



## Integrated Coronary Revascularization

Howard A. Cohen, MD and Marco Zenati, MD

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I want to thank the organizers for the opportunity to participate in what is a very unique symposium that provides an exciting means to exchange ideas between different disciplines. It is an honor to represent my colleagues at the University of Pittsburgh, including both the interventional cardiology group and the cardiac surgeons. In particular, I would like to recognize Dr. Marco Zenati, who has performed the vast majority of our minimally invasive direct coronary artery bypass (MID-CAB) operations. I have been asked to speak about our experience with what we have termed “integrated coronary revascularization” — a better approach to patients with multi-vessel disease and type C lesions of the left anterior descending (LAD) artery. The integrated approach, or what has been called the “hybrid approach”, is a combination of the MID-CAB operation with angioplasty in the non-LAD lesions in patients with multi-vessel disease.

**Background.** It is well known that the left internal mammary artery is an excellent graft with demonstrated long-term patency that confers survival benefit, as has been shown by Dr. Loop and other investigators.<sup>1,2</sup> More recently, the MID-CAB approach has allowed surgeons to utilize the left internal mammary artery to bypass the LAD through a small left thoracotomy without the use of cardiopulmonary bypass. The largest single center series, reported by Dr. Calafiore in Chieti,<sup>3</sup> has

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demonstrated that this is a viable alternative compared to routine bypass surgery. Early in our experience, Dr. Zenati looked at the cost of MID-CAB compared to routine bypass surgery and found that there was approximately a 33% reduction in resource utilization.<sup>4</sup> The BARI trial demonstrated that angioplasty and routine coronary bypass surgery had equivalent 5 year survival with approximately 70% of the patients in the angioplasty arm free of bypass surgery at five years in patients with multi-vessel disease.<sup>5</sup> In addition, this trial revealed that the cost of angioplasty at five years was less than or equal to bypass surgery in patients with 2 and 3-vessel revascularization.<sup>6</sup> More recently, the STRESS<sup>7</sup> and BENESTENT<sup>8</sup> trials demonstrated that restenosis could be reduced with stenting. Furthermore, the results were better in the circumflex and right coronary artery as compared to the LAD.

**What are the potential theoretical advantages of the integrated approach?** This is a minimally invasive approach to multi-vessel disease that enables revascularization without cardiopulmonary bypass. We are all aware of the considerable morbidity associated with cardiopulmonary bypass, not the least of which are the neurological sequelae as recently reported in the *New England Journal of Medicine*.<sup>9</sup> In addition, the integrated approach provides a LIMA graft to the LAD with long-term patency and the survival benefit that the LIMA graft confers. Furthermore, with stenting of the other significantly diseased vessels, restenosis and good long-term results might be expected. The average length of stay of patients undergoing integrated coronary revascularization has been

low, and it is anticipated that the costs of this approach would be lower compared to routine bypass surgery.

**What are the potential disadvantages of the integrated approach?** First, we are not certain at this time that the left internal mammary bypass graft to the LAD as performed by the MID-CAB approach is the same as that performed by routine coronary bypass surgery performed through a mid-line sternotomy on an arrested heart. Another potential disadvantage is, of course, the possibility of restenosis in vessels that have undergone angioplasty and, in particular, the potential of in-stent restenosis, which can be a particularly vexing problem.

**Why might you consider the integrated approach?** Certainly, there is a definite patient preference for less invasive surgery. Patients who have refused routine coronary bypass surgery have been very willing to accept minimally invasive coronary bypass through a small left anterior thoracotomy. I will present several cases that I think will reveal how integrated coronary revascularization can expand treatment options that we can offer patients, and decrease cost at the same time. I believe that cost effectiveness will continue to be a very important issue. Finally, the long-term results of this approach will hopefully be equal to and perhaps better than routine bypass surgery.

Ideally, a simultaneous approach will be the only way to keep costs down. That is to say, performance of integrated coronary revascularization in a single room, whether it be an operating room in the cardiac catheterization laboratory or a cardiac catheterization laboratory in the operating room. There should be no compromise in the ability of either the surgeon or the interventional cardiologist to perform the procedure. In other words, there could be no compromise in the angiography suite and there should be no compromise in the operative suite. There can be cost saving by cross-training personnel so that the nurses and technicians are the same for both the MID-CAB and the angioplasty.

