EDITORIAL

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Treatment Delay in Myocardial Infarction: A Timely Topic

The relative merits of primary angioplasty versus thrombolytic therapy for acute myocardial infarction continue to be debated. Recent clinical trials have demonstrated superior mortality outcomes with primary angioplasty compared with thrombolytic therapy.[1–3] However, physicians should consider several important factors when choosing between these reperfusion options.

Time Matters

In this issue of **ecp**, Kent and colleagues have addressed one of these factors—the difference in treatment time for primary angioplasty versus thrombolysis.[4] For patients receiving thrombolytic therapy, time to treatment is defined as the time from hospital arrival to the initiation of intravenous thrombolysis. For patients undergoing primary angioplasty, the time to treatment is the time from hospital arrival to first balloon inflation. In either case, the shorter the time to treatment, the more rapidly reperfusion can be achieved and the greater the survival benefit.

The time to treatment for thrombolysis is shorter than that for primary angioplasty because thrombolytic therapy can be delivered in the emergency department, whereas patients need to be transferred to a cardiac catheterization laboratory to receive primary angioplasty. Furthermore, thrombolytic therapy is usually available 24 hours a day. Primary angioplasty, in contrast, may not be immediately available if the cath lab is being used for another patient, the staff are outside the hospital (which occurs at some institutions during off-peak hours), or the medical center lacks the facilities or staff to perform the procedure. Therefore, clinicians may be faced with determining what is an acceptable procedure-related delay with primary angioplasty.

By using an innovative modeling technique, Kent and coworkers examined the influence of treatment times on the mortality differences observed in 10 randomized trials that compared primary angioplasty with thrombolytic therapy. The authors estimated that the survival benefit attributed to primary angioplasty is negated when the difference in treatment time between primary angioplasty and thrombolysis exceeds 50 minutes (the time to "equipoise").

Effect of New Therapies

Several issues warrant consideration before we can accept this time threshold in clinical practice. The analysis was based solely on the results of clinical trials completed before the widespread use of coronary artery stents and platelet glycoprotein IIb/IIIa receptor antagonists (e.g., abciximab, eptifibatide, tirofiban, and lamifiban). These newer therapies, which are now widely used, have been associated with improved outcomes following angioplasty, while mortality rates with thrombolytic therapy have remained relatively stable.[5–7] This temporal trend toward lower mortality after angioplasty would be expected to result in a longer time to equipoise between the treatments (i.e., preserving the benefit of primary angioplasty despite longer delays).

Our recent study evaluating outcomes following reperfusion as a function of institutional primary angioplasty volume included data from the coronary artery stent

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and platelet glycoprotein IIb/IIIa receptor antagonist era.[3] Although we did not calculate the "time to equipoise" in our study, our results may shed light on this question. At low-volume hospitals (those performing <16 primary angioplasties per year), there was no significant difference in hospital mortality between primary angioplasty and thrombolysis-treated patients (6.2% vs. 5.9%; $P > 0.2$). The median treatment time was 36 minutes for thrombolytic therapy and 114 minutes for primary angioplasty. Because the mortality rates were similar with this difference in treatment times, the time to equipoise at these low-volume hospitals was approximately 78 minutes.

Effect of Volume

Another important consideration is procedural experience. Kent and colleagues point out that because delay is probably associated with angioplasty experience, they likely overestimated the independent contribution of delay (and underestimated the time to equipoise). Several studies have shown lower rates of mortality following primary angioplasty at hospitals with higher procedural volume.[3, 8, 9] Consequently, the American College of Cardiology and the American Heart Association have recommended that primary angioplasty be considered as an alternative to thrombolytic therapy only when performed by experienced personnel and medical centers.[10]

In our study, hospitals with higher volume (those performing > 17 primary angioplasties per year) had significantly lower mortality rates with primary angioplasty than with thrombolysis (3.9% vs. 5.8%; $P < 0.001$). From our data, we cannot estimate a time to equipoise at the higher-volume institutions, because the mortality rates with the primary angioplasty and thrombolytic therapy were not similar. However, we agree with Kent and coauthors that higher-volume institutions probably have a time to equipoise that is substantially longer than that for low-volume hospitals.

Estimating the Right Time

So what should clinicians do when facing a choice between thrombolysis and primary angioplasty? First, because more than 25% of patients with myocardial

