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INDICATIONS FOR CORONARY ANGIOPLASTY IN ACUTE MYOCARDIAL ISCHEMIC SYNDROMES

Pim J. de Feyter, Patrick W. Serruys, Paul G. Hugenholtz

Thoraxcenter
Erasmus University and University Hospital Dijkzigt
Rotterdam, The Netherlands

SUMMARY. The role of coronary angioplasty for the treatment of patients with evolving myocardial infarction, unstable angina, and early postinfarction unstable angina is discussed.

It has been shown that coronary angioplasty in patients with an evolving myocardial infarction is feasible and can be performed with a high initial success rate. The most beneficial timing of dilatation is still unclear, and acute reocclusion following coronary angioplasty remains a problem. Current data suggest that the left ventricular function is greater improved and peri-infarction ischemia is less with angioplasty when compared with sole thrombolytic treatment.

Coronary angioplasty for unstable angina and early postinfarction unstable angina can be performed with a high initial success rate, but at an increased risk of major complications.

Thus, coronary angioplasty has nowadays obtained a definitive place in the treatment of acute myocardial ischemic syndromes. Further research is needed to improve the initial and late results of coronary angioplasty, and additional randomized clinical studies are necessary to more accurately define the indications and timing of dilatation in these acutely ill patients.

KEY WORDS. unstable angina, angioplasty, angina, acute myocardial infarction, coronary artery bypass grafting

Transluminal angioplasty, performed to widen the lumen of a stenotic vessel by means of an intravascular catheter, was conceived by Dotter and Judkins in 1964 [1]. This technique proved effective in peripheral arteries. However, it took until 1977 before Gruentzig used this method to dilate the coronary arteries of conscious humans [2]. Subsequent improvements in equipment and technique have established coronary angioplasty as a major treatment mode for stable angina in patients with single-vessel disease. Recently, the initial restricted indications have been widened to include dilatation of complex lesions, multivessel lesions, and vein grafts. Furthermore, angioplasty has now been shown to play an important role in the management of unstable angina and acute myocardial infarction. The purpose of this paper is to review recent developments in coronary angioplasty for the management of patients with 1) unstable angina, either refractory to or initially stabilized with optimal pharmacological treatment, 2) early postinfarction angina, and 3) evolving myocardial infarction.

Management of Unstable Angina Syndrome

Unstable angina, defined as chest pain at rest accompanied with significant electrocardiographic ST-T changes, but without enzyme elevation, is a clinical syndrome that requires aggressive management because it carries an increased risk of mortality and morbidity. This is more so when optimal pharmacological treatment with nitrates, beta blockers, and Ca antagonists have proven to be inadequate [3, 4]. Since the causes of unstable angina are multifactorial [5-8], and within the same patient different pathophysiological mechanisms may occur at different times and in succession, it is difficult to decide what the optimal therapy for a particular stage of the disease at a particular moment in time for a patient consists of. Therefore, although treatment must be highly tailored to individual needs, one cannot afford to lose too much time awaiting the response to one or another agent. So when pain persists after initial therapy with nitrates, it usually will be directed against all suspected pathophysiological mechanisms at the same time, e.g., beta blockade, Ca entry blockers, anticoagulants, and sedatives. Basically, such treatment is aimed at restoring coronary blood flow by means of vasodilation, while also reducing overall myocardial oxygen demands. The uncertainty of outcome in a specific patient forces one to provide "maximal" treatment from the outset in order to evaluate its efficacy frequently, and early experience has shown that relief of all signs and symptoms of ischemia should be prompt, i.e., within

Address for correspondence and reprint requests: Pim J de Feyter, M.D., Catheterization Laboratory, Thoraxcenter, Erasmus University, Postbus 1738, 3000 DR Rotterdam, The Netherlands.

24 hours or less. The longer and the more frequent the attacks are, the more likely it is that obstruction of the vessel is increasing. In refractory ischemia, acute revascularization by means of PTCA or CABG should be carried out. Elective revascularization should be performed in patients who are still symptomatic after optimal pharmacological treatment. Coronary angioplasty, as an initial alternative to bypass surgery, has been shown to be effective for the treatment of selected patients with unstable angina, both to relieve acute ischemic symptoms and to prevent progression to (re)infarction or cardiac death. The preference of coronary angioplasty above CABG in these critically ill patients is related to the avoidance of the intrinsic risks of major surgery and anesthesia, its rapid implementation, and its reduction of in-hospital stays and costs.

