) new inversions of previously upright T waves.

The postoperative course of any patient who developed any of the above changes in their ECG or new bundle branch block or arrhythmia was reviewed by two physicians who were blind to the patient's preoperative status and intraoperative course. Patients who had any episode of chest pain, tightness, or discomfort lasting 30 minutes or more, palpitations, or syncope, or whose surgeon suspected that the patient had a myocardial infarction failure also were evaluated by the reviewers. These physician reviewers determined whether the patients who were suspected of having postoperative myocardial ischemia or infarction met the diagnostic criteria.

Definition of Postoperative Infarction and Ischemia

The criteria for myocardial infarction and ischemia[20] were provided to our blinded reviewers and they made the final designation. For example there were six patients who either had new q waves or major consistent ECG change persisting for more than 48 hours associated with 5% or more MB. The one patient with new q waves and one patient with ST-T changes lasting 48 hours or more, with 5% or more MB were designated as having a definite myocardial infarction. None of the four patients with T-wave inversions lasting ≥48 hours or more with 5% or more MB were rated by the reviewers as having a definite myocardial infarction. One patient with ST-T changes that lasted less than 48 hours with 5% or more MB was designated as having a definite infarction. For the sake of clarity, the patients who were finally designated as having definite, probable, or possible myocardial infarction or definite ischemia will be described. The reviewers also classified deaths and arrests as cardiac or noncardiac. A cardiac death was a death in the setting of myocardial ischemia, infarction, ventricular tachycardia, cardiogenic shock, with the clinical events leading to death compatible with a primary cardiac etiology.

Cardiac deaths. There were four cardiac deaths, one of which occurred after intraoperative ventricular tachycardia, one following anginal episode, one after refractory arrhythmias and cardiogenic shock, and one after developing a new Q wave, followed by an arrest.

Cardiac arrest. Two arrests that did not lead to cardiac death occurred in the setting of pulmonary edema and symptomatic myocardial ischemia. Two arrests occurred in the setting of a definite or possible myocardial infarction: one with ST-T depression 48 hours or more with 12% MB (definite), and the other with ST elevation less than 48 hours with 6% MB (possible).

Definite or probable myocardial infarction. There was one definite myocardial infarction without an arrest or death: a patient with ST-T depression less than 48 hours with 5% MB. There were two patients with probable myocardial infarction: one patient had new T inversion more than 48 hours with 25% MB and another had new T inversion more than 48 hours with 8% MB.

Possible infarction and definite ischemia. There were three patients with possible myocardial infarctions, 1 with ST-T depression more than 48 hours with 4% MB, 1 with ST normalization more than 48 hours with 5% MB, and 1 with T inversion more than 48 hours with 5% MB.

There were 18 patients designated as having definite ischemia with ECG changes: 1 patient with T inversion more than 48 hours and 5% MB and 1 with 3% to 4% MB; 1 patient with ST elevation more than 48 hours and 3% to 4% MB and 1 patient with ST elevation less than 48 hours and more than 5% MB; 1 patient with ST normalization more than 48 hours and 3% to 4% MB; 4 patients with ST depression and T wave inversion more than 48 hours with 0% to 2% MB; and 5 patients with T depression more than 48 hours with 0% to 2% MB. One patient had unstable angina without ECG changes, and three patients had definite angina by the Rose criteria.

Listing events hierarchically, among the 278 patients there were 4 cardiac deaths, 4 cardiac arrests, 3 definite or probable myocardial infarctions, 3 possible infarctions, 14 definite ischemias, and 4 anginas.

In 24 (8.6%) of the patients, the research assistant was not present in the operating room to record events and blood pressures. Among those patients, 1 (4%) suffered cardiac death, 1 had a possible infarction, 1 had definite ischemia, and 1 had definite angina. Because the purpose of this analysis is to assess the intraoperative blood pressures and events in relation to cardiac complications, we have omitted these 24 patients and these four cardiac events from this analysis because the intraoperative data was not recorded by an independent observer. The remainder of the paper will concentrate on the 254 patients, for whom intraoperative data was recorded by an independent observer. However, when the 24 patients were included in the analysis, the results did not differ.

