Coronary artery bypass surgery prior to resection of abdominal aortic aneurysm in patients with unstable coronary artery disease

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Coronary artery disease (CAD) is associated with abdominal aortic aneurysm in greater than 60% of cases. CAD continues to affect postoperative complication rates. Half of the deaths that follow resection of abdominal aortic aneurysms are due to perioperative myocardial infarctions. On evaluation for surgical resection of an abdominal aortic aneurysm, six patients were found to have significant CAD. Each underwent coronary artery bypass surgery prior to elective resection of the aneurysm. No deaths or myocardial infarctions occurred following any of the procedures. We restrict our indications for coronary angiography to the evaluation of patients with unstable angina (pain at rest or after minimal exertion) in whom noninvasive studies reveal evidence of CAD, and for patients who are unresponsive to medical management.

Atherosclerosis is a systemic disease that steadily progresses to end organ symptoms. The simultaneous occurrence of coronary artery disease (CAD) and abdominal aortic aneurysm approaches 60%.^{1,2} Myocardial infarction (MI) is the leading cause of death following the resection of such aneurysms.³⁻⁵ Patients with a history of CAD or previous MI also have increased risk of surgical morbidity.^{6,7}

The evaluation of patients with abdominal aortic aneurysms should include a precise cardiac his-

tory. We also believe that patients who have significant CAD and angina that is not well controlled with medical therapy should undergo cardiac catheterization. For patients at greatest risk, coronary artery bypass surgery (CABS) prior to vascular resection affords myocardial protection during the perioperative period. Patients should be evaluated on an individual basis. When appropriate, CABS should be performed six to eight weeks prior to the resection of the aneurysm. Our success and the results that appear in the literature have encouraged us to continue this approach.

Patient selection and results

Six male patients ranging in age from 56 to 69 years were evaluated for abdominal aortic aneurysm; all had significant CAD. In all patients, angiography confirmed the presence of the aneurysms, which had been detected on routine physical examination. The aneurysms measured 8 to 10 cm in their greatest diameters. All patients had unstable angina, either at rest or after minimal exertion. Four patients had a history of MI. In one (patient 4), MI followed an episode of hemorrhage from an active duodenal ulcer. Four patients had positive stress ECGs. At cardiac catheterization, all six patients were found to have triple vessel disease, and patients 4 and 6 had occlusion of the left main coronary artery (Table 1).

CABS was performed six to eight weeks before vascular resection for five patients; at his own request, aneurysmorrhaphy was delayed for one year for patient 2. CABS was accomplished with reversed saphenous vein grafts and cold potassium

TABLE 1. CARDIAC HISTORIES AND CATHETERIZATION RESULTS FOR SIX MALE PATIENTS WHO HAD ELECTIVE RESECTION OF ABDOMINAL AORTIC ANEURYSMS (AAA) WITH 100% POSTOPERATIVE SURVIVAL.

Patient	Age (yr)	CAD symptoms	ECG	Medical therapy	Catheterization data		CAD surgery	AAA surgery
					Artery	% Block		
1	56	Angina, dyspnea	Nonspecific ST segment changes	Verapamil, digoxin	LAD LCx LCx Mg RCA RV Br	100 90 80 100 90	CABS 5	9-cm AAA, 22-mm aortoiliac bifurcation graft
2	66	Angina, dyspnea, previous MI, HBP, positive stress test	LAHB, old MI	Aldomet, NTG, procainamide, digoxin	LMain LCx Mg RCA	100 60 50	CABS 3	8-cm AAA, 19-mm aortoiliac bifurcation graft
3	68	Angina, dyspnea, 2 previous MIs, HBP	Q (II,III), Q (AVF)	Inderal, NTG, Procardia, digoxin	LAD LCx Mg Interm RCA	100 80 100 100	CABS 6 resection LV aneurysm	8-cm AAA, 22-mm aortoiliac bifurcation graft
4	69	MI (GI bleeding) positive stress test	1° AV block, LVH	Procardia, NTG	LMain LAD LAD Dg RCA	90 85 90 100	CABS 6	10-cm AAA, 22-mm straight graft
5	66	Hypotensive, previous laparotomy, HBP, positive stress test	Nonspecific ST segment changes, T wave inversion.	Aldomet, insulin, Timolol	LAD LCx Mg LAD Dg RCA	90 80 75 100	CABS 4	9-cm AAA, 20-mm straight graft
6	69	Angina, HBP, previous MI	Atrial fibrillation, old MI, T wave inversion	Digoxin, Tolinase, Procardia	LMain LAD RCA	90 90 100	CABS 3	8-cm AAA, 20-mm aortoiliac bifurcation graft

