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Intraoperative Contrast Echocardiography: A Direct Approach to Measure Regional Myocardial Perfusion

EVALUATION OF THE EFFECTIVENESS of myocardial revascularization has been limited by an inability to directly assess regional myocardial perfusion. The number of different methods currently used to assess the adequacy of revascularization is indicative of this limitation.

Surgeons have typically used hydraulic or anatomic methods (mass graft flow measurement using electromagnetic flow probes, probing and manual stripping of grafts, and even high-frequency epicardial echocardiography) to detect technical deficiencies at anastomotic sites. Physiologic information has been obtained using intraoperative ultrasonic velocity determinations in bypassed coronary arteries, coupled with an assessment of the postocclusive hyperemic response. Experimentally, radioactive tracers have been used to estimate total transmural perfusion, and a variety of thermal methods have been used to detect regional cooling and rewarming as indicators of regional perfusion. There is no general agreement on the effectiveness, if any, of these methods, and in fact none are universally employed.

The anesthesiologist's best estimates of regional myocardial perfusion have come from electrocardiographic indicators, determinants of global myocardial function, and indirect measures of perfusion such as the detection of regional wall motion abnormalities using echocardiography.

In this issue of ANESTHESIOLOGY, Aronson *et al.*[1] report on the use of contrast echocardiography in an animal model of coronary artery bypass grafting. Employing microbubbles suspended in sonicated Renografin-76® (4.5 $\mu g \pm 2.8$ μg in diameter) injected into the aortic root after aortic occlusion, epicardial echocardiography is used to provide tomographic data regarding the distribution of this echo-reflective agent throughout the imaging plane. Numerous studies have shown that microbubbles of this size behave much like red blood cells in terms of distribution and transit time, permitting regional contrast enhancement to be considered a direct measure of perfusion. Aronson *et al.* demonstrate that it is possible to detect regions of myocardial hypoperfusion caused by total coronary occlusion with a high degree of confidence. Thus, the effectiveness of coronary artery bypass grafting can be assessed directly at the tissue level.

This method is new, exciting, and, we believe, destined to have a major impact in the conduct of cardiac surgery. We have employed this agent in the study of 35 patients undergoing coronary artery bypass grafting and have found it to be safe and effective.[2] By injecting the contrast agent directly into completed coronary artery bypass grafts, we have been able to demonstrate transmural myocardial enhancement consistent with appropriate graft function and appropriate selection of anastomotic site (fig. 1). That this information is qualitative (as Aronson *et al.* point out, limitations in the agent do not permit quantitation at this time) does not detract from its clinical use, in our opinion. The absence of complications in our series and in other series using contrast injection during coronary arteriography indicate that wide application of son-

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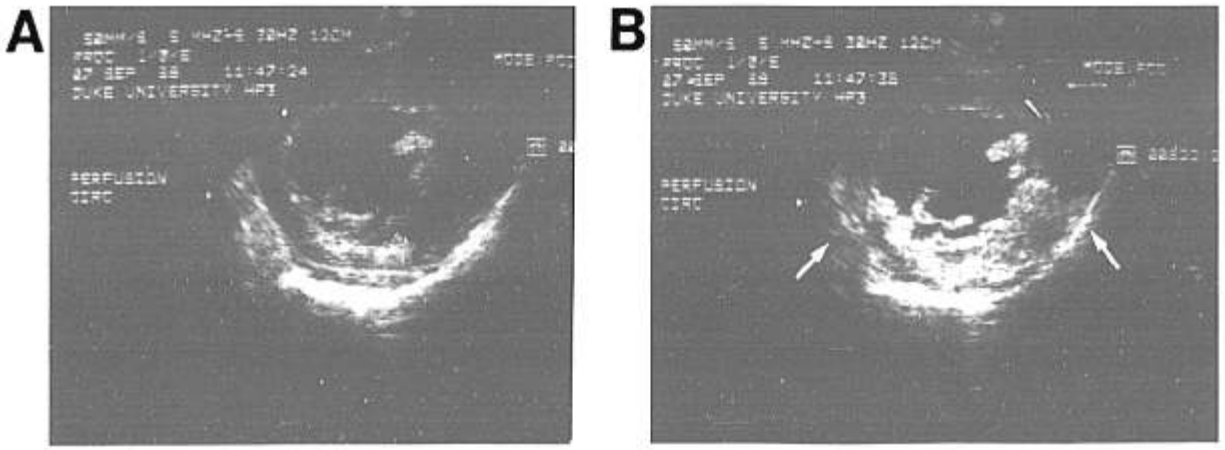

