

## CASE REPORTS

## Ischemic Gastroparesis: Resolution After Revascularization

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Patients with chronic nausea and vomiting frequently present challenging diagnostic and therapeutic problems. In such patients, gastroparesis of unknown cause, or "idiopathic" gastroparesis, may be the only objective finding. Two middle-aged women with nausea, vomiting, and weight loss of 10 and 26 kg over 6 and 18 months, respectively, were evaluated. Routine laboratory and barium study results were normal. Solid-phase gastric emptying studies showed severe gastroparesis in both patients. Upper endoscopies excluded gastric outlet obstruction. Gastric dysrhythmias (4-cpm and 1-cpm patterns) were recorded using cutaneous electrodes. An abdominal bruit was auscultated in one patient. Abdominal arteriograms in both patients showed total occlusion of all three major mesenteric vessels with collaterals supplied via hemorrhoidal arteries. Bypass grafting procedures of the celiac and superior mesenteric arteries in one patient and of the celiac artery in the other patient were performed. Six months after mesenteric artery revascularization, upper gastrointestinal symptoms had resolved and original weights were regained. Furthermore, normal 3-cpm gastric myoelectrical activity and normal gastric emptying of solids were restored in both patients. In these patients, chronic mesenteric ischemia resulted in a novel and reversible cause of gastroparesis, gastric dysrhythmias, and accompanying symptoms.

**G**astric emptying is delayed in a variety of clinical settings, including diabetes mellitus, amyloidosis, scleroderma, systemic lupus erythematosus, dermatomyositis, and myotonic and muscular dystrophy, and in some patients after gastric surgery (1). The pathogenesis of gastroparesis in these conditions is believed to involve neuromuscular abnormalities of the stomach. However, mechanical obstruction of the gastrointestinal tract must be excluded in all patients with gastroparesis. A group of patients with gastroparesis in

which the cause remains unexplained, i.e. idiopathic gastroparesis (1), remains.

Herein we report on two patients with nausea, vomiting and idiopathic gastroparesis in whom three-vessel mesenteric artery occlusions were discovered. Chronic mesenteric ischemia usually occurs in elderly individuals with abdominal pain and weight loss (2-6). Our patients were middle-aged and had symptoms compatible with their documented gastroparesis. Furthermore, after mesenteric revascularization, upper gastrointestinal symptoms and gastroparesis resolved in both patients. Recognition of this entity is important because symptoms and gastroparesis are reversible with corrective vascular surgery.

### Materials and Methods

#### *Gastric Emptying Test*

Patients fasted for at least 8 hours before solid-phase gastric emptying tests were performed. No medications that might affect gastric emptying were allowed for 48 hours before the studies. The standard meal consisted of two eggs mixed thoroughly with 500  $\mu$ Ci of technetium 99m sulfur colloid and then cooked until done. A large-field-of-view camera with a parallel hole collimator was used. The energy range for technetium 99m was preset with a 20% window, and the preset stop was set for 60 seconds. Immediately after the eggs were ingested, a static scintigraphic image was taken in the anterior position and recorded on an  $\alpha$ -microdot computer. The patient relaxed in an upright position until the next 1-minute scintigram was obtained 15 minutes later in the supine position. This procedure continued with 1-minute scans 15, 30, 45, 60, 75, 90, 105, and 120 minutes after ingestion of the eggs. In studies from 10 healthy control subjects, the  $t_{1/2}$  averaged 75 minutes and the percentage

*Abbreviations used in this paper:* EGG, electrogastrogram; RSA, running spectral analysis; SMA, superior mesenteric artery.

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0016-5085/90/\$3.00

emptied at 120 minutes averaged 83%. Patients with prolonged  $t_{1/2}$  or percentage emptied  $<2$  SD above the mean at 120 minutes, i.e.,  $<60\%$  emptied, were considered normal.

