previous study MgSO₄ did not reduce preload.¹⁰ Finally, we cannot completely exclude the possibility of myocardial conditioning. However, the slightly lower values in mean arterial pressure and myocardial oxygen consumption in the 9 group 1 patients at the peak of the second versus the first pacing and the absence of changes in these hemodynamic parameters in group II suggest a link between drug-induced hemodynamic changes and the prevention of angina.

The apparent contrast of our conclusions with those of Kugiyama et al.⁹ showing no prevention of exercise-induced myocardial ischemia in patients with fixed coronary artery disease by MgSO₄ is likely due to the higher infusate concentration adopted by our study and by termination of the infusion 30 minutes before the second exercise test in the study of Kugiyama et al.⁹

In summary, our study shows that MgSO₄ infusion at the rate of 0.4 g/min prevents pacing-induced myocardial ischemia in patients with coronary artery disease, and this effect is not mediated by an increase in coronary blood flow. The mechanism of the beneficial effect of the drug is possibly due to a reduction in myocardial oxygen requirements, but other mechanisms, such as a direct protective effect on ischemic myocardium, cannot be excluded and must be addressed in future studies. These results may provide an additional rationale for treating tachyarrhythmias with high-dose MgSO₄ infusion in patients with coronary artery disease.

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going CABG. All but 4 patients had a clinical history of angina pectoris, and 13 patients had a previous myocardial infarction. Coronary angiography showed a significant stenosis (>50% lumen diameter reduction) of the left main coronary artery in 7 patients, significant 3-vessel disease in 19 patients, 2-vessel disease in 4 patients, and 1-vessel disease in 2 patients. Six of the 32 operations were performed on an urgent basis.

Before anesthesia, patients received diazepam and morphine sulfate. Anesthesia consisted of fentanyl and pancuronium in all patients. After endotracheal intubation, a radial artery catheter and a central venous catheter were inserted in each patient. Ventilation before and after cardiopulmonary bypass was controlled to maintain arterial oxygen and carbon dioxide tensions between physiologic ranges. Routine intraoperative monitoring included an 8-lead electrocardiogram (limb leads plus V5 and V6), arterial pressure, central venous pressure, and esophageal and rectal temperatures.

Cardiopulmonary bypass was performed by means of a membrane oxygenator using hemodilution and moderate systemic hypothermia (28°C). In 12 patients the myocardium was protected by local hypothermia according to the method of Shumway, after a single 1,500 ml bolus dose of cold hyperkalemic cardioplegic solution (St. Thomas, S.A.L F. Bergamo, Italy). Hyperkalemic cardioplegia was repeated every 20 minutes or upon completion of each distal anastomosis. In 20 patients, multidose cold blood with potassium cardioplegia was used. Patients received 93 reversed saphenous vein grafts; sequential grafts were used for marginal branch-diagonal or diagonal-diagonal combinations. The distal anastomoses were all performed first during continuous aortic cross-clamping. Proximal anastomoses were performed during cardiopulmonary bypass and aortic side-clamping, after having restored cardiac activity. Twenty-four patients also received internal mammary artery grafts to the left anterior descending coronary artery. An average of 3.6 vessels were thus revascularized per patient. The pericardium was left open in all patients.

Two-dimensional echocardiograms were obtained by a biplane transesophageal probe, operating at 5.0 MHz, and connected to phased-array sector scanners (Aloka SSD 830 or SSD 870). The probe was positioned in the esophagus soon after the induction of anesthesia, and then advanced into the stomach to obtain a short-axis view of the left ventricle. Echocardiographic images and the electrocardiogram were monitored throughout the period from insertion of the esophageal probe to the cardiac arrest after aortic cross-clamping, and from the time of aortic unclamping to sternal closure. The echocardiographic images were recorded on VHS videotapes during each of the following situations: (1) before cardiopulmonary bypass, (2) after release of the aortic cross-clamp or side-clamp, (3) after cardiopulmonary bypass, and (4) whenever echocardiographic or electrocardiographic abnormalities appeared during on-line monitoring.

Echocardiographic images were reviewed offline by 2 experienced observers. For each sequence of images, the reviewers answered the following questions: Was a regional increment in myocardial reflectivity present, and where was it located within the ventricular walls? What was the presence, type, and extent of ventricular wall motion abnormalities? Only abnormalities detected by the consensus of both observers were accepted. An ST-segment shift from baseline at the J point was considered to be significant if there was >1 mm ST depression and >2 mm ST elevation.

