coronary vein without IABP counterpulsation.

Our article¹ does not support the idea of coronary venous arterialization. We did not ligate the cardiac vein distally to isolate the arterialized venous system from the rest of the venous anatomy and to prevent steal through the coronary sinus to the right atrium, as is performed in surgical or percutaneous arterialization of the coronary venous system. However, even in the presence of the steal to the right atrium, the flow pattern of the arteriovenous graft we demonstrated may give the readers some suggestions regarding the physiology of the arterialized coronary venous system.

To be exact, the main finding of our article¹ is that it is impossible to detect incorrect grafting of the LITA to the coronary vein by flow waveform analysis with the transit time flow measurement under IABP counterpulsation.

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Difficulty of early diagnosis in patients with solitary pulmonary nodule

To the Editor:

We would like to express our opinion about the article by Crestanello and associates.¹ First, we congratulate them for the well-performed study contributing to the early diagnosis of lung cancer. Because an early diagnosis is likely to lead

to better survival, it is necessary to find a useful, easy, low-cost method to obtain better survival in patients with non-small cell lung cancer. But the results of this study seem to indicate that low-dose computed tomography (CT) screening is not the gold standard to obtain an early diagnosis. Low-dose CT screening in a well-selected group of patients detects a large number of indeterminate pulmonary nodules, but the diagnosis is not always made in the early stage; 7 patients (14.5%) had advanced lung cancer in stage IIIA or greater. These patients had a late diagnosis, despite an excellent treatment algorithm and a retrospective analysis of previous thorax CT. The percentage of patients with advanced lung cancer is very high for a well-selected group of patients, how is relatively high (39%) the percentage of benign nodules submitted to surgical operation.² Discussants emphasized that the main problem remains in detecting nodules less than 1 cm in diameter, whereas fortunately no discussion is necessary on the detection of nodules larger than 2 cm.

What is meant by the authors' statement, "morphologic appearance worrisome for cancer"?

Did the authors consider ground-glass opacity or other CT pattern? In their study, did the authors investigate the presence of ground-glass opacity³ in nodules less than 1 cm in diameter? Some recent studies have established a correlation between this CT pattern and the possibility of a malignant pulmonary nodule. If they studied this pattern, was the correlation observed in 37 nodules less than 1 cm in diameter in the patients enrolled in their study?

Last, what do the authors think about a computer-aided diagnosis and serial CT scan? These 2 methods have been proposed to distinguish between benign and malignant nodules.^{4,5} The computer-aided program can predict the histology of solitary pulmonary nodules by means of a simple chest x-ray film, whereas the serial CT scan algorithm enables volumetric modeling and may permit accurate assessment of doubling time over a relatively short period (20 days).

In conclusion, we believe that low-dose CT alone is not adequate to screen for solitary pulmonary nodules because it is possible to miss an early diagnosis and

difficult to differentiate between malignant and benign nodules.

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Reply to the Editor:

We appreciate Sortini and colleagues' comments concerning our report regarding surgical intervention in patients enrolled in a computed tomography (CT) screening trial. The radiographic finding in nodules that we considered worrisome for cancer include spiculation, noncalcification, diameter greater than 7 mm, and enlargement on serial examination.

The question about ground-glass opacities observed on CT is important. Our current policy is to carefully observe ground-glass opacities that are less than 7.0 mm in diameter. If they enlarge, we would either perform a percutaneous needle biopsy or thoracoscopic wedge resection of the nodule to establish a histologic diagnosis.

Our report included 16 patients in the surgical group with ground-glass opacities. Six of these patients had nodules that were

smaller than 1.0 cm; the stage was IA in 5 patients and IIIA in 1 patient. For the entire 16 patients with ground-glass opacities, the stage was IA in 13, IB in 1, and IIIA in 2. Our report, however, only examined those patients who underwent surgical intervention, so it does not represent a complete description of all patients in our CT screening trial with ground-glass opacities. We eagerly await continued reporting from the radiology literature about the entire spectrum of patients found to have ground-glass opacity on a screening CT.

The question regarding computer-aided diagnosis for enlargement of small nodules is provocative. Three-dimensional computer-aided diagnosis is clearly superior to 2-dimensional human measurement. This would be the preferred technique only when it can be smoothly automated for efficient use in day-to-day practice.¹

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Why clopidogrel failed to inhibit platelet function early after coronary artery bypass surgery: To load or not to load, and is it a question of resistance?

To the Editor:

Antiplatelet therapy remains a topic of much-deserved attention and debate. We read with interest the recent article by Lim and associates¹ in which they found that clopidogrel after coronary artery bypass grafting failed to inhibit platelet function, on the basis of the percentage platelet aggregation on day 5. Patients were randomized to receive 100 or 325 mg of aspirin daily or 75 mg of clopidogrel daily for 5 days after coronary artery bypass grafting.

It is not clear whether patients in the clopidogrel arm received a loading dose before the daily maintenance dose. Several similar studies assessing platelet inhibition, albeit in the context of percutaneous coronary intervention, have demonstrated the importance of appropriate loading of 300 to 600 mg if steady-state levels of platelet aggregation are to be achieved within the first 24 hours.²⁻⁴ Daily maintenance dosing with 75 mg of clopidogrel without preloading, as in this study, has been shown to result in steady-state levels of platelet inhibition only after 3 to 7 days.⁵

The second observation with regard to this study is that the investigators did not state whether a baseline pretreatment sample was taken before surgery or before administration of the antiplatelet therapy. Whether this would have added much to the final analysis remains unclear, but evidence, again drawn from studies in the percutaneous coronary intervention setting, have suggested pretreatment platelet reactivity to be an important determinant of posttreatment reactivity.⁶

The final comment is the most elusive, namely, the issue of "clopidogrel resistance." Although it was not directly mentioned by the authors, we can assume that it was alluded to in their discussion. It is likely that a correlation exists between a laboratory measure of clinical clopidogrel nonresponsiveness and the clinical outcome. However, until such time as there is greater understanding of the likely mechanisms of clopidogrel responsiveness and the individual heterogeneity that is apparent, can we totally dismiss the efficacy of clopidogrel in the early postoperative period?

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Reply to the Editor:

In our reply to Raja, we have addressed a similar query with regard to the dosing regimen of clopidogrel. It is vitally important to appreciate that the study in which Hunt and associates quote the time to the onset of the effects of clopidogrel (4 to 7 days) is from a sample of healthy subjects.¹ Nonrandomized studies after coronary artery bypass surgery suggest that it takes 9 to 28 days.² Our results are consistent with the latter.

In our article, you will note that we reported all measurements as the percentage change compared with baseline.³ The baseline sample was taken on the day before surgery.

We respectfully disagree with the final comment of Hunt. A previous observational study and our randomized data are consistent regarding the inefficacy of clopidogrel early after coronary surgery assessed on aggregometry. At present, we are unaware of any evidence to the contrary; therefore, the onus should be to prove that an effect exists before prescribing clopidogrel (as the sole antiplatelet in this time frame), rather than subjecting patients to the possibility of ineffective treatment while awaiting a "greater understanding of the likely mechanisms of clopidogrel responsiveness."

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