**The sequence of the procedures.** Generally, we have performed angioplasty first, followed by the MID-CAB. When the revascularization is performed in a single room, it really makes no difference which part of the procedure is performed first. When the MID-CAB is performed first, LIMA angiography prior to PTCA can then be undertaken to confirm the patency of the bypass and the quality of the anastomosis. The patient may be extubated and returned to a monitored bed at the conclusion of the procedure, but not necessarily to an intensive care unit. In our experience, patients can be discharged in two to three days.

In fact, some patients do so exceedingly well that they could be discharged on the following day. Whether or not an institution decides to have a single room dedicated to this approach depends upon the volume of cases performed. Such a room could also serve as an interventional suite for peripheral vascular surgeons as well. If the integrated approach becomes an accepted and frequent event in any given institution, then I believe that institution should consider having a single room where the MID-CAB and the angioplasty can be performed in the same setting.

Returning to the issue of the sequence of the procedure; we do angioplasty first, with the exception of patients with unstable or critical LAD disease or patients with left main coronary artery disease. Obviously, the MID-CAB to the LAD should be performed first in the latter circumstance. Generally, we do angioplasty first so that the patient can be converted to routine surgery via mid-line sternotomy in the unlikely event of emergency surgery.

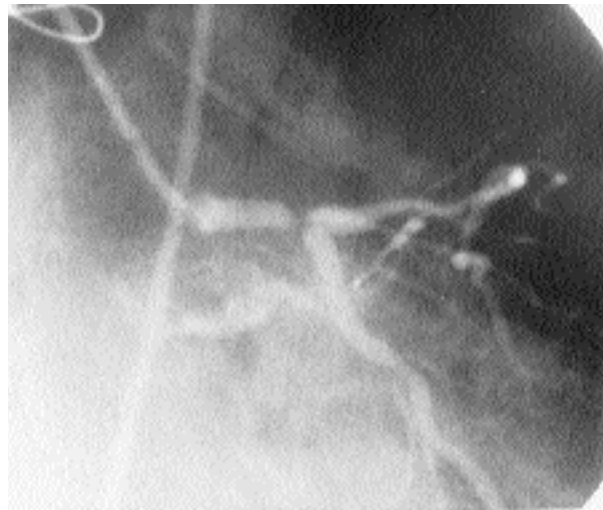
In our initial experience of 25 patients, approximately two thirds were male with the age ranging between 46 and 86 years old. All had evidence of ischemia involving the LAD with significant disease in at least one other vessel. The LAD was felt not to be favorable for routine angioplasty. Many of these patients had high-risk characteristics, including congestive heart failure and ejection fraction less than 35%, advanced age and a high frequency of chronic obstructive pulmonary disease, peripheral vascular disease, and carotid arterial disease. A significant number of patients also had chronic renal deficiency with a creatinine level greater than 2.0 mg/ml. Out of these 25 patients, the MID-CAB was performed to the LAD in 23, with one patient with a Y-graft to the diagonal and one patient with the MID-CAB by intention to the diagonal since it was a larger vessel and thought to be better suited for bypass.

Angioplasty was performed on the circumflex coronary artery in eleven patients, on the right circumflex artery in nine patients, on the diagonal in three patients, on the ramus intermedius in two patients, and on the left main coronary artery in three patients. Slightly more than 50% of these patients had coronary stenting, twelve had routine angioplasty alone and two had rotational atherectomy with adjunctive balloon angioplasty. In our institution, MID-CAB experience has been growing, with an increasing percentage of all coronary bypass operations performed. In one particular month, MID-CAB represented 25% of all coronary bypass surgeries performed. Our surgeons have accordingly become increasingly experienced with this operation. I believe that this is an operation that does have a steep learning curve. It is not an operation that all surgeons like, but those that are good at it are able

to perform the LIMA take down and anastomosis very successfully. I will now present several instructive cases that I believe will demonstrate how this approach can expand treatment options.