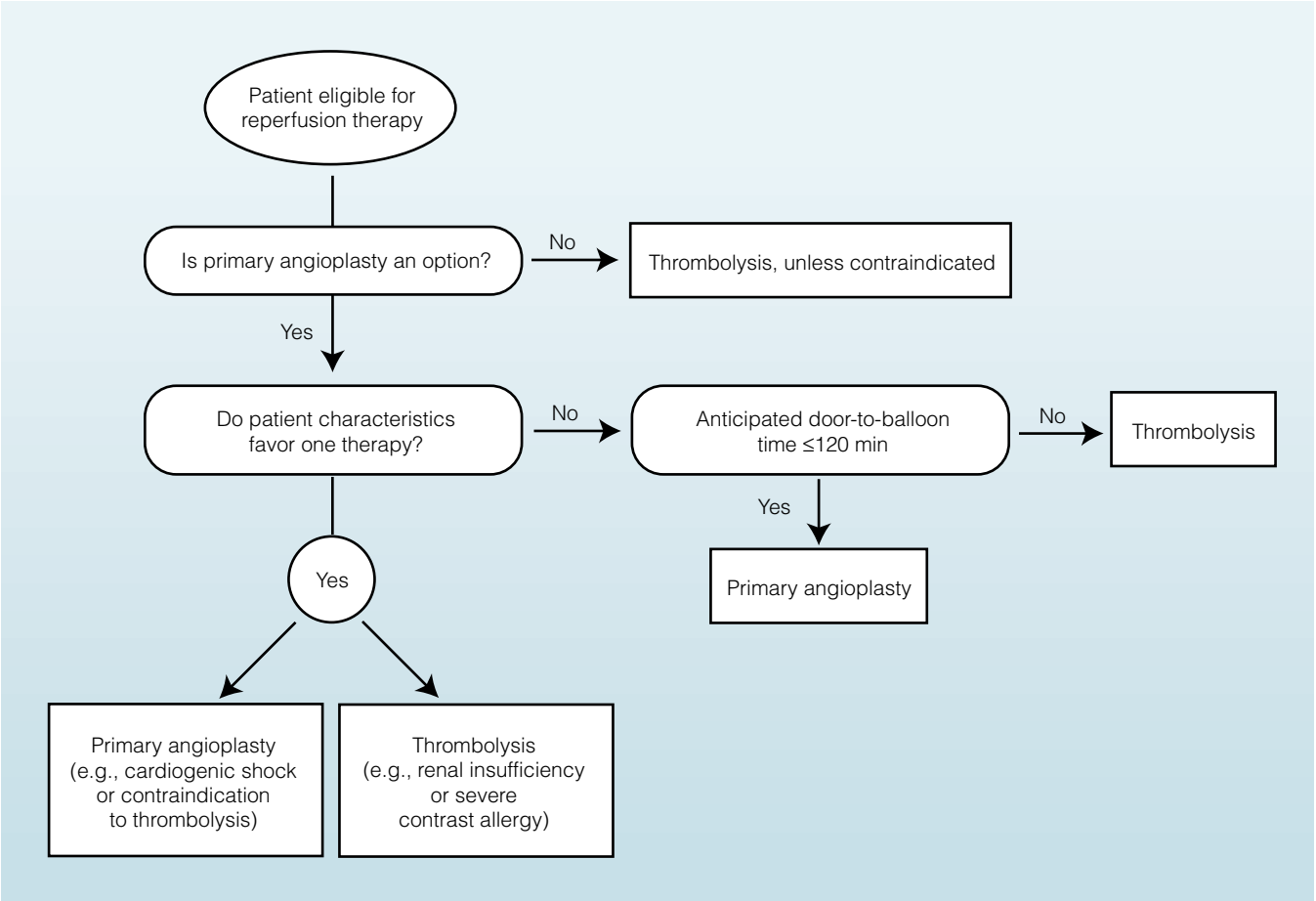

FIGURE 1. Decision tree for primary angioplasty versus thrombolysis.

infarction who are eligible do not receive reperfusion therapy,[3] efforts to increase the use of either therapy should be the priority. If angioplasty is an option, we suggest that patient characteristics be considered next (**Figure 1**). Primary angioplasty is the best option for patients with cardiogenic shock or with a contraindication to thrombolytic therapy. Alternatively, thrombolysis may be preferred for patients with diminished renal function or severe allergy to intravenous contrast dye.

Treatment times for primary angioplasty and thrombolysis should be considered next. The absolute time threshold for the difference in treatment times that would favor thrombolysis remains unknown, but the guidelines of the American College of Cardiology and American Heart Association for percutaneous coronary intervention provide some direction.[11] These guidelines suggest that the maximum door-to-balloon time acceptable for primary angioplasty is 120 minutes. Given that the recommended treatment time for thrombolysis is 30 minutes, this suggests an acceptable difference in treatment times of up to 90 minutes. Again, acceptable differences in treatment times may vary according to institutional procedural volume; that is, the acceptable time may be shorter at lower-volume centers and longer at higher-volume centers. For cases in which all other factors are equal and the likely difference in treatment time is less than 90 minutes, primary angioplasty should be considered as the reperfusion option of choice.

This discussion has focused on mortality, but nonfatal outcomes are also important considerations in selecting a reperfusion therapy. For example, hemorrhagic stroke is more common with thrombolytic therapy (with approximately one additional nonfatal stroke for every 200 patients treated with thrombolysis instead of primary angioplasty).[3] In addition, because initial reperfusion rates are lower with thrombolytic therapy, patients who receive thrombolysis are more likely to require subsequent revascularizations. On the other hand, successful thrombolysis may obviate the need for an invasive procedure with its attendant risks.

In the future, primary angioplasty and thrombolytic therapy may be combined (so-called "facilitated" percutaneous coronary intervention), reducing the need to choose between therapies. In this case, thrombolysis could be initiated and followed by percutaneous coronary intervention, providing greater options regarding time delay and transfer.

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