Analysis

The preoperative pressures were all obtained by mercury manometer and the intraoperative pressures were obtained either by mercury manometer (n = 121), intra-arterial catheter (n = 51), or indirect oscillometric device (n = 71). Because there are some systematic differences in the systolic, diastolic, and mean pressures obtained using the different techniques,[16] the analysis was performed in several ways. First the differences in MAPs were evaluated without any adjustment. Second the MAPs were evaluated after adjustment for the systematic differences between methods of measurement. For example the mean intra-arterial pressure was 3.4 mm Hg lower than simultaneous assessments with a mercury manometer; thus for the adjustment 3.4 was added to all intraoperative pressures obtained by arterial catheter. Similarly the Omega mean pressure was 0.4 mm Hg lower than the mercury manometer pressure, so 0.4 was added to all pressures obtained using the Omega device. Second the intraoperative MAPs were also adjusted using the regression equations developed in a study comparing the devices;[16] however for the added complexity, there was no particular advantage of using regression instead of the simpler method of adjustment. Therefore the results are presented with the first method of additive adjustment. The rate–pressure product was calculated as the pulse multiplied by the MAP.

Logistic regression was performed using PROC LOGIST, available in the Statistical Analysis System.[21] For logistic regression at least five to ten outcome events must be available for each variable examined.[22,23] Therefore only four or five covariates could be evaluated. The approach developed by Harrell for creating clusters of related phenomena before evaluation using logistic regression was used to reduce the number of separate variables examined.[22]

Results

Four per cent (10 of 254) of the patients had a perioperative cardiac death, cardiac arrest, or a definite or probable myocardial infarction. Eight per cent (20 of 254) had a possible myocardial infarction or definite myocardial ischemia. Thus 12% of patients had a perioperative ischemic cardiac event. Most of these events occurred within the first three days after surgery, with the risk declining sharply after the second postoperative day.[24]

Table 2 shows the ischemic complications according to the duration of increases and decreases of 20 mm Hg or more in intraoperative MAP. At the beginning of the study, the hypothesis was that this magnitude of change in MAP would be associated with increased cardiac complications. Sixty per cent of patients had intraoperative increases (154 of 254) and 62% (159 of 254) had decreases of this magnitude. However ischemic complications were increased in only two groups of patients: 19% among the 43 patients who had decreases in MAP lasting 60 minutes or more ($p = 0.03$); and 20% among the 41 patients with decreases in MAP lasting 5 to 59 minutes who also had increases in MAP for 15 minutes or more ($p = 0.02$).

The complication rates were also evaluated with definitions of changes in MAP used in other studies.[7,12,13] An intraoperative fall in blood pressure of 50% or more occurred in 15 patients; 15% of these patients had ischemic complications. A fall of 33% for ten minutes or more occurred in 36 patients; 19% had complications. Similarly 14% of 56 patients who had intraoperative diastolic pressures rise over 110 and 17% of 41 patients whose systolic pressures rose over 200 had ischemic complications.

Table 3 shows the total rates of perioperative cardiac death, arrest, myocardial infarctions or ischemia according to the preoperative characteristics of the patients. The third column shows that total ischemic cardiac complication rates were increased among patients with severe hypertension (23%), those with previous myocardial infarction (27% and 22%), those in Canadian cardiovascular classes III-IV (22%), those with chronic renal disease (27%), with left ventricular hypertrophy on ECG (23%), or cardiomegaly on chest x-ray (24%). As might be anticipated, there was considerable correlation between these findings. For example when the complication rates for patients with left ventricular hypertrophy on ECG or cardiomegaly on chest x-ray were analyzed jointly, cardiomegaly on chest x-ray had the predominant impact: patients with left ventricular hypertrophy by ECG without cardiomegaly on chest x-ray did not have higher complication rates. Among patients with cardiomegaly the higher rates were not attributable to congestive heart failure; the rates were essentially identical among the 36 patients with cardiomegaly without congestive failure (25%) and the 14 patients with congestive failure (21%).