**Patient #1.** An 86-year-old female patient one year post 3-vessel coronary bypass surgery performed for severe left main coronary disease and diffuse disease of the RCA. She received three saphenous vein bypass grafts. She recently presented to another institution with subendocardial myocardial infarction and had post-infarction unstable angina pectoris. Repeat angiography was performed and revealed occlusion of all three bypass grafts with a 90% stenosis of the left main coronary artery. The RCA had diffuse 50% stenoses, but no critical disease. What is the best treatment for this 86-year-old patient who is now one year post bypass surgery status and post subendocardial myocardial infarction with post infarction unstable angina pectoris? In Figure 1, the severe obstruction of the left main coronary artery is evident. Should this 80-year-old patient have repeat coronary bypass surgery? Our approach was to perform MID-CAB to the LAD. The success of this procedure was confirmed by LIMA injection, which demonstrated an excellent anastomosis and TIMI 3 flow into the LAD (Figure 2). We then proceeded with angioplasty of the left main coronary artery and the proximal circumflex. There was no fear of occluding the proximal left anterior descending coronary artery, since this vessel was already successfully bypassed. Figure 3 demonstrates the excellent angioplasty result with stenting of the left main coronary artery and proximal circumflex. The patient is now nine months post integrated revascularization and remains asymptomatic.

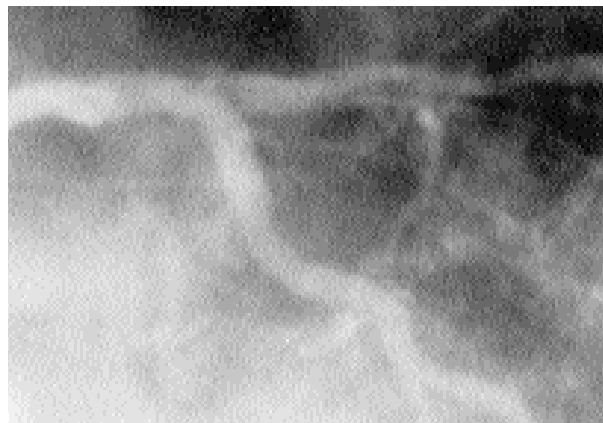
**Patient #2.** This 40-year-old fireman presented with a very complex lesion of the proximal LAD involving the large first diagonal with an eccentric plaque proximal to the bifurcation involving the LAD as well as the diagonal (Figures 4A and 4B). This is a lesion that is technically possible from an interventional point of view, but is likely to take at least several hours and must certainly be deemed high risk even with stenting and bifurcation stenting. If we are to perform debulking prior to stenting, as suggested by Dr. Colombo earlier, then the procedure is going to be prolonged even further. In summary, this is a difficult lesion that is going to be resource intensive with a higher than average restenosis rate. Another approach to this patient would be MID-CAB to the LAD with stenting of the diagonal, which is the approach that we decided upon. The LIMA graft to the LAD took approximately one hour and the angioplasty with stenting into the diagonal took 15 minutes. Following MID-CAB to the LAD, angioplasty was performed into the diagonal (Figures 5A and 5B). As



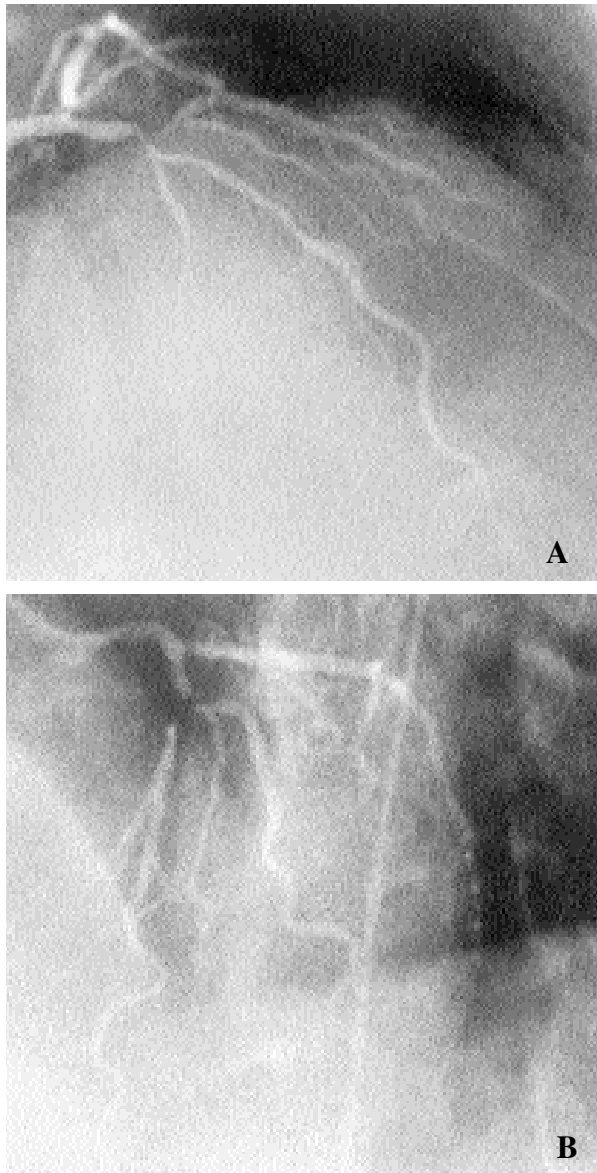
**Figure 1.** Severe stenosis of the distal left main coronary artery with occlusion of all saphenous vein bypass grafts.