CAD = coronary artery disease; MI = myocardial infarction; HBP = high blood pressure; GI = gastrointestinal; LAHB = left anterior hemiblock; AVF = atrioventricular fibrillation; AV = atrioventricular; LVH = left ventricular hypertrophy; NTG = nitroglycerin; LAD = left anterior descending; LCx = left circumflex coronary artery; LCx Mg = left circumflex coronary artery, marginal; RCA = right coronary artery; RV Br = right ventricular branch of the right coronary artery; LMain = left main artery; Interm = intermediate branch; LAD Dg = left anterior descending; CABS = coronary artery bypass surgery; LV = left ventricular.

Fig 1. Survival rates of patients with and without surgical resection of abdominal aortic aneurysms, from time of diagnosis or surgery to death.

cardioplegia. After systemic heparinization, patients underwent aneurysmorrhaphy with woven Dacron grafts. All of the procedures were performed on an elective basis.

Following the operative procedures, the patients received appropriate intensive care monitoring. Pneumonia developed in patient 6 subsequent to resection. He had no other postoperative complication during recovery. The other patients had no significant complications postoperatively, and none of the patients had ECG changes after surgery. All patients are alive and well at this time of the writing of this article.

Discussion

Mortality rates

Over the past 30 years, the mortality rates for elective resection of abdominal aortic aneurysms have declined from approximately 15% during the early years (1950s) to 3% to 5% at present.

Several reviews illustrate the progressive improvement in mortality rates.⁸⁻¹⁵

Improvements in fluid management, precise perioperative hemodynamic monitoring, and newer anesthetic agents have helped to minimize operative mortality. Improvements in prosthetic materials,

refinements in surgical techniques, and a trend toward resecting smaller aneurysms also have enhanced survival in patients undergoing elective resection.

One factor not to be discounted is the much improved therapy of associated disease. Careful screening of patients for cardiac risk factors has had a significant impact on patient survival.

The incidence of MI following elective resection of abdominal aortic aneurysms is 4%, in contrast to an expected 0.1% to 0.7% incidence of MI for all surgical procedures performed for patients receiving a general anesthetic. Also, MI accounts for 50% of the postoperative deaths, which is significantly greater than the 15% to 20% mortality rates associated with MI in the nonsurgical population.^{1,3,6,10-14,16-21}

Surgical risk

At greatest risk are patients with significant CAD. For patients who have survived a previous MI who undergo general anesthesia for a surgical procedure, the reinfarction rate is 6% to 7%, with an expected mortality rate of 65%.²²

The unresected abdominal aortic aneurysm also carries a high mortality rate. From the time of diagnosis, only 55% of patients with aneurysms ≥ 5 cm, as demonstrated on plain abdominal radiography, will survive one year without surgery (Fig 1).^{8,14,16-20,23-36} By three and five years after diagnosis, the survival rate declines to 34% and 19%, respectively. Although 21% will die as a result of MI, 30% will die of a ruptured aneurysm. The mortality rate for ruptured abdominal aortic aneurysms requiring emergency surgery is approximately 50%. Without surgery, ruptured aneurysms invariably prove fatal.

In the past, many patients with advanced CAD had been refused surgery for abdominal aortic aneurysm. However, after the first postoperative year, survival rates for these patients who have undergone resection approaches that of the normal, age-related population (Fig 1). The three- and five-year survival rates for patients who have resected aneurysms [v] those for patients with unresected aneurysms (70% [v] 34% and 53% [v] 19%, respectively) clearly demonstrate the benefit of elective surgical resection of abdominal aortic aneurysms.

