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Cardiac Risk of Noncardiac Surgery in Patients with Asymmetric Septal Hypertrophy

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Background: Many data are available regarding cardiac risk in patients with coronary artery disease undergoing noncardiac surgery, but few data are available regarding risk for patients with hypertrophic cardiomyopathy and asymmetric septal hypertrophy.

Methods: Seventy-seven patients with asymmetric septal hypertrophy were identified in whom an echocardiogram had been performed within 24 months of noncardiac surgery. Patients' charts were reviewed for data regarding surgical operations, including length of surgery, type of anesthesia, and intravascular monitoring used. Data regarding adverse perioperative cardiac events also were gathered.

Results: Forty percent (n = 31) of patients had one or more adverse perioperative cardiac events, including one patient who had a myocardial infarction and ventricular tachycardia that required emergent cardioversion. There were no perioperative deaths. All 31 patients had minor outcomes. Of the 77 patients, perioperative congestive heart failure developed in 12 (16%). Factors associated with adverse cardiac events were increasing length of surgical time ($P < 0.01$) major surgery ($P < 0.05$), and intensity of monitoring ($P < 0.05$). Age, gender, resting outflow tract gradient, systolic anterior motion of the anterior mitral leaflet, prior myocardial infarction, severity of mitral regurgitation, type of anesthetic, septal thickness, and the interval between echocardiogram and surgery were not associated with the occurrence of adverse cardiac events.

Conclusion: Patients with asymmetric septal hypertrophy undergoing noncardiac surgery have a high incidence of adverse cardiac events, frequently manifested as congestive heart failure. However, irreversible cardiac morbidity and mortality was extremely low. Important independent risk factors for adverse outcome in all patients include major surgery and increasing duration of surgery. (Key words: Anesthesia, general: spinal. Complications: postoperative. Heart: cardiomyopathy cardiovascular diseases; coronary artery disease. Monitoring, echocardiography: transthoracic. Surgery: noncardiac.)

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HYPERTROPHIC cardiomyopathy is a rare, genetic myocardial abnormality with an autosomal dominant pattern of inheritance, defined by the presence of a hypertrophied, nondilated left ventricle in the absence of other known causes.[1] A minority of these patients (approximately 25%) manifest a dynamic left ventricular outflow tract (LVOT) gradient. This gradient may exist at baseline or be provokable by a number of physiologic changes that are prone to occur during anesthesia and surgery, including reductions in preload and afterload or increases in contractility. There are few data, however, examining cardiovascular outcomes in a large group of patients with hypertrophic cardiomyopathy.[2] In addition, there has been no systematic investigation of clinical or echocardiographic correlates that might identify a subgroup of these patients at increased risk for cardiac events.

Although the morphologic pattern of wall thickening is quite heterogeneous, patients with hypertrophic cardiomyopathy often manifest hypertrophy that involves the intraventricular septum and anterolateral left ventricular walls with relative sparing of the posterior left ventricular wall.[3] This disproportionate increase in septal wall thickness relative to the posterior left ventricular free wall may be quantified by M-mode echocardiography and has led to the use of the term asymmetric septal hypertrophy (ASH) to describe this condition.[4] In an effort to identify potential perioper-