### Electrogastrography

Standard electrodes (Miniature Skin Electrodes, SensorMedics Corp., Anaheim, CA) were positioned on the abdomen to record the electrogastrogram (EGG). Three electrodes were placed in the left upper quadrant and epigastric regions: the first electrode was positioned below the left rib margin in the midclavicular line, the third electrode was placed equidistant between the xiphoid process and the umbilicus, and the second electrode was positioned along a line between the first and third electrode. The fourth electrode served as a reference electrode and was positioned in the right upper quadrant along the line formed by the other three electrodes. The skin beneath the electrodes was abraded gently before attaching the electrodes. The electrodes were connected to a rectilinear recorder (R611, SensorMedics) through direct nystagmus couplers (9859, SensorMedics). The low-frequency cutoff was 0.016 Hz, and the high-frequency cut off was 0.30 Hz. The EGG signals were recorded simultaneously on magnetic tape (Honeywell 101, Honeywell Instruments, Denver, CO) for computer analysis.

Each patient ate a 200-kcal breakfast (juice and toast) 2 hours before the EGG recording. After a 20-minute baseline recording, the patients ingested 240 mL of water in a 2-minute period. The recording channel with the clearest EGG signal was chosen for visual and computer analysis. Approximately 3-cpm EGG waves (2.5–3.5 cpm) were considered normal; 4–9-cpm waves were considered tachyarrhythmias/tachygastrias; and from 0–2.5-cpm waves were considered bradygastrias (7–9). Visual inspection of the EGG recording was used to determine the predominant gastric rhythm. Computer analysis representing approximately 40 minutes of EGG signals recorded from each subject were compared with the visual interpretation of the EGG signal to confirm the predominant frequency peaks and to ascertain shifts in EGG frequency that were not appreciated by visual inspection. Computer analysis of EGG records using analog to digital transformation, Fourier analysis, and running spectral analyses has been described previously (10).

### Case 1

A 56-year-old white woman presented with a 6-month history of nausea, vomiting of undigested foods, and occasional crampy epigastric to right lower quadrant pain. During this period, she lost 10 kg. Diagnostic studies included a normal upper gastrointestinal series with small bowel follow-through, normal abdominal ultrasound, and normal computed tomographic scan of the abdomen. She reported no relief of symptoms after antacids, ranitidine, and empiric trials of metronidazole for suspected giardiasis. She had a 40-pack-year smoking history and reported no alcohol use. Review of systems was remarkable for Raynaud's phenomenon. She was referred to the gastroenterology clinic to consider a drug trial for chronic unexplained nausea and vomiting.

Physical examination was notable for weight of 35 kg and right upper abdominal and right femoral bruits that had not been appreciated previously. Blood count, liver enzymes, protein, albumin, serum electrolytes, and glucose were normal. A 0.5 × 0.5-cm superficial antral ulceration was found by esophagogastroduodenoscopy; the pylorus was patent and the duodenum was normal. Solid-phase gastric emptying time was markedly delayed, with  $t_{1/2} >120$  minutes and 32% emptied 2 hours after ingestion. A Doppler study of the mesenteric arteries failed to define vascular flow. An arteriogram showed total occlusion of the celiac artery, superior mesenteric artery (SMA), and inferior mesenteric artery (Figure 1) with collaterals supplied by the left middle hemorrhoidal artery.