Presurgical evaluation

How extensive should the investigation of CAD be? Several vascular surgical centers perform simultaneous cardiac and abdominal aortic angiography. At the Cleveland Clinic, preoperative cardiac catheterization revealed triple-vessel CAD in 31% of 91 patients who had no clinical indication of

TABLE 2. CORONARY ARTERY BYPASS SURGERY PRIOR TO RESECTION OF ABDOMINAL AORTIC ANEURYSM

Study	No. of cases	Mortality	No. of myocardial infarctions
Hertzer et al (1984) ⁵	61	1	...
Crawford et al (1978) ³⁸	49	0	0
Kramer et al (1982) ¹	29	0	0
Hertzer et al (1979) ³⁹	21	0	0
McCollum et al (1977) ⁴⁰	17	0	0
Edwards et al (1978) ⁴	9	0	0
Brown et al (1981) ⁶	6	0	0
Chang et al (1978) ²¹	3	0	0
Szarnicki et al (1971) ⁴¹	2	0	0
Present study	6	0	0
Total	203	1	0

CAD.³⁶ However, none of these patients had disease of the left main coronary artery without some clinical evidence of CAD.

We believe that electrocardiography should be performed routinely, and we find gated pool nuclear (MUGA) scanning with cardiac output determination helpful. Stress electrocardiography and stress thallium scanning may be done selectively.

Reports from two large series (422⁶ and 517⁹ of patients) in which unstable angina (pain at rest or after minimal exertion) was the principal consideration for cardiac angiography and in which nearly all patients had not undergone CABS prior to aneurysm resection, overall mortality was 1.7% (7 deaths, 4 from MI) and 2.3% (12 deaths, 9 from MI), respectively.

Conclusions

We believe that these mortality rates are acceptable, but we do not believe that proceeding with CABS in patients with CAD who are clinically asymptomatic would provide any significant benefit, especially in view of the 3% to 5% mortality attendant to CABS.

We further believe that coronary angiography (and CABS) is unnecessary in patients with CAD who have their disease well controlled on a medical regimen, who have no significant past cardiac history, and who have normal findings on noninvasive cardiac evaluation.

Advanced CAD should not serve routinely as a contraindication to aneurysmorrhaphy. CABS may be performed with an acceptable degree of safety. Review of the literature confirms that CABS prior to resection of abdominal aortic aneurysms affords excellent myocardial protection (Table 2).^{1,4-6,21,38-41}

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CAUTION: Federal law prohibits dispensing without prescription.

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Seldane (terfenadine) is available as tablets for oral administration. Each tablet contains 60 mg terfenadine. Tablets also contain, as inactive ingredients: corn starch, gelatin, lactose, magnesium stearate, and sodium bicarbonate.

INDICATIONS AND USAGE

Seldane is indicated for the relief of symptoms associated with seasonal allergic rhinitis such as sneezing, rhinorrhea, pruritus, and lacrimation.

CONTRAINDICATIONS

Seldane is contraindicated in patients with a known hypersensitivity to terfenadine or any of its ingredients.

PRECAUTIONS

Information for patients

Patients taking Seldane should receive the following information and instructions. Antihistamines are prescribed to reduce allergic symptoms. Patients should be questioned about pregnancy or lactation before starting Seldane therapy, since the drug should be used in pregnancy or lactation only if the potential benefit justifies the potential risk to fetus or baby. Patients should be instructed to take Seldane only as needed and not to exceed the prescribed dose. Patients should also be instructed to store this medication in a tightly closed container in a cool, dry place, away from heat or direct sunlight, and away from children.

Carcinogenesis, mutagenesis, impairment of fertility

Oral doses of terfenadine, corresponding to 63 times the recommended human daily dose, in mice for 18 months or in rats for 24 months, revealed no evidence of tumorigenicity. Microbial and micronucleus test assays with terfenadine have revealed no evidence of mutagenesis.

Reproduction and fertility studies in rats showed no effects on male or female fertility at oral doses of up to 21 times the human daily dose. At 63 times the human daily dose there was a small but significant reduction in implants and at 125 times the human daily dose reduced implants and increased post-implantation losses were observed, which were judged to be secondary to maternal toxicity.

