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Should community hospitals perform angioplasty for acute myocardial infarction?

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I F ANGIOPLASTY produces better results than thrombolytic therapy in acute myocardial infarction, and if time is precious in this situation, then perhaps community hospitals should perform angioplasty, even if they have no facilities for heart surgery. In this Cardiology Dialogue, W. Douglas Weaver, M.D., from the University of Washington, argues in favor, while Joseph M. Sutton, M.D., from the Cleveland Clinic, voices some reservations.

THE ARGUMENT IN FAVOR

DR. WEAVER: The guidelines from the American College of Cardiology and the American Heart Association state that angioplasty should not be done without surgical backup,[1] but in the community hospitals in the Primary Angioplasty in Myocardial Infarction (PAMI) study relatively few patients needed emergency surgery after unsupported angioplasty, and the outcomes appeared very good.[2,3]

■ This series is based on the Cleveland Clinic Heart Center's "Controversies in Cardiology" conferences, at which a visiting clinician-professor and a Cleveland Clinic Heart Center clinician give contrasting perspectives on the application of a current technology or the management of a cardiologic disease.

In the Seattle area, we have kept a registry of all patients with acute myocardial infarction who were admitted to 19 different hospitals since 1988. We initially compared the data from 441 patients who underwent angioplasty either in unsupported laboratories or in tertiary centers,[4] and we currently have data on about 1100 such patients.[5] After controlling for baseline characteristics, we found that performing angioplasty in the community setting had no adverse effect on outcome. If anything, the results were a little better in the secondary centers (*Figure*).[4]

Only six patients (1.4%) needed emergent surgery after angioplasty. Most of these were patients for whom angioplasty had failed and who continued to be unstable or have chest pain. No patients were sent for surgery because of complications of primary angioplasty. To our surprise, primary angioplasty was usually done because of the physician's choice, not because of a contraindication to thrombolytic therapy. In only about one fourth of cases could a contraindication to thrombolysis be found such as bleeding or history of stroke.

Occasionally, emergency angiograms uncover something unexpected, such as three-vessel disease, that leads one to intervene earlier than if emergent angiography had not been done. So if we are going to do angiography, we might as well do it right away and triage these patients to appropriate treatment.

Therefore, provided the operators are trained in angioplasty (and not in emergent angioplasty only), and provided there is a mechanism to transfer the
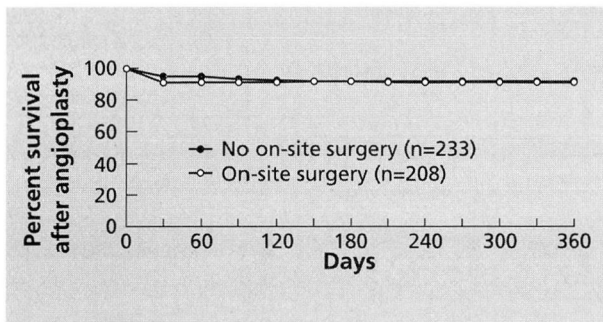
FIGURE. Unadjusted 1-year survival rates after direct angioplasty in hospitals with or without on-site surgery. The survival rate (with and without adjustment for baseline characteristics) was not significantly different between the two groups. Almost all deaths occurred in the first 15 days. From Weaver et al, reference 4.

patient, primary unsupported angioplasty may be a good option, at least for some patients. In patients who are hemodynamically unstable or are otherwise not candidates for thrombolytic therapy, doing angioplasty at the local hospital might be better than delaying for several hours while transferring them.

THE ARGUMENT AGAINST

DR. SUTTON: I agree about patients who are ineligible for thrombolytic therapy because of recent surgery, stroke, or circulatory collapse. But one problem with doing primary angioplasty on a more general basis is practicality. Fewer than 15% of all hospitals in the United States have catheterization laboratories.[6] If rural hospitals that do not have them begin to transfer patients to secondary and tertiary centers for angioplasty instead of giving them thrombolytic therapy, needless delays could be introduced. Further, the trials to date have involved a select group of very experienced operators only, and may not be widely transferable.