One patient was excluded from analysis because of inadequate quality of the echocardiographic images. Of the 31 patients studied during CABG, 7 (23%) had an abrupt, marked increase in regional myocardial reflectivity (Figure 1), which was accompanied by attenuation of posterior structures in 3 patients. This phenomenon was observed upon release of either aortic cross-clamp (5 patients) or side-clamp (2 patients). Myocardial opacification involved ventricular walls only reperfused with venous grafts (inferolateral wall in 2 patients, inferoseptal wall in 2, posterior papillary muscle in 1, and anteroseptal wall in 2). In 4 patients these findings were accompanied by ST-segment changes: elevation in 3 and depression in 1. Regional akinesia accompanied the increase in myocardial reflectivity in 2 patients with ST-segment elevation. These echocardiographic changes were fully and spontaneously reversible within a mean of 6 minutes (range 80 seconds to 12 minutes).

FIGURE 1. Sequence of left ventricular short-axis views recorded by transesophageal echocardiography before and after release of aortic side clamp. Soon after release (right upper panel), myocardium of the inferolateral wall shows an abrupt increase in myocardial reflectivity, which was not present before release (left upper panel). The increase in myocardial reflectivity is still present 30 seconds (left lower panel) and 90 seconds (right lower panel) after release of clamp. LV = left ventricle.
The foregoing episodes of increased myocardial echo intensity occurred during only a portion of the episodes of intraoperative myocardial ischemia. In fact, ventricular wall motion abnormalities—not associated with visible changes in myocardial reflectivity—were observed on 17 occasions in 13 patients. Regional hypokinesia, akinesia, or dyskinesia were observed on 3, 12, and 2 occasions, respectively. As previously described, these ischemic episodes occurred more frequently in the postoperative period. Specifically, 4 episodes occurred before cardiopulmonary bypass, 8 after aortic unclamping, and 5 after termination of cardiopulmonary bypass. Thirteen of these 17 episodes were accompanied by ST-segment elevation, and 1 by ST depression. Regional wall motion abnormalities were fully reversible in all but 1 patient who developed postoperative myocardial infarction. This ischemic episode began after cardiopulmonary bypass and was not preceded by any changes in myocardial reflectivity. No patient died during hospitalization.

This study reports marked regional increments in myocardial reflectivity occurring during coronary surgery which were easily identified by visual inspection. This phenomenon likely represents gaseous embolism of the coronary circulation, since it is similar to that observed during venous air embolism, during intracardiac air retention in open heart surgery, and after injection of gaseous contrast agents into venous grafts. The increase in video density involved walls revascularized only with venous grafts and only occurred after release of aortic cross-clamp or side-clamps. Thus, gas was probably accidentally introduced into the coronary circulation during surgical maneuvers and caused the regional increment in myocardial intensity.

Gaseous embolism of the coronary circulation does not represent an echocardiographic curiosity; in fact, it was able to induce true myocardial ischemia, as demonstrated by the transient ST-segment shifts and regional wall motion abnormalities that accompanied visualization of increased video density. Furthermore, this phenomenon occurred most often during a period of the surgical procedure, when loading conditions were still low and regional wall motion abnormalities were difficult to detect. Although gas embolization was able to induce ischemia, it resolved within a few minutes without requiring any therapeutic maneuvers. Thus, gaseous coronary embolism did not produce major cardiac events, nor was it the cause of postoperative myocardial infarction. However, the effects of air on coronary circulation may be different if a greater amount of gas is accidentally introduced.

One might ask why a similar phenomenon was not reported in previous studies employing transesophageal echocardiography during CABG. The standard marker for myocardial ischemia by ultrasound is classically represented by regional wall motion abnormalities. Thus, echocardiographic monitoring has thus far excluded the time interval of cardiopulmonary bypass, starting again at least after completion of the last proximal graft insertion. This study was unique in that it was able to detect truly myocardial ischemia, as demonstrated by on-line reading. In addition, electrocardiographic data were obtained by a conventional monitoring system, with a paper printout to record selected time periods, whereas Holter monitoring might have allowed beat-by-beat analysis of the entire perioperative period. Finally, the monitoring period we explored was shorter than in previous studies, and was not extended to the postoperative phase in the intensive care unit.