**Figure 2.** Patent left interior mammary artery graft to the mid left anterior descending artery creating a "protected left main coronary artery."



**Figure 3.** Widely patent distal left main coronary artery after stenting into the proximal circumflex. There is reduced antegrade flow in the left anterior descending artery, but this is of no consequence since this vessel now fills via the left interior mammary artery graft.



**Figure 4.** Left coronary artery in the (A) right anterior oblique and (B) left anterior oblique projections. Note the severe bifurcation stenosis in the proximal left anterior descending artery involving the large diagonal.



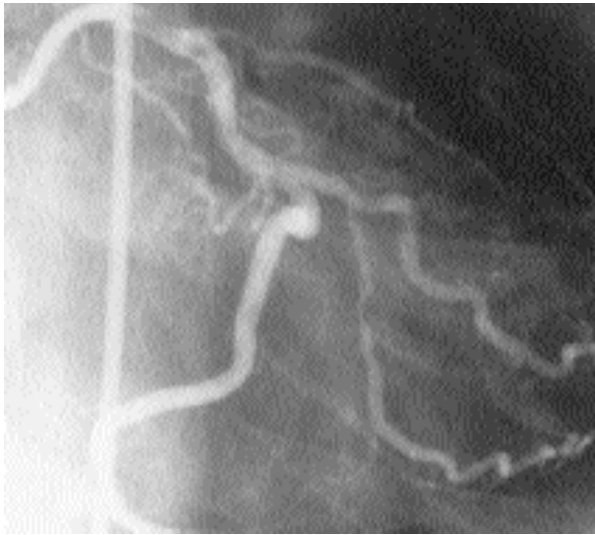
**Figure 5.** Post MID-CAB to the left anterior descending (LAD) artery followed by angioplasty with stenting of the LAD into the diagonal. (A) right anterior oblique view and (B) left anterior oblique view demonstrate a widely patent first diagonal with the LAD occluded just beyond. The LAD now fills only via the patent left internal mammary artery graft.

you can see, there is no antegrade flow into the LAD, since this vessel is occluded proximally with all of the flow occurring via the LIMA graft. There is 0% stenosis in the LAD diagonal after PTCA and stenting.

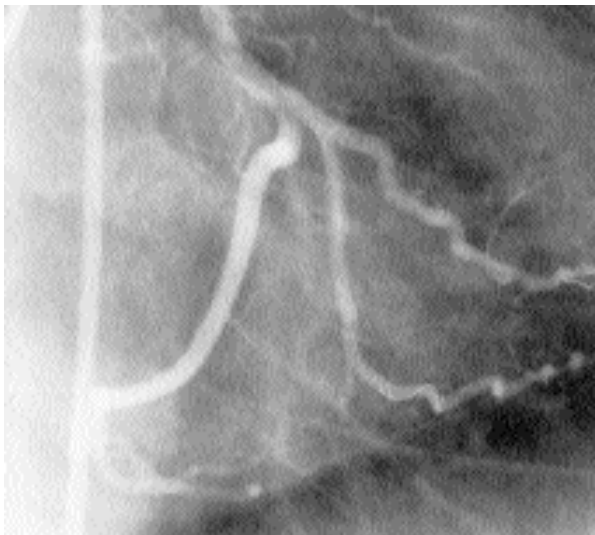
**Patient #3.** This 42-year-old laborer presented with a totally occluded LAD at its origin, a left dominant circulation, and the LAD filling via left to left collaterals. There is a long lesion in the second marginal involving the ostium of the first marginal (Figure 6). I do not believe that this patient is a good candidate for routine angioplasty, since it would be very difficult to revascularize the LAD with a long