Patients with preoperative angina did not have a higher rate of ischemic cardiac complications. The slightly higher

TABLE 2. *Rates of Postoperative Myocardial Infarction, Ischemia, Cardiac Arrest or Death According to the Duration and Magnitude of Intraoperative Changes in Mean Arterial Pressure in Relation to Preoperative Baseline*

Intraoperative MAP Rises ≥ 20 mm Hg Above Baseline	Intraoperative MAP Falls ≥ 20 mm Hg Below Baseline				
	None	5–14 Minutes	15–59 Minutes	≥60 Minutes	Total
None	12% (33)	12% (8)	6% (32)	15% (27)	11% (100)
5–14 minutes	7% (28)	18% (11)	4% (24)	30% (13)	12% (76)
≥15 minutes*	6% (34)	26% (19)	14% (22)	0% (3)	13% (78)
Total	9% (95)	18% (38)	7% (78)	19% (43)	11% (254)

* There were 7 patients with increases lasting >60 minutes.

TABLE 3. *Perioperative Cardiac Death, Arrest, Myocardial Infarction, and Ischemia According to Preoperative Characteristics of Patients*

Preoperative Characteristics	Cardiac Death Arrest or Definite MI (%)	Probable MI or Definite Ischemia (%)	Total (%)	Number of Patients
Age				
<70	2	9	11	(162)
≥70	7	6	13	(92)
Sex				
Male	6	9	15	(97)
Female	3	7	10	(157)
Hypertension				
Not severe	3	8	11	(152)
Severe*	8	15	23	(39)
Diabetes				
No end organ damage	7	5	12	(73)
End organ damage	4	11	15	(27)
Dyspnea				
Walk without stopping for breath	3	7	11	(179)
Stop while walking	2	9	11	(56)
Short of breath dressing	16	11	27	(18)
12-minute walking distance				
≥640 meters	5	6	11	(17)
400–640 meters	2	7	9	(55)
<400	9	13	22	(45)
Not done	3	6	9	(137)
Cardiac comorbidity				
Angina	6	8	14	(48)
Myocardial infarction				
<6 months	9	18	27	(11)
≥6 months	18	4	22	(22)
Congestive heart failure				
Compensated	5	11	16	(18)
Decompensated	0	0	0	(14)
Valvular heart disease	7	4	11	(27)
Goldman's cardiac risk class				
Class I	3	8	11	(146)
Class II	4	8	12	(76)
Class III/IV†	6	10	16	(32)
Canadian cardiovascular classification				
I	3	8	11	(217)
II	6	7	13	(15)
III–IV	11	11	22	(22)
Other comorbidity				
Peripheral vascular disease	4	5	9	(92)
Cerebrovascular accident	6	7	13	(31)
Chronic bronchitis	3	7	10	(63)
Chronic renal disease	9	18	27	(22)
Comorbidity index				
0–2	5	5	11	(163)
3–4	5	5	10	(73)
>5	11	11	22	(18)
Electrocardiogram				
Q waves on EKG	5	3	8	(38)
Infarct on EKG	10	6	16	(64)
Any abnormality	10	8	18	(84)
Left ventricular hypertrophy‡	11	12	23	(26)
APC's or VPC's on EKG	0	8	8	(12)
Chest X-ray				
Cardiomegaly‡	6	18	24	(50)

* History of diastolic blood pressures > 120 mm Hg or hospitalization for hypertension.

† Only two patients were in class IV.