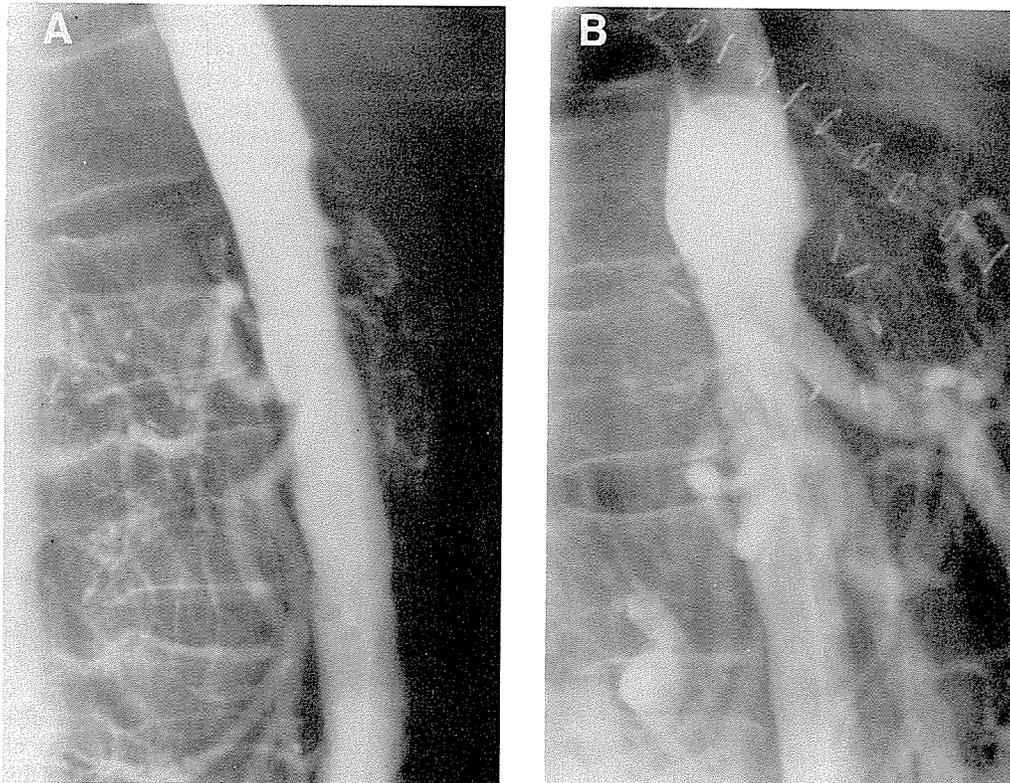
The patient underwent abdominal revascularization with an antegrade bifurcated graft from the aorta to the celiac axis and SMA. After surgery, her symptoms resolved, and by 6 months after revascularization her weight had increased 6 kg and gastric emptying was normal;  $t_{1/2}$  improved from  $>120$  minutes to 75 minutes, and the percentage emptied at 120 minutes improved from 32% to 80% (Figure 2).

Electrogastrograms and the running spectral analysis (RSA) of the EGG signal from this patient before revascularization are shown in Figure 3. The EGG shows rhythmic waves at 4 cpm (inset); the RSA also indicates that the predominant frequency is near 4 cpm. After ingestion of water, the amplitude of the EGG waves increases and the frequency remains 4 cpm; the RSA also shows that the predominant EGG rhythm is near 4 cpm. Smaller peaks are also seen in the  $<2$ -cpm and  $>4$ -cpm ranges. Figure 4 shows the EGGs and RSA recorded from 6 months after revascularization when the patient was symptom-free. The EGG shows rhythmic waves at 3–3.5 cpm, and the RSA also indicates regular peaks at 3–3.5 cpm, a frequency slightly slower than the preoperative rates and now within the normal range.

### Case 2

A 55-year-old white woman with a surgical history of cholecystectomy, appendectomy, and removal of a Meckel's diverticulum had an 18-month history of nausea, vomiting of undigested food, and constant "nagging" discomfort in the right upper quadrant that was sometimes relieved by vomiting. She lost approximately 26 kg during this period. Diagnostic studies included a normal upper gastrointestinal examination with small bowel series, barium enema, abdominal ultrasound, and computed tomographic scan. Fecal fat and 24-hour urine collections for 5-HIAA were negative. Several esophagogastroduodenoscopies showed varying degrees of mild superficial gastric and pyloric channel ulcerations but no evidence of pyloric or duodenal obstruction. Results of an endoscopic retrograde cholangiopancreatogram (ERCP) were normal. Symptoms did not improve with ranitidine, famotidine, sucralfate, or metoclopramide. She had a 30-pack-year history of smoking. She was referred to the gastroenterology clinic for treatment of idiopathic nausea and vomiting.

Physical examination showed a cachectic woman weighing 34 kg. Results of her examination were otherwise normal, and no abdominal bruits were auscultated. Routine laboratory studies were within normal limits. A solid-phase gastric emptying study was abnormal with  $t_{1/2} >120$  minutes,



**Figure 1.** A. Aortogram (lateral view) showing occlusions at the origin of the celiac artery, SMA, and inferior mesenteric artery (case 1). The patient in case 2 had similar angiographic findings.