Table 1. Definitions of Major and Minor Adverse Outcomes

Major outcomes	
Myocardial infarction	New Q waves on ECG of at least 0.04 s in duration and 1 mm or more in depth, or new ST-segment depression or T-wave inversion that either was associated with chest pain typical of myocardial ischemia or could not be explained on the basis of medications or electrolyte imbalance and was associated with elevations of serum creatine phosphokinase isoenzymes (MB fraction)
Life-threatening dysrhythmia	Supraventricular or ventricular dysrhythmia requiring urgent cardioversion
Cardiac death	Patient death within 72 h of surgery from an arrhythmia or from refractory low cardiac output that was not part of an inexorable downhill course primarily caused by some noncardiac condition, such as sepsis, respiratory failure, or metastatic cancer
Minor outcomes	
Congestive heart failure	Chest x-ray changes consistent with pulmonary edema or respiratory distress and rales that improved promptly with diuretic therapy
Myocardial ischemia	Chest pain typical of myocardial ischemia in patient with history of angina pectoris On ECG, the presence of reversible ST-segment changes lasting at least 1 min and involving a shift from baseline of either >1 mm ST depression or >2 mm ST elevation 60 msec after the J point
Stable dysrhythmia	Supraventricular or ventricular dysrhythmia not requiring urgent cardioversion
Transient hypotension	Reversible reduction in systemic blood pressure not related primarily to changes in heart rhythm that is corrected through pharmacologic therapy or expansion of intravascular volume

ative risk factors associated with ASH, we reviewed the adverse cardiac outcomes in the patients identified by our database as having ASH.

Materials and Methods

A database containing summarized information from 20,914 echocardiographic reports, representing all studies performed at our institution between 9/1/85 and 11/30/93 was searched. Asymmetric septal hypertrophy was defined to be present when the ratio of septal thickness to posterior left ventricular wall thickness equaled or exceeded 1.5 on two-dimensional guided M-mode echocardiography.[5] Ninety-nine patients with ASH were identified. Seventy-seven of these patients had undergone one or more noncardiac surgical procedures, having had an echocardiogram within 24 months of surgery. The data on these 77 patients represent the basis for this report. If patients had more than one surgical procedure, only the first was used for analysis to avoid the confounding influence of the first surgery (and events) on subsequent surgeries (and events).

The patent's hospital record was reviewed from the time of preoperative evaluation. The anesthetic and/or surgical preoperative evaluations were used. Abnormal left ventricular function was defined as echocardiographic evidence of global or focal left ventricular systolic dysfunction. Hypercontractility was not considered systolic dysfunction. The intensity of intravascular monitoring also was noted, and four levels of monitoring were defined: patients without intravascular monitoring, patients with intraarterial pressure monitoring, patients in whom right atrial pressure was monitored, and patients in whom pulmonary artery catheters were inserted. Intraabdominal and intrathoracic procedures were classified as major surgeries. All others were considered minor procedures.

The medical record was examined for evidence of either intraoperative or postoperative adverse cardiac events. Major events were defined as myocardial infarction, life-threatening dysrhythmias, and cardiac death.[6] Congestive heart failure (CHF), myocardial ischemia, stable dysrhythmias, and transient hypotension constituted minor events (table 1).

Continuous variables are summarized as mean ± standard deviation. Univariate testing of the association of type of surgery or of adverse events used Wilcoxon's rank sum test (for continuous variables), Fisher's exact test (for binary variables) or extensions (for unordered, categorical variables), or Cochran-Mantel-Haenszel test for trend (for ordered discrete variables, *e.g.*, intensity of invasive monitoring). Logistic regression was used for multivariate modeling of predictors of adverse events. Because of the importance of duration of surgery as a predictor and its extremely strong association with type of surgery, the log duration was standardized for type of surgery in the logistic regression model. All analyses used SAS V6.10 statistical software (SAS Insti-

Table 2. Clinical and Echocardiographic Data

Mean age (yr) (range)	71 ± 13 (36–96)
Male (%)	43
Clinical history of syncope (%)	9
Dyspnea (%)	39
Prior MI (%)	36
Mean septal thickness (mm)	20 ± 3
SAM (%)	45
LVOT gradient ≥ 10 mmHg (%)	39
LV dysfunction (%)	20

MI = myocardial infarction; SAM = systolic anterior motion of the anterior mitral leaflet; LVOT = left ventricular outflow tract gradient; LV = left ventricle.

tute, Cary, NC). $P < 0.05$ (two-sided) was used to determine statistical significance.