‡ Definite and probable.

rates among patients with ECG evidence of infarction were attributable to patients who also had a clinical history of an infarction; among patients whose ECG provided the only evidence of a previous infarction, the complication rate was only 9%. Similarly once the history of a previous infarction was taken into account, patients with an abnormal ECG did not have increased complication rates. The higher rate of complications in cardiac risk class III-IV was similarly attributable to patients with a previous infarction; 22% (n = 23) of those with a previous MI in class I-II, and 30% (n = 10) in class III had ischemic complications. The higher rates in Canadian cardiovascular class III-IV were also attributable to patients with a previous infarction.

Once the presence of cardiomegaly was taken into account, severe hypertension was not an independent predictor of ischemic complications. Cardiomegaly was found in 36% of patients with severe hypertension, but in only 19% of patients without severe hypertension. Among the 39 severe hypertensives, 38% of the eight patients with a previous myocardial infarction and 20% of the ten patients with cardiomegaly but without infarction had ischemic complications. Among 21 severe hypertensives without cardiomegaly or infarction, the complication rate was only 14%. Logistic regression confirmed that among the preoperative characteristics of patients, only previous myocardial infarction ($p = 0.055$) and cardiomegaly ($p < 0.01$) were independent predictors of ischemic complications.

Table 4 shows the patients stratified hierarchically according to whether they had a previous infarction or cardiomegaly and according to intraoperative changes in MAP. Overall 7% of patients without cardiomegaly or previous myocardial infarction, but 25% of those with one of those conditions had cardiac complications. The ten patients who had both cardiomegaly and previous myocardial infarction who had a 20% postoperative ischemic complication rate were grouped together with the 23 patients who had a previous myocardial infarction but

TABLE 4. *Ischemic Cardiac Complications According to Preoperative Characteristics and Intraoperative Changes in MAP*

A. Patients Without Previous Myocardial Infarction or Cardiomegaly

Intraoperative MAP Rises ≥20 mm Hg Above Baseline	Intraoperative MAP Falls ≥20 mm Hg Below Baseline			
	None	5–59 Minutes	≥60 Minutes	Total
0–14 minutes	3% (40)	6% (52)	11% (26)	6% (118)
≥15 minutes	0% (27)	16% (32)	0% (4)	8% (63)
Total	1% (67)	10% (84)	10% (30)	7% (181)

B. Patients with Cardiomegaly Without Infarction

Intraoperative MAP Rises ≥20 mm Hg Above Baseline	Intraoperative MAP Falls ≥20 mm Hg Below Baseline			
	None	5–59 Minutes	≥60 Minutes	Total
0–14 minutes	18% (11)	8% (13)	44% (9)	21% (33)
≥15 minutes	25% (4)	67% (3)		43% (7)
Total	20% (15)	19% (16)	44% (9)	25% (40)

C. Patients with Previous Myocardial Infarction*

Intraoperative MAP Rises ≥20 mm Hg Above Baseline	Intraoperative MAP Falls ≥20 mm Hg Below Baseline			
	None	5–59 Minutes	≥60 Minutes	Total
0–14 minutes	33% (9)	10% (10)	40% (5)	25% (24)
≥15 minutes	33% (3)	16% (6)		22% (9)
Total	33% (12)	13% (16)	40% (5)	24% (33)

* Includes 23 patients with previous myocardial infarction alone and 10 patients with both previous MI and cardiomegaly.