B. Postoperative aortogram showing celiac artery and SMA grafts in case 1.

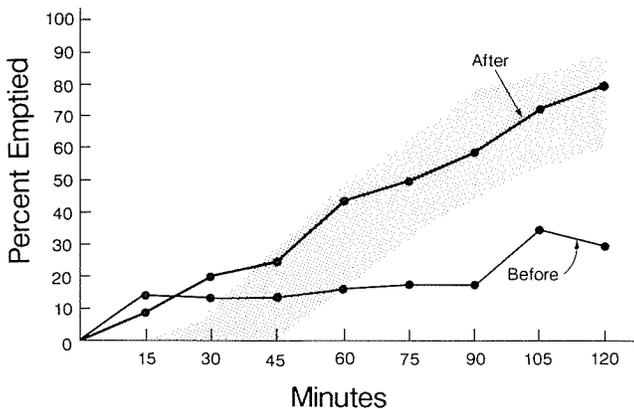
and only 44% of the meal emptied 2 hours after ingestion (Figure 5).

Vague lower abdominal discomfort developed and abdominal arteriograms were obtained. The radiographic findings were similar to those in case 1 and showed occlusion of the celiac artery, SMA, and inferior mesenteric artery with collaterals supplied by the middle hemorrhoidal artery. During surgery the celiac axis was absent and a calcified plaque was found at the origin of the SMA. The splenic and hepatic arteries arose from the proximal SMA. An aorto-SMA Dacron bypass graft was placed.

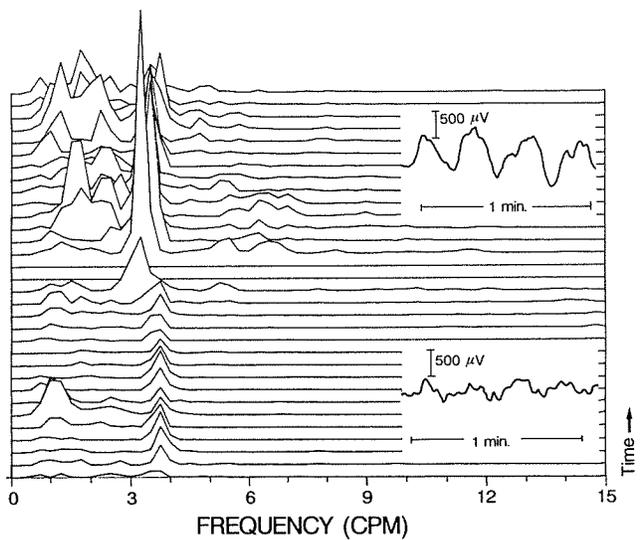
Six months after revascularization, the patient was symptom-free and had gained 17 kg. Figure 5 shows the solid-

phase gastric emptying results after mesenteric revascularization:  $t_{1/2}$  improved from 120 minutes to 85 minutes, and the percentage emptied at 120 minutes improved from 44% to 82% after revascularization.

Figure 6 shows the patient's EGGs and RSA before revascularization. The baseline EGG shows large 1-cpm waves (inset). The RSA shows predominant EGG frequen-



**Figure 2.** Solid-phase gastric emptying study before and after surgery shows improvement in gastric emptying after mesenteric revascularization (case 1).



**Figure 3.** Preoperative EGGs (insets) and RSA of EGG signal (case 1). The two flat lines indicate the time when 240 mL of water was ingested. The predominate EGG rhythm is regular at approximately 4 cpm; a similar frequency is apparent in the series of RSA peaks.

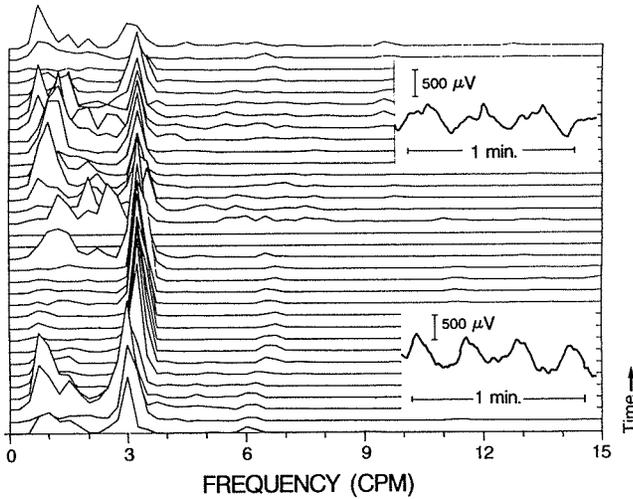


Figure 4. Postoperative EGGs (insets) and RSA (case 1) show predominantly rhythmic EGG waves at 3-3.5 cpm and corresponding peaks at 3 cpm in the RSA.

cies near 1 cpm; no 3 cpm waves or peaks are seen. After ingestion of water, the EGG waves and the RSA show no changes in frequency and no evidence of normal 3-cpm rhythms. Electrogastrograms obtained six months after revascularization (Figure 7) show rhythmic EGG waves within the normal range at 3-3.5 cpm; the RSA shows some 1-2-cpm peaks and many regular peaks at the normal 3-cpm range.