Results

Population Description and Echocardiographic Data

Clinical and echocardiographic data are presented in table 2. Prior myocardial infarction had occurred in 28 patients (36%), including three who had experienced a myocardial infarction within the previous 6 months. The time between echocardiogram and surgery was 5.2 ± 6.4 months, with a range of 0–24 months. Eleven patients (14%) were tested within 1 or 2 yr of surgery.

The ratio of septal-to-posterior wall thickness was 1.7 ± 0.2. Thirty patients (39%) had a peak, resting LVOT gradient of 10 mmHg or greater as measured by continuous-wave Doppler echocardiography. The peak resting LVOT gradient in these 30 patients was 31 ± 22 mmHg on average (range 10–100 mmHg). Twenty-three (30%) patients had at least mild to moderate mitral regurgitation. Resting left ventricular systolic function could not be assessed on echocardiogram in two patients.

Surgery and Anesthesia

Thirty-five patients (45%) had surgery classified as major; 42 (55%) had surgery classified as minor. Thirty-nine patients (51%) had no intravascular monitoring, 16 (21%) had invasive monitoring of arterial blood pressure, in 8 patients (10%) right atrial pressure was measured, and in 14 (18%) patients pulmonary artery catheters were inserted. There was a significant association of intensity of monitoring with major/minor surgery ($P < 0.001$).

Sixty-two patients (81%) had general anesthesia with or without regional anesthesia. Twelve (16%) had regional techniques alone (7 spinal, 3 epidural, 2 upper extremity blocks); and three patients (4%) had monitored anesthetic care (MAC). The mean duration of surgery was 151 ± 102 min, with a range of 10–450 min. Major surgeries lasted an average 2 h longer than minor surgeries ($P < 0.001$).

Adverse Events

Overall, 31 (40%) patients had at least one adverse cardiac event (table 3). There was one patient with two major events (myocardial infarction and ventricular tachycardia requiring emergent cardioversion). This patient also developed postoperative CHF, a minor outcome. There were no intraoperative or postoperative deaths. All 31 patients had at least one minor outcome. Twelve of the 77 patients (16%) developed perioperative CHF.

Predictors of Adverse Events

Among 35 patients undergoing major surgical procedures, 20 (57%) had some adverse event. In contrast, only 11 of 42 (26%) patients undergoing minor procedures had some adverse event ($P < 0.01$). There was also a significant association of intensity of monitoring with the likelihood of adverse outcome ($P < 0.001$) overall, and this trend was found both in patients with minor surgery and with major surgery separately. Increasing length of the surgical procedure was associated with adverse outcome ($P < 0.001$) overall, and similar differences were found for both types of surgery. Increasing age was associated with adverse outcome ($P < 0.05$ overall), but this association was found only in patients with minor surgery ($P < 0.05$) and not in patients with major surgery ($P > 0.50$).

Table 3. Adverse Events

Adverse Outcome	% Patients with Outcome
Death	0
MI	1
Life-threatening dysrhythmia	1
CHF	16
Myocardial ischemia	12
Stable dysrhythmia	25
Transient hypotension	14

MI = myocardial infarction; CHF = congestive heart failure.

Gender, magnitude of resting LVOT gradient, systolic anterior motion, severity of mitral regurgitation, left ventricular dysfunction, history of prior myocardial infarction, time between echocardiogram and surgery, and septal thickness were not related to the occurrence of adverse cardiac events (all $P > 0.15$). There were no significant differences in outcome in patients having general anesthesia, regional anesthesia, or MAC ($P > 0.15$). There was a suggestion that patients having general anesthesia fared worse, with 28 (45%) having an adverse event compared to 3 (20%) of those who had regional anesthesia or MAC, but this difference was not statistically significant ($P = 0.09$).

Because of the association between the predictive variables, a multivariate model was developed. In this model, we found that important predictors of adverse outcome were: type of surgery (major *vs.* minor; $P < 0.05$), log duration of surgery (standardized for type of surgery; $P < 0.01$), and intensity of monitoring ($P < 0.05$). Age was not a significant predictor of outcome after adjustment for other variables ($P > 0.25$). In addition, general *versus* regional and MAC anesthesia was not an important predictor after adjustment for other variables ($P > 0.05$).