Model $X^2 = 19.01$; $p < 0.001$; $R = 0.244$

	Beta	p
Myocardial infarction	0.95 ± 0.49	p = 0.055
Cardiomegaly	1.14 ± 0.44	p = 0.01

	Beta	p
≥20 mm Hg decreases in MAP ≥60 min.	1.09 ± 0.49	p = 0.03
≥20 mm Hg decreases in MAP <60 min. *and* ≥20 mm Hg increases in MAP >15 min.	1.19 ± 0.51	p = 0.02

who did not have cardiomegaly. Twenty-six per cent of these latter patients had a postoperative ischemic event. When these preoperative characteristics are taken into account, the same pattern emerged, as was apparent in Table 1. Patients with 5 to 59 minutes of decreases in MAP ($p = 0.03$) and those with less than 60 minutes of decreases who also had 15 minutes or more of increases in MAP ($p = 0.02$) had higher complication rates. Patients with either cardiomegaly or previous infarction who had more than 60 minutes of low MAPs had particularly high complication rates—40% to 44%. There were no important differences in the percentage of patients with cardiomegaly or previous infarction who had 60 minutes or more of decreased MAPs in relation to those without either condition, but these patients did not tolerate such changes.

Table 5 shows the ischemic complications in relation to the type of operation and anesthesia, the length of surgery, intraoperative events, medications, fluid management, and intraoperative changes in pulse. The ischemic complication rates were slightly but not significantly higher among patients who underwent general anesthesia because of a higher proportion of patients with previous myocardial infarction or cardiomegaly in this group. The patients who had narcotic agents (*e.g.*, fentanyl with nitrous oxide) used as the primary anesthetic were included in this group; however there were too few patients to evaluate its impact on postoperative ischemic complications. The complication rates were higher among patients who underwent abdominal, peripheral vascular, or aortic aneurysm surgery. Not surprisingly, among patients who had aortic aneurysm repair, 40% (10 of 25) had cardiomegaly or a previous infarction. However aneurysm patients did not experience complications unless they had important changes in intraoperative MAP: of 11 patients who had prolonged (60 minutes or more) decreases in MAP, 36% had complications; and of the eight patients who had increases and decreases in MAP, 38% had complications. Only six patients undergoing aneurysm repair did not have either of these hemodynamic patterns.

Among patients who did not have major intra-abdominal or vascular surgery, complications occurred only among patients who had either cardiomegaly (22%; $n = 9$) or previous myocardial infarction (33%; $n = 9$). Once intraoperative hemodynamic patterns were taken into account, patients with longer operations did not have higher complication rates—although obviously patients with longer operations had a greater opportunity for prolonged changes in MAP. Although patients who received vasoactive agents or fluid challenges appear to have higher complication rates, when the preoperative characteristics and intraoperative hemodynamic patterns were taken into account, those receiving any of these interventions had complication rates similar to those of other patients in the same group. Although the numbers involved were small, the impact of such interventions appeared to depended on the hemodynamic result (*i.e.*, whether prolonged hypotension or hypertension was avoided). Ischemic complication rates did not vary significantly according to net fluid intake or net hourly blood loss; patients with larger hourly urine output did have a higher rate of ischemic complications, although this did not reach significance.

Table 6 shows the cardiac complication rates in relation to the preoperative characteristics, changes in intraoperative MAP, and to intraoperative changes in pulse of more than 20 beats per minute. In this table the intraoperative changes in blood pressure were reduced to the three important groups: prolonged decreases (≥60 minutes), increases of 15 minutes or more and decreases of 5 to 59 minutes, and patients with neither of those patterns. There were only eight patients who had both intraoperative increases and decreases of 20 or more beats per minute in pulse; they have been included with the patients whose pulse decreased. Pulse increases or decreases did not carry increased risk of developing cardiac complications when other variables were taken into account, except among patients with a previous myocardial infarction. Among patients with a previous infarction, only 6% of 16 patients without pulse changes had a postoperative ischemic complication, while 41% of the 17 patients who had either an increase or decrease in pulse of 20 or more beats per minute had complications. The changes in pulse and MAP that were examined in this table were not simultaneous; that is the changes in MAP occurred in different time intervals than the changes in pulse.