Another problem is that we still have no data from large studies to tell us that primary angioplasty affects the mortality rate as profoundly as thrombolysis does, whereas we do have unequivocal evidence for the benefit of thrombolysis.[7] The primary angioplasty arm of the second Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries trial (GUSTO-2) will take us in that direction. Smaller studies have indicated that, under optimum circumstances (in patients who present when the catheterization labora-

tory is open and who can be accommodated quickly), primary angioplasty gives a superior patency rate at 90 minutes: 95% vs approximately 70% with thrombolysis.

As you showed in your fibrinolytic trial, the first 2 hours are crucial.[8] It often takes us an hour or more to mobilize the catheterization laboratory in the middle of the night. If we delay therapy until the third or fourth hour because we are mobilizing the laboratory, it would be more prudent to go ahead and start thrombolytic therapy. By the time we are ready, the patient may be pain-free with ST-segment resolution.

New thrombolytic agents and regimens may make thrombolysis nearly as effective as primary angioplasty. Recombinant plasminogen activator (r-PA), which has been studied extensively in Germany, seems to produce a very high patency rate early on—90% at 30 minutes in some reports, and about 85% at 90 minutes in a recently completed trial.[9] Tissue plasminogen activator given as a double bolus (50 mg initially and 50 mg 30 minutes later) has a reported patency rate of 80% to 85%.[10]

Finally there is the issue of reimbursement. We make more money from primary angioplasty than from thrombolysis. I have been alarmed to hear my colleagues say that is one of the reasons they have given up on thrombolytic therapy. Some centers perform primary angioplasty exclusively.

MORE TRIALS NEEDED

DR. WEAVER: I agree, we have only a few randomized trials with a few hundred patients with primary angioplasty.[2,11] Most of us have interpreted the results as saying angioplasty is as good as thrombolytic therapy or better, but there are a few reasons why it could be worse. One is time to treatment. In our registry, only half of the patients were treated by 90 minutes; the median time to treatment—from when the emergency room record was time-stamped until angioplasty was begun, not from when symptoms began until reperfusion was achieved—was 88 minutes. Twenty-five percent of the patients had to wait 2 hours or longer. It is almost impossible to begin sooner than 60 minutes. On the other hand, investigators who have addressed this question could not find any relationship between time to angioplasty treatment and outcome.[11] It could be that achieving grade 3 on the Thrombolysis in Myocardial Infarction (TIMI) scale is more important than time to treatment.

DR. SUTTON: Could it also be that they just did not have enough patients treated within the first 2 hours to demonstrate time-dependent results?

DR. WEAVER: Yes, or the spectrum of times was not wide enough to show a difference. Another possibility is that all cardiologists may not get the same results. In our registry, for instance, the patency rate is 88%, not 95%.

As for the cost issue, in the few economic analyses that have been done, routine angioplasty was cheaper than thrombolysis.[12,13] I am not sure that is true in the real world. But in the recent PAMI trials, two thirds of the low-risk patients were discharged by day 3.[14] That is very good.

Only 15% of hospitals have catheterization laboratories, but 85% of people in the United States live within 1 hour of one. So why not just drive them all to these cath labs and do angioplasty? If we believe that angioplasty is better than thrombolytic therapy, and if patient outcomes are at least equal and costs and length of stay are lower, is that not justification enough?

A trial being planned should be very helpful. The PAMI group is planning to take patients that come to community hospitals and randomly give half of them thrombolysis and send the others to tertiary centers for primary angioplasty.

QUESTIONS FROM THE AUDIENCE

AUDIENCE: This study will be an artificial situation, because everyone will try hard to move the angioplasty patients along quickly, without the usual delays. It will have to show a dramatic advantage for angioplasty over thrombolysis, because if the results are equivalent, in the real world things will be worse. If angioplasty proves dramatically better, we should try to change the system.