Discussion

This study demonstrates that patients with ASH, whether or not they have LVOT obstruction have frequent perioperative, adverse cardiac events when undergoing noncardiac surgery. Common adverse events include CHF, myocardial ischemia, perioperative hypotension, and stable dysrhythmia. Patients with ASH at particular risk for these outcomes are those undergoing longer procedures and those undergoing major surgeries. It should be emphasized, however, that the incidence of severe outcomes such as death and myocardial infarction in these patients is extremely low.

Many data are available concerning cardiac risk for patients with coronary artery disease undergoing noncardiac surgery,[6,7] but few are available regarding such risks for patients with ASH. Prospective data are completely lacking in this group of patients. One reason for this is clear: ASH is a rare abnormality with a reported incidence of 0.1% and 0.5% in the general populace and in patients with cardiac disease, respectively.[8] In our group of patients undergoing echocardiography in a tertiary care center, there was an incidence of 0.47%, (99 of 20,914).

Thompson *et al.* retrospectively examined their experiences with 35 patients with ASH who underwent one or more surgical procedures between 1961 and 1983.[2] Asymmetric septal hypertrophy was defined as the presence of an outflow tract gradient at cardiac catheterization and/or echocardiographic evidence of ASH (intraventricular septum to posterior wall thickness ratio of >1.3:1) and systolic anterior motion of the mitral valve. The peak resting outflow tract gradient was 30 mmHg on average and varied from 0 to 150 mmHg, similar to the values obtained in our current study. There were no perioperative cardiac deaths. One patient sustained a myocardial infarction and CHF diagnosed 4 h after receiving a spinal anesthetic. The most common complications were atrial dysrhythmias requiring treatment (14%) and hypotension requiring vasoconstrictors (14%), each occurring in 5 of 35 patients. By comparison in our study, one patient had a myocardial infarction, 16% of patients manifested CHF, 25% had stable dysrhythmias, and 14% became transiently hypotensive. The authors concluded from these data that anesthetic risk in these patients is low. They advised against spinal anesthesia, because of the fear that sympatholysis would cause ventricular hypovolemia and because of its association with the only myocardial infarction in their series of 35 patients. The remainder of the anesthetic literature consists largely of anecdotal case reports.[9–14]

We have confirmed Thompson's observation of a very low rate of postoperative death and myocardial infarction in patients with ASH. In contrast to their findings, we have found a greater risk of complications in patients with ASH undergoing anesthesia and surgery. Forty percent had some adverse event, including 16% who developed postoperative CHF. The possible explanations for these differences between our study and Thompson's likely result from differences in patient characteristics. The patients in the current study have a mean age of 71 yr, 18 yr older than the mean age of 53 yr in Thompson's study. Although data exist that both support and refute age as a predictor of adverse cardiac outcome, some may contend that this difference alone would predict the difference in findings between the two studies.[7] Increasing age, however, did not predict poor outcome in our group of patients after adjusting for other factors. The specific surgical procedures performed are not mentioned in the study by Thompson, making it impossible to directly compare differences in the surgical procedures between the two cohorts. Differences in the results of these two studies, therefore, may be attributable to differences in surgical severity. We have used a two-dimensional guided, M-mode derived septal-to-posterior wall thickness ratio of 1.5 or greater to define ASH in our cohort. A septal-to-posterior wall thickness ratio >1.3, as used by Thompson *et al.*[2] would not meet the criteria currently used to make this diagnosis.[5] In addition, the current availability of two-dimensional guided M-mode largely precludes inadvertent off-axis measurements of wall thickness. Off-axis measurement in Thompson's study might have given a false-positive diagnosis of ASH and therefore tended to reduce the observed complication rate.