To evaluate the impact of simultaneous changes in intraoperative pulse and MAP, the changes in the intraoperative rate–pressure product (MAP × pulse) were also examined. Table 7 shows ischemic complications according to whether patients had 20% or more increases or decreases in the rate–pressure product. The major finding was that patients who had a decrease of 20% or more in the rate–pressure product for more than 30 minutes had greater complication rates. Table 8 shows ischemic complications according to whether patients had 20% or more increases or decreases in intraoperative rate–pressure product that lasted for 30 minutes or more according to the preoperative characteristics. The predominant finding was that patients with cardiomegaly or previous infarction had increased complications when they had intraoperative decreases in rate–pressure product that lasted for more than 30 minutes.

Discussion

The preoperative characteristics of patients likely to experience postoperative ischemia after noncardiac surgery have been studied by a number of investigators. Previous

TABLE 5. *Perioperative Cardiac Death, Arrest, Myocardial Infarction, and Ischemia According to Type and Duration of Operation, Anesthesia, and Intraoperative Events*

	Cardiac Death Arrest or Definite MI (%)	Probable MI or Definite Ischemia (%)	Total (%)	Number of Patients
Type of operation				
Peripheral vascular	5	5	11	55
Aortic aneurysm	8	20	28	25
Abdominal	2	10	12	96
Other operations	4	2	6	78
Length of operation				
<2 hours	3	3	6	79
≥2 < 4 hours	4	9	13	110
≥4 hours	6	11	17	65
Type of anesthesia				
Local or regional	4	0	4	27
Spinal or epidural	5	5	10	20
General	4	9	13	207
Intraoperative events				
Aortic cross clamping	8	14	22	27
Cardiac arrest	100	0	100	2
Intraoperative medications				
Any hypotensive agent*	7	14	21	28
Any pressor†	4	11	15	26
Pressors & hypotensive agents	29	0	29	7
Fluid challenge‡				
No	3	7	9	216
Yes	8	16	24	38
Hourly blood loss				
0–49 cc/hour	3	7	10	119
50–99 cc/hour	6	8	14	35
100–249 cc/hour	4	8	12	59
≥250 cc/hour	4	10	14	41
Hourly urine output				
0–49 cc/hour	3	4	7	136
50–99 cc/hour	2	10	12	41
>100 cc/hour	8	14	22	49
No Foley	4	14	18	28
Net intraoperative fluid infusions§				
<300 cc/hour	2	9	11	45
300–499 cc/hour	7	10	17	42
500–749 cc/hour	7	3	10	41
750–999 cc/hour	4	10	14	46
≥1000 cc/hour	3	7	10	60
Intraoperative pulse change of ≥20 beats				
Decrease in pulse‖	7	8	15	69
Increase in pulse				
5–14 minutes	5	2	7	44
≥15 minutes	0	14	14	55

* Hydralazine, nitroprusside, beta-blocker, nitropaste.
† Neosynephrine, ephedrine, dopamine, norepinephrine.
‡ >500 cc in 15 minutes or 1000 cc in 30 minutes.
§ Isotonic saline, Ringer's lactate, D_5 Ringer's lactate, Normosol.
‖ No decrease in pulse of >20 beats lasted longer than ten minutes.

studies have agreed that patients with a previous myocardial infarction, particularly those who had an infarction within 6 months of surgery, are at increased risk for postoperative infarction,[4–7,12,13,25] while those with angina alone were not.[6,7,12] Several studies have found that the risk of ischemic events was higher among patients with greater functional impairment.[7,8,26] Age over 70 years, shortness of breath, mitral regurgitation, more than 5 PVCs per minute, and a tortuous or calcified aorta were identified by Goldman[7] as risk factors for postoperative myocardial infarction. Most patients who had either a cardiac death or postoperative infarction had either pre-

TABLE 6. *Ischemic Complications According to History of Previous Infarction and Cardiomegaly, Intraoperative Changes in MAP, and Intraoperative Changes in Pulse*