DR. WEAVER: I would bet there will still be a 2-hour delay at least. Many institutions are addressing this issue and are trying to respond more quickly.

'Rescue' angioplasty
DR. SUTTON: The apparent synergism between thrombolysis and angioplasty also confounds this issue. If angioplasty after thrombolysis ("rescue" angioplasty) gave results as good as those of primary angioplasty, we could give thrombolysis in the emer-

gency room as soon as the patient comes in, and then assemble the catheterization laboratory team. I have done this a few times in the middle of the night, knowing it would take 1.5 to 2 hours to start angioplasty. However, the success rates are only 70% to 80% with this approach. Something about thrombolytic agents, even the fibrin-specific ones, primes the clotting cascade, so that after the infusion is stopped, the reocclusion rate is much higher.

I have been fortunate: my patients had perfusion re-established by the time I got here. But if they had not, I shaved at least 10% off the likelihood of getting a good early angiographic result in exchange for the favorable (70% success) gamble that thrombolytics might have worked more quickly to re-establish flow. There have been no large randomized trials of rescue angioplasty to tell me whether I increased those patients' mortality risk by 1% or 2%.

DR. WEAVER: Unfortunately, we do not have the same incentive from the Food and Drug Administration to study angioplasty as we do for the pharmaceuticals. We would know a lot more about primary angioplasty if catheter companies were required to provide the same level of proof. I would also like to know the results of community hospital angioplasty. Angioplasty has many technical nuances, which may relate to outcomes. In Germany, the typical community interventionalist does approximately 200 angioplasties a year, whereas in the United States that number is 22. Less-experienced operators may not get the same results as in the published studies.

On the other hand, I am not convinced we can make a perfect thrombolytic regimen. Some patients have terrible atherosclerosis and some have mechanical flaps caused by dissection, which thrombolytic agents will never affect. Perhaps there is a plateau beyond which thrombolysis cannot go.

TIMI grade and survival
DR. WEAVER: The GUSTO trial results seem to indicate that we need to increase the percentage of patients who achieve TIMI grade 3 flow from 54% to 75% or 80% to reduce the mortality rate by 1%.[15] Angioplasty does produce that patency rate, and just might make a difference in outcome. Or it is possible that we do not understand the mechanism by which angioplasty works, and TIMI grade 3 flow rates do not tell the whole story.

TABLE
TIMI[†] GRADE DEFINITIONS USED AT THE CLEVELAND CLINIC[*]

Grade	Definition
0	No antegrade flow through a total occlusion
1	Contrast material penetrates the lesion but does not perfuse the distal beds
2	Partial perfusion: the contrast material crosses the obstruction and opacifies the coronary bed distal to the obstruction, but the rate of entry of contrast material into the vessel distal to the obstruction or its rate of clearance from comparable areas not perfused by the previously occluded vessel is reduced compared with the opposite coronary artery or coronary bed proximal to the obstruction
2a	Artery fills slowly, but within five beats
2b	Artery fills slowly, takes longer than five beats
2c	Artery fills as quickly as TIMI grade 3, but the rate of clearance is slower
3	Complete perfusion: antegrade flow into the coronary bed distal to the obstruction occurs as promptly as into the bed proximal to the obstruction, and clearance of the contrast material occurs as promptly as clearance of material from an uninvolved bed in the same vessel or opposite artery

[†]TIMI, Thrombolysis in Myocardial Infarction
[*]Table courtesy of Stephen G. Ellis, MD

DR. SUTTON: The TIMI flow grade data from GUSTO were sobering in the angiographic subset, because TIMI grade 2 flow was just as bad as TIMI grade 1 and grade 0 flow with respect to late mortality. Only with TIMI grade 3 flow was there was a statistical reduction in mortality. Possibly, chest pain and ST-segment elevation could resolve after thrombolytic therapy with TIMI grade 2 flow, but the patient's mortality risk would not be reduced. Primary angioplasty does achieve that known TIMI grade 3 flow in all patients.