In both patients, follow-up Doppler studies have shown continued graft patency and normal flow patterns.

**Discussion**

An association between chronic mesenteric ischemia and gastroparesis has not been described previously. Thus, the major new findings provided by these studies are that (a) chronic mesenteric ischemia is a pathophysiological mechanism that may result in gastroparesis, and (b) ischemia-related gastroparesis,

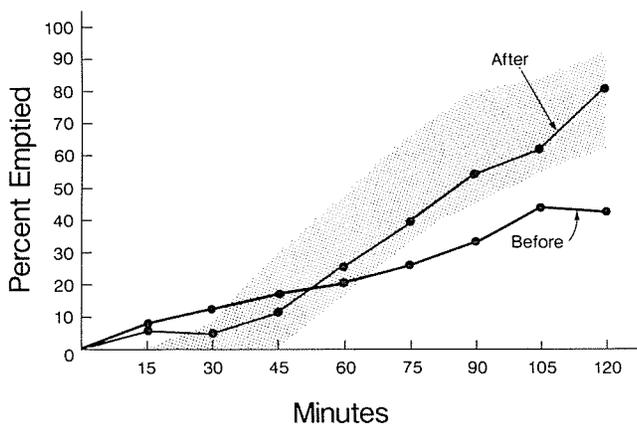


Figure 5. Solid-phase gastric emptying study (case 2) before and after mesenteric revascularization shows delayed emptying improved to within the normal range after operation.

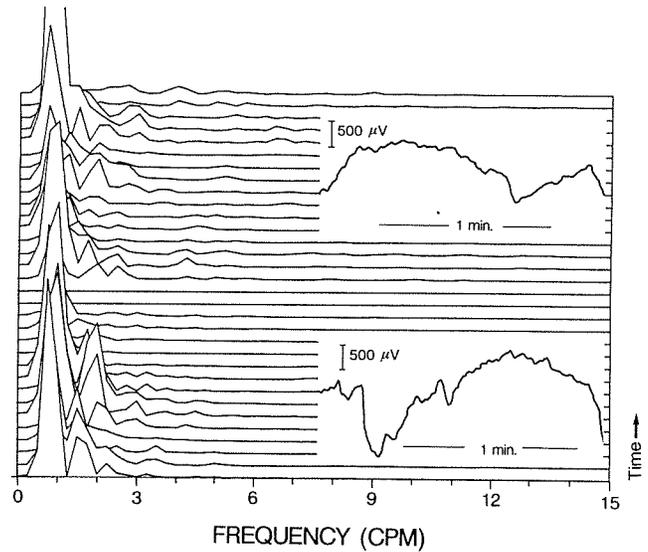


Figure 6. Preoperative EGGs (insets) and RSA of 30 minutes of EGG signal in a patient with mesenteric ischemia (case 2). Baseline EGG shows large 1-cpm waves. The RSA also indicates predominant frequencies near 1 cpm; no 3-cpm waves or peaks are seen. The two flat lines in the RSA indicate the point where 240 mL of water was ingested by the patient.

gastric dysrhythmias, and upper gastrointestinal symptoms are reversible after mesenteric artery bypass graft surgery.

Ingestion of meals normally stimulates a fed pattern of 3/min gastric peristalses that mix and empty the chyme into the small intestine where a fed pattern of segmental contractions continues the digestive and absorptive process. Our patients had abnormal preoperative solid-phase gastric emptying, but emptying