Coronary Angioplasty for Initially Stabilized Unstable Angina and Refractory Unstable Angina

The need for surgery or, alternatively, coronary angioplasty is obvious in patients with unstable angina who are refractory to optimal pharmacological treatment. Although initial pharmacological treatment may relieve the acute phase symptoms, patients remain at high risk for progression to myocardial infarction or cardiac death, and the need for coronary bypass surgery is not reduced [9]. The coronary artery obstruction in patients with unstable angina is at risk of becoming a permanent occlusion leading to myocardial infarction or death [10, 11]. It has now been shown that coronary angioplasty is relatively safe and can be performed with a high success rate in unstable angina that is either refractory to optimal pharmacological treatment [12-14] or is initially stabilized after treatment [15-17] (Table 1). The reported lower success rate of 63% to 76% was achieved with a nonsteerable

Table 1. Coronary angioplasty for initially stabilized unstable angina, refractory unstable angina, and early postinfarction unstable angina

Author	No. PT	Success rate %	Major complication rate death %	MI %	acute surgery %	Coronary events after successful angioplasty death %	MI %	AP %	Follow-up months mean
INITIALLY STABILIZED UNSTABLE ANGINA									
Faxon[1, 2] 1983 [15]	442	63	0.9	8	—	1.7	1.5	18	18
Quigley 1986 [16]	25	81	4	12	12	0	0	32	18
De Feyter 1987 [17]	71	87	0	10	12	2	2	23	12
REFRACTORY UNSTABLE ANGINA									
Williams[1] 1981 [12]	17	76	0	0	6	0	0	8	10.5
Meyer[1] 1983 [13]	50	74	0	4	2	0	0	36	6
de Feyter 1985 [14]	60	93	0	7	7	2	0	13	9
EARLY POSTINFARCTION UNSTABLE ANGINA									
de Feyter 1986 [40]	53	89	0	8	8	0	4	26	9
Gottlieb 1986 [41]	47	91	0	—	—	2	5	21	7.5
Holt 1986 [42]	69	80	2	—	12	0	4	24	21

[1]Use of a nonsteerable dilatation system
[2]Majority of the patients were initially stabilized
No. PT = number of patients; MI = myocardial infarction; AP = angina pectoris