Intraoperative Changes in MAP ≥20 mm Hg	Intraoperative Changes in Pulse: None	Any Increase ≥20 Beats	Any Decrease ≥20 Beats	Total
	A. Patients Without Cardiomegaly or Previous Infarction			
Neither	4% (49)	5% (40)	0% (30)	3% (119)
Increase ≥15 minutes and decrease ≥5 minutes	11% (9)	12% (16)	29% (7)	16% (32)
Decrease ≥60 minutes	0% (11)	22% (9)	10% (10)	10% (30)
Total	4% (69)	9% (65)	6% (47)	7% (181)
	B. Patients with Cardiomegaly Without Infarction			
Neither	23% (13)	13% (8)	0% (7)	14% (28)
Increase ≥15 minutes and decrease ≥5 minutes		100% (1)		100% (1)
Decrease ≥60 minutes	50% (6)	0% (1)	50% (4)	36% (11)
Total	31% (19)	20% (10)	18% (11)	24% (40)
	C. Patients with Previous Infarction			
Neither	9% (13)	40% (5)	50% (4)	23% (22)
Increase ≥15 minutes and decrease ≥5 minutes	0% (2)	0% (2)	50% (2)	16% (6)
Decrease ≥60 minutes	0% (1)	100% (1)	33% (3)	40% (5)
Total	6% (16)	38% (8)	44% (9)	24% (33)

operative congestive heart failure or ischemic heart disease.[7] Congestive heart failure was identified as a risk factor in another study.[13] In this study, which consisted mainly of hypertensive and diabetic patients, those with a previous myocardial infarction and those with greater functional impairment had increased ischemic complications, but age and congestive heart failure were not significant risk factors. The number of patients with PVCs on preoperative ECG or mitral regurgitation was too small to draw any conclusions. Because the majority of our patients had hypertension, a substantial proportion of patients had cardiomegaly on chest x-ray or left ventricular hypertrophy on ECG. Goldman found that 8% of patients with cardiomegaly had postoperative infarction or cardiac death, in contrast to 2% of patients without cardiomegaly; however this difference did not retain significance in a multivariate analysis.[7] In this study cardiomegaly was a significant predictor of ischemic complications.

The type and duration of operation have also been evaluated as predictors of ischemic complications. Patients undergoing upper abdominal or intrathoracic surgery were found to be at higher risk for cardiac death or infarction in several retrospective[4,5] and one prospective study;[13] but this was not confirmed in two other prospective studies.[7,12] In the earliest studies[1,2] the duration of surgery was related to ischemic complications, but later studies[7,12,13] have not confirmed this. In this study the type and duration of surgery did not predict ischemic complications once hemodynamic events during surgery were taken into account.

In most studies of noncardiac surgery, patients who had intraoperative hypotension, defined as a 30% decrease

TABLE 7. *Perioperative Cardiac Death, Cardiac Arrest, Myocardial Infarction, or Ischemia According to Intraoperative Changes in the Rate-Pressure Product*

≥20 Increase in the Rate-Pressure Product	≥20% Decrease in the Rate-Pressure Product: <5 Minutes	5–29 Minutes	30–59 Minutes	≥60 Minutes	Total
<5 minutes	0% (11)	7% (14)	0% (6)	20% (40)	13% (71)
5–29 minutes	9% (23)	4% (28)	18% (23)	12% (33)	10% (107)
30–59 minutes	7% (15)	10% (10)	20% (5)	20% (5)	11% (35)
≥60 minutes	18% (22)	7% (15)	—	50% (4)	15% (41)
Total	10% (71)	6% (67)	15% (34)	18% (82)	11% (254)

TABLE 8. *Perioperative Ischemic Complications According to History of Previous Infarction and Cardiomegaly and Intraoperative Changes in Rate-Pressure Product*