total occlusion and lack of a “stump” at the origin. We therefore elected to proceed with integrated coronary revascularization. The patient underwent LIMA graft to the LAD performed by the MID-CAB approach. Angioplasty with stenting was then performed in the circumflex marginal with a T-stent placed in the first marginal with excellent angiographic result (Figure 7). The patient left the hospital two days following his surgery.

**Success with the integrated approach.** Finally, I would like to relate to you a brief experience that we



**Figure 6.** Left coronary artery in the right anterior oblique projection. Note that the left anterior descending artery (LAD) is occluded at its origin without a "stump." The LAD fills via left to left collaterals from the circumflex. There is a severe stenosis in the mid second large marginal with disease extending back to the origin of this vessel.



**Figure 7.** Post PTCA and stenting of the second marginal with a bifurcation stent placed in the origin of the first large marginal after its origin was compromised by placement of the first stent.

had with left main coronary artery disease and integrated coronary revascularization. The object of this approach is to provide a "protected" left main coronary artery prior to proceeding with angioplasty of the left main coronary artery and the circumflex as well as the right coronary artery as necessary. Between January and September 1997, twelve consecutive patients with left main coronary artery disease were referred for integrated coronary revascularization. These were, for the most part, an

elderly group of patients; approximately 50% were male. The left ventricular ejection fraction was low; 58% of the patients had an ejection fraction of less than 35%. By the system 96 risk model, the mortality risk for this elderly group of patients with routine bypass surgery was 32%. Seventy-five percent of these patients had documented history of prior cerebral vascular disease with TIA or stroke and 75% had severe chronic obstructive pulmonary disease defined by an FEV1 of less than 50% of predicted. In some patients, MID-CAB to the LAD alone was sufficient, since the left main disease involved only the ostium of the left main coronary artery. Post-operative adenosine stress thallium perfusion scan did not reveal any reversible defect and hence an integrated coronary revascularization was not performed with the LIMA graft alone resolving the patients ischemia. No further intervention was therefore pursued in these patients. All of the five patients treated in this fashion were alive and well at an average of nine months post-operatively. Seven additional patients had an integrated coronary revascularization angioplasty (performed on day one in 4 patients and on day two or three in 3 patients). All patients had demonstration of the left internal mammary artery anastomosis and flow at the time of angioplasty. One patient had an 80% stenosis of the mid portion of the LIMA graft caused by a hemoclip. This area was dilated with restoration of the LIMA to normal patency. The site of the PTCA was the body of the left main in three patients and the distal left main and the ostium of the circumflex in four patients. Five patients received a stent and two had angioplasty alone. Currently, I think that we would make an attempt to place stents in all these patients. All patients were discharged on aspirin and Ticlid and had no problems at an average of 5 months post-integrated coronary revascularization. All patients were extubated in the operating room. The average length of stay for the 12 patients was 3.2 days. This was a very high-risk cohort with a predicted 30 day operative mortality of 36%. Four patients were home on post-operative day 1 or 2 and there were no strokes despite the high incidence of cerebral vascular disease. The preliminary data, therefore, on this high-risk group of patients with left main disease suggests that they may be successfully treated with MID-CAB alone in some cases and with integrated coronary revascularization in others.

**The MORE trial.** This initial experience has been encouraging and we therefore proposed the Myocardial Optimal Revascularization (MORE) trial, which is a prospective randomized trial in patients with multi-vessel disease involving the LAD and one other

vessel and comparing the integrated approach standard coronary bypass surgery. The integrated approach can be performed simultaneously or as a staged approach during the same hospitalization. From a cost effective point of view, it would be hoped that the combined therapy in the integrated arm would be performed as expeditiously as possible and ideally in the same setting. Inclusion criteria include a significant stenosis greater than 50% involving 2 or more vessels (including the LAD) with functional Canadian cardiovascular class 3 or 4 or with objective evidence of ischemia either on clinical grounds or with stress testing. The patient must be a candidate both for MID-CAB and routine bypass surgery with an equivalent revascularization anticipated with both approaches. The non-LAD lesion must, of course, be suitable for angioplasty. The proposed endpoints are survival, coronary event-free survival, resource utilization and cost, quality of life and LIMA patency. The real issue is whether you can get "more" for less. We hope to obtain equivalent outcomes with decreased costs.