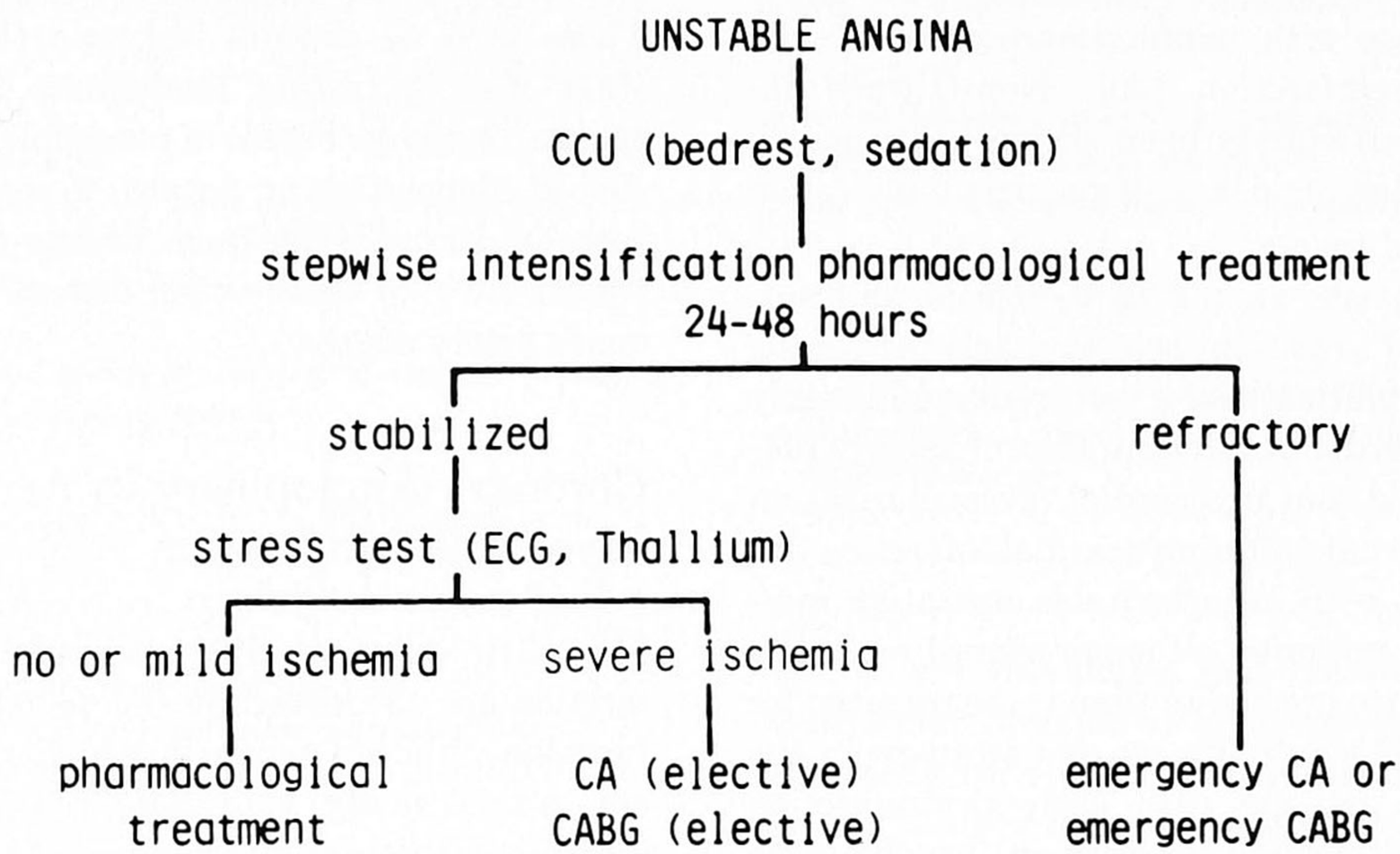

Fig. 1. Proposed management of patients with unstable angina. For all patients with unstable angina inclusive of early postinfarction angina. Pharmacological treatment includes, in all patients, anticoagulation (heparin, aspirin) and individually tailored therapy of either nitroglycerin (s.l., i.v.), beta-adrenoceptor agonists, and calcium antagonists, either alone or in combination. CA: coronary angioplasty; CABG: coronary artery bypass grafting; CCU: coronary care unit.

dilatation catheter, whereas the initial success rate of 81% to 93% was achieved with a steerable dilatation catheter. The latter figure reflects the current state-of-the-art, and the initial success rate achieved in unstable angina is somewhat lower than the greater than 90% success rate reported in series of patients with stable angina pectoris [18, 19].

A significant amount of complications (death, myocardial infarction, urgent bypass surgery) occurred more often in patients with unstable angina than in patients with stable angina [18-20]. Procedure-related death occurred between 0% and 4%; this is less than 1% for stable angina [18-20]. The procedure-related myocardial infarction rate varied from 0% up to 12%; this rate is substantially higher than the 4% rate reported for stable angina [18-20]. In addition, the need for urgent bypass surgery is higher (2% to 12% versus 4%) for an elective procedure. An explanation for the higher complication rate may be due to, besides the clinical instability, the presence of severe or eccentric lesions being higher in patients with unstable angina [21]. These lesions have been shown to be associated with a higher rate of major complications [20, 22]. The angiographic restenosis rate and recurrence of angina after an initial successful coronary angioplasty is favorable and appears to be comparable to those of patients with stable angina. [15, 17].

Thus coronary angioplasty can be performed at an acceptable risk and with a high initial success rate in patients with unstable angina either refractory to or stabilized after pharmacological treatment. However, these results are obtained in selected patients and those with predominantly single-vessel disease and well preserved left ventricular function.

Coronary Angioplasty for Early Postinfarction Angina

The recurrence of angina after sustained myocardial infarction, but still during the hospitalization period, is reported to be between 18% and 57% [23-28]. Early postinfarction angina is considered to have a poor short-term and long-term prognosis [23-27]. The incidence of early nonfatal reinfarction in patients with early postinfarction angina ranges between 19% and 34% [23, 24]. Reinfarction in these patients is therefore a serious complication, as it carries an in-hospital mortality of 20% to 36% versus 9% to 13% for patients

without reinfarction [24, 26]. The 1 year survival rate was 76% for those with reinfarction versus 91% for those without reinfarction [26]. Non-Q-wave infarctions have particularly been shown to be associated with a higher incidence of recurrent infarction [24, 28-31].