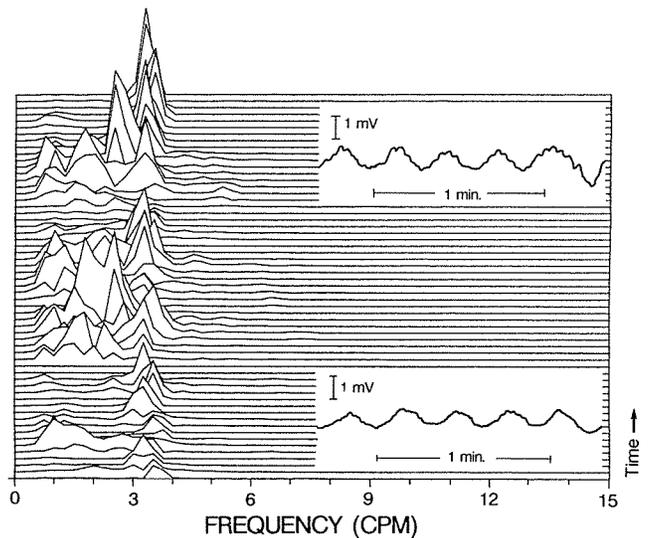


Figure 7. Postoperative EGGs (insets) and RSA (case 2) show rhythmic EGG waves at the normal rate of 3-3.5 cpm; RSA also shows predominantly regular peaks at 3-3.5 cpm, with occasional 1-2-cpm peaks.

returned to normal after mesenteric revascularization. Thus, these findings suggest that mesenteric ischemia inhibits gastric contractility and results in delayed gastric emptying. The incidence of chronic mesenteric ischemia in patients with idiopathic nausea, vomiting, and gastroparesis is unknown, but in patients at risk for vascular diseases the possibility should be considered.

Slow waves are generated by oxygen-requiring metabolic activity of smooth muscle cells located in the pacemaker region of the stomach (11). In healthy subjects, normal slow wave frequency is approximately 3 cpm (7-13). However, our patients with ischemic gastroparesis had gastric dysrhythmias. Bradygastrias and tachygastrias are associated with symptoms of nausea (7-11,13,14) and may also contribute to gastroparesis by interfering with normal gastric contractile activity (14,15). Gastric dysrhythmias reflect a disruption of normal gastric myoelectrical activity, but the underlying mechanisms of gastric dysrhythmias in humans are poorly understood. However, normal slow wave activity in the small bowel is reduced or abolished by ischemia and hypoxia resulting from chronic decreases in mesenteric blood flow (16). The normal postoperative slow wave signals reported here suggest that chronic ischemia is one mechanism that disrupts normal gastric myoelectrical activity.

Blood flow increases immediately and transiently in canine celiac artery after meals, whereas the increase in blood flow is sustained in the SMA for several hours after a meal (17,18). As recorded in Doppler studies in humans, blood flow in the SMA increases significantly 10 minutes after ingestion of a nutrient meal (19). Postprandial increases in celiac blood flow were not detected; selective increases in flow to the stomach could not be excluded by this technique (19). Increases in blood flow to the stomach after meals in our patients were apparently insufficient to support normal gastric motility, as evidenced by delayed gastric emptying. Any increase in blood flow in the SMA after ingestion of meals also may have reduced the limited blood flow to the stomach, thereby creating a potential "steal" syndrome that would lead to gastric ischemia, impaired contractility, and gastroparesis. These putative effects of chronic ischemia on gastric emptying and myoelectrical activity are supported by the fact that gastroparesis and gastric dysrhythmias resolved or improved after revascularization.

The resected arteries in cases 1 and 2 showed organized thrombus and an isolated arteriosclerotic plaque, respectively. Chronic mesenteric ischemia is commonly caused by arteriosclerotic processes; more unusual causes of arterial occlusion include embolism, external compression, thromboangitis obliterans, aortitis, chronic aortic dissection, and congenital abnor-

malities of the vessels (20). Potential risk factors for arterial lesions in our patients were their smoking histories. Cigarette smoking and nicotine alter intestinal blood flow and platelet aggregation (21-24) and increase vascular resistance (23), events that may contribute to atherosclerosis and thrombosis. Thus, it is conceivable that cigarette smoking contributed to the vascular lesions found in these two patients.

The possibility of mesenteric ischemia should be considered in patients with idiopathic gastroparesis, nausea, and vomiting, particularly if the patients are middle-aged women with marked weight loss, smoking histories, or other risk factors for vascular disease. Identification of such patients is important because symptoms, gastric dysrhythmias, and gastroparesis are potentially reversible with vascular bypass graft surgery.

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Received August 13, 1989. Accepted December 5, 1989.

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