Pregnancy Category C

There was no evidence of animal teratogenicity. Reproduction studies have been performed in rats at doses 63 times and 125 times the human daily dose and have revealed decreased pup weight gain and survival when terfenadine was administered throughout pregnancy and lactation. There are no adequate and well-controlled studies in pregnant women. Seldane should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nonteratogenic effects

Seldane is not recommended for nursing women. The drug has caused decreased pup weight gain and survival in rats given doses 63 times and 125 times the human daily dose throughout pregnancy and lactation. Effects on pups exposed to Seldane only during lactation are not known, and there are no adequate and well-controlled studies in women during lactation.

Pediatric use

Safety and effectiveness of Seldane in children below the age of 12 years have not been established.

General

Consideration should be given to potential anticholinergic (drying) effects in patients with lower airway disease, including asthma.

ADVERSE REACTIONS

Experience from clinical studies, including both controlled and uncontrolled studies involving more than 2,400 patients who received Seldane, provides information on adverse experience incidence for periods of a few days up to six months. The usual dose in these studies was 60 mg twice daily, but in a small number of patients, the dose was as low as 20 mg twice a day, or as high as 600 mg daily.

In controlled clinical studies using the recommended dose of 60 mg b.i.d., the incidence of reported

adverse effects in patients receiving Seldane was similar to that reported in patients receiving placebo. (See Table below.)

ADVERSE EVENTS REPORTED IN CLINICAL TRIALS

Adverse Event	Percent of Patients Reporting			All Clinical Studies**	
	Seldane N=781	Placebo N=665	Control N=626***	Seldane N=2462	Placebo N=1478
Central Nervous System					
Drowsiness	9.0	8.1	18.1	8.5	8.2
Headache	6.3	7.4	3.8	15.8	11.2
Fatigue	2.9	0.9	5.8	4.5	3.0
Dizziness	1.4	1.1	1.0	1.5	1.2
Nervousness	0.9	0.2	0.6	1.7	1.0
Weakness	0.9	0.6	0.2	0.6	0.5
Appetite Increase	0.6	0.0	0.0	0.5	0.0
Gastrointestinal System					
Gastrointestinal Distress (Abdominal distress, Nausea, Vomiting, Change in Bowel habits)	4.6	3.0	2.7	7.6	5.4
Eye, Ear, Nose, and Throat					
Dry Mouth/ Nose/Throat	2.3	1.8	3.5	4.8	3.1
Cough	0.9	0.2	0.5	2.5	1.7
Sore Throat	0.5	0.3	0.5	3.2	1.6
Epistaxis	0.0	0.8	0.2	0.7	0.4
Skin					
Eruption (including rash and urticaria) or itching	1.0	1.7	1.4	1.6	2.0

*Duration of treatment in "CONTROLLED STUDIES" was usually 7-14 DAYS.

**Duration of treatment in "ALL CLINICAL STUDIES" was up to 6 months.

***CONTROL DRUGS: Chlorpheniramine (291 patients), d-Chlorpheniramine (189 patients), Clemastine (146 patients)

In addition to the more frequent side effects reported in clinical trials (See Table), adverse effects have been reported at a lower incidence in clinical trials and/or spontaneously during marketing of Seldane that warrant listing as possibly associated with drug administration. These include: alopecia, (hair loss or thinning), anaphylaxis, angioedema, arrhythmia (including ventricular tachyarrhythmia), bronchospasm, confusion, depression, galactorrhea, hypotension, insomnia, menstrual disorders (including dysmenorrhea), musculoskeletal symptoms, nightmares, palpitation, paresthesia, photosensitivity, prolonged QT interval, seizures, sweating, syncope, tachycardia, tremor, urinary frequency, and visual disturbances. In clinical trials, several instances of mild, or in one case, moderate transaminase elevations were seen in patients receiving Seldane. Mild elevations were also seen in placebo treated patients. Marketing experiences include isolated reports of jaundice, cholestatic hepatitis, and hepatitis; in most cases available information is incomplete. In neither the clinical trials nor marketing experience is a causal relationship of liver abnormalities to Seldane use clear.

OVERDOSAGE

Information concerning possible overdose and its treatment appears in Full Prescribing Information.

DOSAGE AND ADMINISTRATION

The usual dosage for adults and children 12 years and older is 60 mg (1 tablet) twice daily.

Product Information as of June, 1988

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