DR. WEAVER: The two r-PA trials were the only ones in which TIMI grade 2 flow did not portend a bad outcome. Where TIMI grade 2 flow looked like TIMI grade 3 flow, the mortality rate was low.[16]

DR. SUTTON: Our team splits antegrade TIMI grade 2 into 2a, 2b, and 2c, depending on how many beats it takes for the artery to fill completely (*Table*). TIMI grade 2 flow also is a washout phenomenon, and reflects both inflow and outflow. If rapid inflow is restored but the capillary bed is already destroyed and necrosis has already occurred, this is still TIMI grade 2 flow—TIMI grade 2c. I think this distinction between TIMI grade 2 flow on an outflow basis vs an inflow basis makes a difference in outcome.

AUDIENCE: For the inflow problem angioplasty should give better results, but for the outflow problem nothing will help, because the muscle is damaged.

DR. SUTTON: It is more complex than that, because flow can improve. In the TIMI-V trial comparing hirudin vs heparin after thrombolysis, of the patients who had TIMI grade 2 flow at 60 minutes, the conversion to TIMI grade 3 flow was dramatically higher after 24 to 36 hours in the hirudin group. Impaired inflow may benefit from pharmacologic intervention as well, and may depend on the specific agents used.

AUDIENCE: Do you think there might be a built-in illusion in comparing thrombolysis and angioplasty, which are theoretically different? We worry about the time to treatment in angioplasty, but thrombolysis does not have an immediate effect: it takes about 45 minutes to work. If we compare times to patency instead of times to treatment, the differences may diminish or even disappear.

DR. WEAVER: I am not so sure about that. In the last fibrinolytic trial we did together we did not study many arteries at 30 minutes, but two thirds of them were open. Even in the earliest studies, the patency rates were at least 50% in the first 30 to 60 minutes. In contrast, in angioplasty, very few arteries are opened before 90 minutes.

Angioplasty in bypass grafts
AUDIENCE: Does the location of the infarct affect your decision to use angioplasty or thrombolysis? Also, what about a patient with previous bypass surgery or known coronary artery disease?

DR. WEAVER: For an inferior myocardial infarction, I would choose angioplasty over thrombolytic therapy, but on the basis of risk, not of benefit. The mortality rate in this situation is so low that we will probably never demonstrate a statistical difference.

Thrombolytic therapy does not work as well in bypass grafts, but angioplasty does not work very well either. Angioplasty is particularly difficult in bypass grafts. The available case series indicate that ST-segment elevation in patients with bypass grafts is statistically more likely to be due to occlusion of the graft than of the native coronary. But that may be because the surgeons have bypassed everything and all the native coronaries are gone. We do not have very much information about what the best approach is. Extraction catheters, which just get rid of the clot, may be appropriate here.

AUDIENCE: We lose a certain amount of success when we tackle difficult cases. The PAMI trial demonstrated a 95% patency rate for angioplasty, but it included native coronaries only. A series in Germany included grafts, and had a patency rate of 88%.

'REAL WORLD' DATA NEEDED

DR. SUTTON: If one of us were having an MI, and if it were daytime and we were right here at the Cleveland Clinic, most of us would prefer angioplasty rather than thrombolysis. But if it were the middle of night, out in a rural area, I would rather have thrombolysis right away than wait to be transferred for angioplasty.

DR. WEAVER: We always say we would take primary angioplasty over thrombolytic therapy, but mishaps do happen, such as clots pulled back into another artery and made worse.[17] Only a few procedure-related deaths could wipe out the advantage of primary angioplasty. As hospitals begin to report their experiences, we may find that the results of primary angioplasty in the real world are not as good as in the published trials. This information should stimulate more critical evaluation.

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