Before cardiopulmonary bypass became widespread, some groups in Italy² and the United States³ performed ligation of the ITAs in canine models and human subjects with ischemic heart disease. Reported results were promising: angina disappeared, correlating with the disappearance of ischemic signs at electrocardiography. We believe that these data should be re-explored with the help of modern technology. Our hypothesis^{4,5} has been that administration of angiogenic growth factors combined with distal occlusion of the ITAs might enhance angiogenesis of NCCC. We performed surgical ligation of the ITAs distally, and vascular endothelial growth factor was administered into the occluded arteries. Intuitively, occlusion by means of endovascular embolization is possible as well. It is known that the ITAs have high plastic potential, being capable of developing major branches that work as the only source of blood in extreme cases of lower limb ischemia.⁶ Hence myocardial ischemia should also be able to stimulate noncoronary collateral blood flow, preferably diverting this to the diseased area rather than to the chest wall.

It will be neither easy nor quick to demonstrate such theories, but our current studies represent a parallel, alternative research field, moving in the same direction of laser transmyocardial revascularization.

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Reply to the Editor:

With great interest, we read Picichè and associates' letter entitled, "Angiogenesis and surgical or endovascular enhancement of noncoronary collateral circulation: a new research field." We thank the authors for their kind comments regarding our article on the neovascuogenic effects of transmyocardial revascularization. We agree wholeheartedly with the authors that in patients with coronary artery disease, noncoronary collateral circulation and the microvasculature comprise critical components of myocardial perfusion and viability and hence greatly affect cardiomyocyte and ventricular function. Although surgical and percutaneous coronary therapy and investigative research are focused predominantly on large epicardial coronary vessels, the small collat-

erals and microvasculature are greatly underappreciated and understudied.

Certainly there are abundant clinical anecdotes of patients surviving on various permutations of coronary and noncoronary collaterals. Clinicians have all encountered the patient with an angiographically absent major coronary artery yet with the subtended myocardium demonstrating completely normal contractility on echocardiographic analysis. Is such a large region supplied through coronary collaterals, noncoronary collaterals from the base of the heart and posterior pericardial reflection or perhaps through the highly vascularized adhesions that surgeons encounter when operating on patients with prior cardiac surgery, renal failure, or myocardial infarction and Dressler syndrome? In older patients and in states of chronic disease, the ability to generate such collaterals can be impaired.^{1,2} Researchers are beginning to understand the critical interrelated roles of endogenous myocardium-mediated proangiogenic signaling and bone marrow-derived endothelial progenitor cells.^{3,4} Although initially very promising, the results of clinical trials aimed at harnessing this intrinsic revascularization machinery have been clinically equivocal.⁵⁻⁷ Perhaps what is needed is a refocus on augmenting noncoronary collaterals as an additional driving force in therapeutic neovascularization.

The authors present a very intriguing strategy of ligating both distal internal thoracic arteries to produce a regional state of hypertension and hyperperfusion around the mediastinum. Coupled with local delivery of angiogenic cytokines, the authors propose to enhance the development of noncoronary collaterals to reperfuse the ischemic myocardium in 2 large animal models. The preliminary background data presented by the authors is encouraging. Although critics will focus on the preclusion of a future left internal thoracic artery-left anterior descending coronary artery graft, the cornerstone of coronary artery bypass grafting

surgery, the experimental hypothesis is conceptually exciting and should be carefully investigated. The authors' proposal is uniquely novel and highly innovative, and we certainly look forward to the findings with great anticipation.

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