**The L'MORE trial.** We have also proposed the L'MORE trial, which is an adjunct to the MORE trial in patients with left main coronary artery disease with MID-CAB creating a protected left main coronary artery followed by angioplasty and stenting of the left main and circumflex and potentially the RCA as well, should that be required by the clinical situation. Since we believe it will be difficult to randomize patients, we will also have a parallel registry. Currently, the University of Pittsburgh, the Mayo Clinic, Washington Hospital Center and Lenox Hill Hospital are involved in the planning and implementation of these trials.

**Summary.** It must be reiterated that integrated coronary revascularization does not require abandoning angioplasty of the LAD in patients with multivessel disease. It does, I believe, require abandonment of angioplasty of the LAD in patients with unfavorable lesions and multivessel disease. It does not imply the abandonment of angioplasty in general in multivessel disease. On the contrary, I believe this approach has expanded the number of patients who can be treated with angioplasty as part of their revascularization. Most of these patients would have been referred to surgery alone because of the unfavorable disease in the LAD.

**What are the unfavorable lesions?** The long, diffuse, calcified LAD lesions, the severe bifurcation lesions, and the lesions involving the ostium of the LAD and the distal left main coronary artery. This

approach does not mean that these lesions are not amenable to percutaneous intervention, but this approach does imply that a better long-term result may be achieved with integrated revascularization.

**What is required for integrated coronary revascularization?** It obviously requires a surgeon who is skilled at performing the MID-CAB operation. At the present time, I do not think this group includes every heart surgeon. There is a steep learning curve and in our institution there is really only one surgeon who is committed to this approach and to whom I routinely refer patients. Obviously, the integrated approach also requires interventional cardiology expertise as well. It is essential that there is good rapport between the cardiologist and the surgeon. You need to have mutual respect for the ability of each member of the team. Ideally, a single room, whether a cardiac catheterization laboratory that is certified as an operating room or an operating room with a full-fledged cardiac catheterization laboratory, should be utilized. I do not believe portable angiography in the operating room is adequate in complex angioplasty.

The ideal revascularization is the one that is most effective, most durable, least invasive and least expensive. At the end of the day, we all know that angioplasty has its potential problems. I think we can best avoid the problems and complications by avoiding those lesions of the LAD that are less than ideal for angioplasty and that are associated with a high restenosis rate despite inadequate or even a good initial angiographic result. I hope that we can perhaps avoid complications and provide better revascularization for patients with this integrated approach, but this remains to be tested in randomized clinical trials.

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## PANEL DISCUSSION

THOMAS LINNEMEIER: I would like to make several comments about MID-CAB. At the Indiana Heart Institute, our cardiovascular surgeons have performed nearly 200 cases of MID-CAB and we have learned a great deal in the process. First, always visualize the actual LIMA with a pre-operative angiogram. You would be surprised how many LIMAs are too small to take down and perform an adequate anastomosis. Second, always visualize the LIMA post-operatively. In the early experience with MID-CABs, distal anastomotic insertion lesions are quite possible and should be identified clearly before patient discharge. Likewise, although rare, it is possible that the LIMA may be anastomosed to the wrong vessel, such as the diagonal branch of the LAD instead of the LAD proper. Third, if you are contemplating starting a MID-CAB program, I would advise that the initial patient population be older rather than younger. The LIMA is a precious vessel and you only get one crack at it. If an anastomotic lesion occurs, or if the wrong vessel is bypassed, then a 40-year-old patient might be left with a shorter life expectancy if a vein graft must be used because the LIMA was inadvertently destroyed. A vein graft to the LAD of a 70-year-old patient may exceed the life expectancy of the patient. A wise approach would be to perform your first 10–15 MID-CABs on patients with quite large LIMAs by angiography on an older patient population with a large target vessel LAD. As time progresses and confidence is gained, expansion into the younger patient population could be accomplished. Finally, at least in the early experience, it is possible for one of these MID-CAB LIMAs to completely go down in the early post-operative period. One must be prepared to complete a “perfect” procedure only to require an emergency redo with a vein graft or an emergency angioplasty in the early experience. At our institution, the number of emergency PTCAs for failed CABG is about equal to the number of emergency CABGs for failed PTCA. I completely agree

with Howard that a cooperative effort between interventional cardiology and cardiovascular surgery is critical in the early stages of this new technique, but because it is a new technique and because large experiences have been gained at other large institutions, some pitfalls can be avoided by following the above recommendations.