The high incidence of CHF in the current study is remarkable and may be related to the frequent finding of diastolic dysfunction in patients with ASH. It is possible that the changes in intravascular and ventricular volume that occur during major operative procedures may surpass the limit of effective cardiovascular compensation in this disorder. Both increased and decreased intraventricular volume potentially threaten the patient with ASH with left ventricular failure. With a sufficient reduction in intraventricular volume, the likelihood of a new or increased systolic LVOT gradient is increased. If volume is increased, left ventricular diastolic dysfunction ensures that end diastolic pressure (and therefore pulmonary capillary pressure) will rise disproportionately. It must be emphasized that our definition of CHF does not allow differentiation of true systolic or diastolic dysfunction from alveolar edema that results from volume overload. Therefore, the frequent occurrence of CHF in this study may result from aggressive fluid therapy during anesthesia in an attempt to sustain preload. Whatever the etiology of this outcome, the clinician is well-advised to be particularly watchful for signs of CHF in these patients during the postoperative period.

Increasing length of surgery was a strong independent predictor of poor outcome in this group of patients. In fact, it was a stronger predictor of adverse cardiac events than whether the patient had major or minor surgery. Patients with increasing degrees of intravascular monitoring had significantly more adverse outcomes than patients who received less intensive monitoring. It is unlikely that increased monitoring itself contributes to poor outcome, but rather may reflect that anesthesiologists often can identify the high-risk patients and operations, leading them to use invasive monitoring.

Two measures often used clinically to quantify the severity of ASH are septal thickness and severity of resting LVOT gradient. Neither was related to adverse outcome in our cohort. This may reflect that septal thickness does not necessarily imply obstructive physiology and that the LVOT gradients measured in these patients at rest may not reflect the degree of obstruction seen with physiologic stress encountered perioperatively.

Thompson *et al.*[2] recommended avoidance of spinal anesthesia in patients with ASH. In our series, 15 patients had anesthetics other than general anesthesia (7 spinal, 3 epidural, 2 upper extremity blocks, and 3 MAC). Type of anesthesia was not an important predictor of outcome after adjusting for major *versus* minor surgery. Of the ten patients who received spinal or epidural anesthesia, only one developed postoperative CHF and one developed intraoperative hypotension with the onset of the regional block. We found no reason to advise against the use of regional anesthesia in patients with ASH as long as hemodynamics are controlled. In fact, given the paucity of severe outcomes, we find it difficult to advise against major surgery in these patients. A high incidence of CHF in the postoperative period should be anticipated, however.

Limitations. Data gathered retrospectively may be flawed. For example, only one patient met our definition of myocardial infarction. Because clinical detection of myocardial infarction may be insensitive, there may have been a number of events (particularly smaller infarctions) that were clinically missed. Similarly, our definition of CHF does not allow us to differentiate true systolic or diastolic dysfunction from alveolar edema that results from volume overload. Complete and rigorous data regarding perioperative fluid administration were not available. Because much of what we define as "heart failure" may be fluid overload with resultant alveolar and interstitial edema (a diagnosis with presumably less dire consequences), we classified this outcome as minor.

The interval between echocardiographic testing and surgery was longer than 1 yr in 11 (14%) patients (range 0–24 months). We included these patients, in part, to derive data on as many patients as possible, realizing that ASH is a chronic and very slowly progressive disease in adults. Asymmetric septal hypertrophy is a disease that is generally morphologically apparent in the third decade of life with appearance of symptoms 20–30 yr later.[15] Consistent with the chronic nature of this pathologic process, annual mortality in this patient population is reported to be approximately 1%.[16,17] The length of the interval between echocardiogram and surgery was not predictive of outcome in this group of patients.

We conclude that patients with ASH, with or without LVOT obstruction, are at risk for perioperative adverse cardiac events when undergoing noncardiac surgery. Common adverse events include CHF, myocardial ischemia, perioperative hypotension, and stable dysrhythmias. Important predictors of adverse outcome were major surgery and duration of surgery. The incidence of severe outcomes such as death and myocardial infarction in these patients is extremely low.

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