In conclusion, this study establishes the presence of gaseous embolism as a cause of transient ischemia during coronary surgery, and demonstrates the relation of gaseous myocardial opacification to venous bypass grafts and to the period after release of aortic clamps.

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The Physiologic Meaning of Relative
Coronary Flow Reserve

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Relative coronary flow reserve (CFR) is a new physiologic measure of coronary stenosis, recently proposed by Gould et al. It is defined as maximal flow in a stenosed artery divided by the (theoretically predicted) maximal flow in a similar artery without stenosis. Whereas traditional absolute CFR was shown to be sensitive to aortic pressure and heart rate, relative CFR was shown to be relatively independent of physiologic conditions. Both absolute and relative CFR can be calculated from stenosis geometry, under certain assumptions, including a predefined value of normal absolute CFR. A provocative maneuver is required for direct measurement of absolute CFR from flow measurements during resting conditions and after induced vasodilatation.

The well-established index absolute CFR (defined as flow during maximal vasodilatation divided by flow at rest) has a clear physiologic meaning as a descriptor of coronary reserve. Coronary reserve is defined as the ability to increase coronary blood flow by means of arteriolar vasodilatation during stressful events that require larger oxygen supply to the heart. The increase in coronary resistance by a stenotic lesion results in compensatory distal vasodilatation, which maintains the basal coronary flow but decreases the available flow reserve. Severe stenosis finally results in maximal distal vasodilatation and "consumption" of the coronary reserve during rest. At this stage, absolute CFR equals 1 (i.e., basal flow equals the maximal available flow). Further narrowing of the stenosis results in a decrease of basal flow; however, the absolute CFR does not change and cannot be used to quantify the additional reduction in basal flow.

Normal arteries have absolute CFR in the region of 3 to 5; thus, flow can be increased 3 to 5 times by vasodilatation of the peripheral coronary bed. In severe

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ly stenosed arteries with exhausted coronary reserve, maximal induced vasodilatation does not result in flow increase; hence, absolute CFR has the limiting minimal value of 1. A normal absolute CFR of 4 is used in the following analysis to allow comparison between the predicted results and published experimental data.

The ratio between absolute CFR of a stenosed artery (ACFRs) and absolute CFR of a normal artery (ACFRn) is:

$$\frac{ACFR_s}{ACFR_n} = \frac{Q_{ms}/Q_{rs}}{Q_{mn}/Q_{rn}}$$

(1)

where Qms and Qrs are maximal and resting flows in the stenosed artery, respectively, and Qmn and Qrm are maximal and resting flows in a normal artery, respectively. Meaningful range of this ratio is between 1 (for normal arteries) and 1/4 (for severely stenosed arteries, with no reserve, assuming normal absolute CFR of 4).

The entire group of stenosed arteries can be grossly divided into arteries that still have functional coronary reserve and those with no effective reserve.

For arteries with functional coronary reserve, flow during rest in the stenotic artery (Qrs) is assumed to be approximately equal to flow during rest in a similar artery without stenosis (Qrn). This assumption is based on the concept of coronary autoregulation, which stabilizes coronary flow and can compensate the effect of proximal stenosis by distal vasodilatation. In these arteries, the CFR ratio is equivalent to the relative CFR (RCFR):

$$\frac{ACFR_s}{ACFR_n} = \frac{Q_{ms}/Q_{rs}}{Q_{mn}/Q_{rn}} = \frac{Q_{ms}/Q_{rn}}{Q_{mn}/Q_{rn}} = \frac{Q_{ms}}{Q_{rn}} = RCFR$$

(2)

Thus, in these mildly to moderately stenosed arteries (up to 85% to 90% diameter stenosis, when absolute CFR is not yet exhausted), relative CFR represents the ratio between the absolute CFR of the stenosed artery and the absolute CFR of a normal artery. In these arteries, the term "relative CFR" has its literal meaning.

The second group comprises severely stenosed arteries with exhausted CFR (over 90% to 95% diameter stenosis). In these arteries, flow during rest is reduced compared with flow in normal arteries, which may induce ischemic events and anginal symptoms during rest. In all arteries with exhausted flow reserve, absolute