FIG. 1. Epicardial short-axis echocardiograph of the left ventricle at the midpapillary level (anterior structures at top). *A.* During cardiopulmonary bypass immediately prior to contrast injection into a sequential saphenous vein graft to the second and third circumflex marginal coronary arteries. *B.* Same view at peak contrast intensity after the injection of 2 ml of sonicated Renografin directly into the bypass graft. Perfusion of the entire posterior left ventricle, the posterior septum, and both papillary muscles is clearly visualized (area between white arrows).

icated Renografin can be justified. In fact, at our institution, investigational consent is no longer required for its intraoperative use.

In our opinion, contrast echocardiography has a great deal of potential in the operating room during coronary artery bypass surgery, where it is possible to completely define and control many physiologic parameters that affect the coronary circulation. In addition, there is ready access to the heart for echocardiography. Although Aronson *et al.* employed epicardial echocardiography (as have we), transesophageal echocardiography is ideally suited for this application. Although available image planes and image quality will always be slightly inferior to those obtained with epicardial echocardiography, these disadvantages will be off-set by the following significant advantages of transesophageal echocardiography: 1) minimal interference with the procedure; 2) real-time analysis by the anesthesiologist, with comparison to regional wall motion abnormalities.

Despite the great potential of contrast echocardiography, a large number of obstacles must be overcome to achieve the goal of quantitation of regional myocardial perfusion. Sonicated Renografin is currently the only agent available that is approved for this use. While the microbubble size is similar to that of red blood cells, the variance of size is too large for quantitative purposes. Echo-scattering is nonlinearly related to microbubble size, such that size-related rheologic factors that are known to exist in the microcirculation cannot be satisfactorily compensated for in analysis. A significant proportion of the microbubbles produced by sonication are of such size as to fail to transit the microcirculation, skewing the contrast washout curve and making indicator-dilution principles inapplicable. In addition, the half-life of sonicated Renografin is approximately 100 s, which adds further complexity to the analysis of sequential images following injection. This short half-life also implies that the agent must be prepared in the operating room, which is a formidable task requiring dedicated personnel and a research environment.

Fortunately, a number of stable agents will soon be available, all being developed to minimize the limitations mentioned above. Albunex® (Molecular Biosystems, Inc., San Diego, California), an air-encapsulating albumin microsphere manufactured from human serum albumin, is currently undergoing clinical trials as an FDA investigational device. These microspheres are of suitable size to ensure complete transit of the microcirculation and are stable with a shelf life of approximately 3 months. In addition, this agent has been shown capable of transpulmonary passage,[3] which may permit contrast enhancement of the left ventricular myocardium following iv injection. Other agents, including polysaccharide microspheres (SHU-508),[4] are also under development at this time.

Although the technique described has many limitations, this should not detract from the fact that it is able to easily provide information regarding the results of coronary artery bypass grafting that is otherwise impossible to obtain directly. This information can be acquired at a time where intraoperative revision is not only possible, but may be indicated. The use of this technique provides yet another reason to emphasize the importance of transesophageal echocardiography as a tool to assist both anesthesiologist

and surgeon in the performance of cardiac surgery. The coming of age of this technique, and the development of new agents capable of transpulmonary passage, will permit the assessment of regional myocardial function and perfusion in patients undergoing noncardiac surgery, as well.

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