≥20% Increase in the Rate-Pressure Product	≥20% Decrease in the Rate-Pressure Product		
	<30 Minutes	≥30 Minutes	Total
A. Patients Without Cardiomegaly or Previous Infarction			
<30 minutes	4% (55)	9% (69)	8% (124)
≥30 minutes	8% (48)	0% (9)	7% (57)
Total	6% (103)	8% (78)	7% (181)
B. Patients with Cardiomegaly Without Infarction			
<30 minutes	9% (11)	32% (19)	23% (30)
≥30 minutes	25% (8)	50% (2)	30% (10)
Total	16% (19)	33% (21)	25% (40)
C. Patients with Previous Infarction			
<30 minutes	10% (10)	29% (14)	21% (24)
≥30 minutes	16% (6)	67% (3)	33% (9)
Total	13% (16)	35% (17)	24% (33)

in the systolic pressure, have had higher postoperative ischemic complications,[1-4,12] particularly if the hypotension was prolonged.[3] One study found that such changes predicted cardiac death, but not infarction.[7] Only two studies of noncardiac surgery specifically evaluated the impact of intraoperative hypertension, and neither found increased complications with hypertension.[7,13] Goldman did examine patients who had both intraoperative hypertension (systolic pressure of 200 mm Hg or more, or more than 40 mm higher than preoperative systolic pressure) and hypotension (33% fall in intraoperative systolic pressure) and found that such patients did not have an increased risk of complications. In this study both intraoperative hypotension and hypertension were defined in terms of the MAP. Patients with 60 minutes or more of 20 mm Hg or more decrease in MAP were at increased risk. Patients with 15 or more minutes of 20 mm Hg or more increases in MAP and 20 mm Hg or more decreases in MAP lasting less than 60 minutes were at increased risk for ischemic complications. Intraoperative changes in pulse were less helpful in identifying patients at risk, with the important exception of patients with a previous infarction. The rate–pressure product was also evaluated, although the rate–pressure product has been criticized as a potentially misleading method of assessing intraoperative myocardial oxygen consumption because of the differential impact of changes in pressure and pulse in the anesthetized patient.[27-29]

Intraoperative decreases in pressure occur almost universally during inhalation anesthesia because halothane, isoflurane, and enflurane all produce a dose-related depression of myocardial contractility.[30-33] With inhalation anesthesia hypertensives, especially those with left ventricular hypertrophy, are prone to the development of intraoperative hypotension, which occurs as a result of decreased systemic vascular resistance and vasodilation of capacitance vessels.[34] This is a potential explanation for the greater risk of ischemic complications among patients with cardiomegaly. Intraoperative hypotension is known to occur as a result of surgical stimulation (*e.g.*, skin incision)[35,36] and unclamping of the aorta.[37] Apart from surgical events, Prys-Roberts et al.[38] have also show that intraoperative hypocapnia may produce an increase in systemic vascular resistance, a fall in cardiac output, and resultant hypotension. This effect is more pronounced in the hypertensive than in the normotensive patient because of the greater reactivity of smooth muscle in the hypertensive patient.[38] Intraoperative hypertension was relatively common in this study because of the substantial proportion of hypertensive patients. Hypertensives have an exaggerated increase in pressure during anesthesia to noxious stimuli.[32-34] Thus the large proportion of hypertensives in the study probably increased the rate at which intraoperative hypotension and hypertension occurred.

Evidence has emerged from studies of patients undergoing noncardiac surgery that used continuous monitoring devices to record intraoperative ECGs linking intraoperative hypertension[39-41] and tachycardia[40,41] with ST-T segment changes. In these studies no reference was made to relationships between ST-T depression and hypotension. However the data supports other studies in hypertensives that such hemodynamic changes may precipitate myocardial ischemia.[32,33,38]

Efforts to prevent perioperative ischemic complications among hypertensives and diabetics should be focussed on patients with cardiomegaly and previous myocardial infarction. Among patients without either cardiomegaly or previous infarction, the risk of ischemic complications was high only among those patients with prolonged hypotension or both hypertension and hypotension.

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