GERALD DORROS: Floyd Loop’s data tell us that LIMAs are the appropriate conduit for the left coronary. Revascularization of the left anterior descending artery is the most important determination of survival. We know that Dr. Johnson and Dr. Tector (Milwaukee, Wisconsin) have used the left internal mammary for many years before its renaissance, which began with PTCA. But it’s also surprising for Dr. Zapolanski, who has a large experience with LIMA, to tell you that some of the surgical literature does not concur with what you are saying. The LIMA does not hypertrophy — that is, have increased flow — in the absence of a proximal obstruction. When you remove the proximal obstruction (using PTCA/stent), then the LIMA’s flow will not increase. If you had an 86-year-old patient and you do enlarge the lumen, why would you have to do anything else at that point? Now that the patient is doing well, I don’t see any reason to increase that patient’s morbidity and potential mortality with additional procedures. I think the MID-CAB is very good and the LIMA is an excellent bypass procedure, but I’m not sure that we have to do all of the other things that you are describing since some of it is apparently cosmetic. I am really concerned about placing a LIMA and then relieving the proximal obstruction.

ALEX ZAPOLANSKI: I would like to expand on these issues. I agree with Dr. Dorros. I started 3 years ago with many other surgeons, but certainly not the majority. There are no data that support the idea that the LIMA to the LAD performed off pump is as good as that performed with the heart arrested. Subramanian had a significant incidence of reoperation in his initial experience, but Calafiore recently reported more than 300 cases done in Italy that did not develop symptoms and did not require recatheterization. The fact is, that from time to time, the recipient vessel is not adequate for grafting with the heart beating due to its intramyocardial position or diffuse disease, making the quality of the anastomosis less predictable. Dr. Cohen, you report that 7 out of 7 arteries were patent; this number is not sufficient to achieve statistical validity. How is it possible to reduce the cost of heart surgery when you are performing two procedures and must therefore deal with the possible complications of two procedures and the cost of two professionals? How could this be less expensive than a conventional opera-

tion? Also, how do you envision that the combination of a mammary and angioplasty would do better than a total arterial reconstruction in a 38-year-old man?

HOWARD COHEN: The patent LIMA angiograms refer only to the left main subgroup of patients that I described with all the grafts demonstrated to be patent by angiography post-operatively. We have had a larger series of 80 consecutive patients with 98% patency confirmed by post-operative angiography. I am confident that the surgeon at my institution will have a patent mammary following the MID-CAB operation. Regarding young patients, I think the idea of total arterial revascularization is certainly a viable alternative. Some of our surgeons are convinced of this and are now attempting to do total arterial revascularization in many of our patients. I think there is a lot to be said for this approach, but the long-term results need to be confirmed. In terms of cost, at our own institution there was a 33% reduction in cost in MID-CAB compared to routine coronary bypass surgery for a matched group of

patients. As I indicated, if you do two separate operations on two different days or two operations on the same day with two room costs and two sets of personnel, it is going to be difficult to save money. But if you perform the integrated revascularization in a single room at the same time with the same personnel and the patient can be extubated in the operative suite and discharged in 2 or 3 days, there is a definite opportunity for cost saving. One of the benefits of this approach is that I believe it does provide a definite treatment option for patients who otherwise would have difficult choices to make. The 86-year-old patient that I presented with left main coronary artery disease and failed bypass surgery certainly makes the point. Finally, with regard to Dr. Dorros's question, we are not really talking about doing a MID-CAB to the LAD and angioplasty of the LAD as well. The MID-CAB is performed to the LAD and angioplasty, with stenting when possible, is performed on the non-LAD vessels. I would agree that performing angioplasty on the LAD following a MID-CAB operation would compromise the flow via the LIMA graft.