Uncertainty exists among cardiologists and surgeons with regard to patient selection and the timing of surgical revascularization for recurrent angina early after acute myocardial infarction. Recent reports [34-39] have suggested that myocardial revascularization within the first 30 days after myocardial infarction can be accomplished with an acceptable operative mortality in selected patients, although overall mortality and morbidity rates are higher than those reported for elective surgery. Accordingly, current strategy for the management of patients with early postinfarction angina is aimed at delaying surgery until such a time when it can be performed with less inherent risks. However, in patients with severe recurrent angina, one is forced to perform immediate coronary angiography to clarify the anatomical cause(s). This is more so since coronary angioplasty, as an alternative to bypass surgery, is now an attractive option. The initial and long-term results of coronary angioplasty in small series of patients with early postinfarction unstable angina [40-42] are shown in Table 1. A myocardial infarction occurred in 8%, and acute surgery was required in 8% to 12%, rates that are definitely higher than those for elective coronary angioplasty [18-20]. The reason for this may be that in early postinfarction angina, the ischemia-producing lesion is still "active," and intracoronary instrumentation may more readily induce total obstruction with resulting myocardial reinfarction. These data suggest that coronary angioplasty performed early after acute myocardial infarction is relatively safe and effective in the majority of patients who have preserved left ventricular function with predominant single-vessel disease. Whether angioplasty can be performed with safety and efficacy in patients with multivessel disease or with reduced left ventricular function in the immediate postinfarction phase remains to be determined. The following management scheme for patients with unstable angina is proposed (Figure 1). Initial treatment should consist of bed rest and sedation with stepwise intensification of pharmacological treatment, highly tailored to the individual needs of a patient. If the patient is refractory to this treatment, emergency revascularization should be carried out. Patients with one- or two-vessel disease should undergo PTCA, and those with two- or three-vessel disease or left main coronary artery disease should undergo CABG. Patients who are initially stabilized should undergo exercise testing (ECG or Thallium-201 scintigraphy) to provoke ischemia. Those with no or mild ischemia (ischemia at early stage of stress testing, inadequate blood pressure response, or a large extent of reversible perfusion defect) should, depending on extent of coronary artery disease, undergo PTCA (one- or two-vessel disease) or CABG (two- or three-vessel disease or left main coronary artery disease).

Coronary Angioplasty in Acute Myocardial Infarction

Mortality and morbidity after acute myocardial infarction are influenced by the degree of residual dysfunction of the left ventricle, which, in turn, is dependent on the size of the ultimate infarct. The concept of limiting infarct size by early recanalization of blocked coronary arteries in evolving myocardial infarction has been proven in clinical practice to be effective, and randomized studies have shown that early recanalization with streptokinase within the first few hours after the onset of symptoms will preserve left ventricular function [43-51]. In addition, in-hospital complications are reduced and 1-year follow-up survival has been shown to be improved [43-51]. Coronary angioplasty has been shown to play an (additional) important role in the management of patients with acute myocardial infarction [52-68]. The basis for this position is that with angioplasty a more complete opening of the vessel is achieved. However, the rationale for coronary angioplasty in acute evolving myocardial infarction requires further evaluation: Is direct recanalization of a blocked coronary artery without initial thrombolytic treatment preferred, or should it be instituted after failed thrombolytic treatment only?; Is dilatation of residual stenosis to optimize antegrade flow essential in order to achieve better myocardial recovery? Finally, can this procedure prevent postinfarction ischemia or reocclusion?

Advantages and disadvantages of early and delayed coronary angioplasty either in association with thrombolytic treatment or without thrombolysis are listed in Tables 2—4.

Severe residual stenosis of the infarct-related vessel is frequently present after successful thrombolysis. While initially only 40% of these patients were thought to be suitable for coronary angioplasty [52], more recently, almost all lesions are considered amenable to the procedure.

The initial success rates of coronary angioplasty with or without preceding thrombolytic therapy are listed in Table 5. This rate appears to be lower than the greater than 90% success rate that has been

Table 2. Immediate coronary angioplasty without preceding thrombolysis (i.v. or i.c.)

ADVANTAGES
Optimizes antegrade flow
Potentiates mechanically the natural lysis phenomenon
Avoids the bleeding complications of thrombolytic therapy
Applicable to patients with contraindication for thrombolytic therapy
Economizes time and money by combining a single diagnostic and therapeutic laboratory session
DISADVANTAGES
Is a potentially lethal procedure in the setting of an acute myocardial infarction
Is a "blind procedure": distal anatomy unknown; proper size of balloon unknown
Can cause dislocation of thrombotic material
May lead to all too sudden reperfusion with reperfusion damage (O_2 and Ca^{2+} paradox)?
Provides no alteration of thrombogenic state
Requires staffing and maintenance of an interventional laboratory around-the-clock

achieved in elective procedures [69, 70]. The initial success rate after a preceding failed thrombolysis was lower and varied between 57% and 83%. Apparently, these lesions are also more resistant to mechanical recanalization. Procedure-related death and other major complications were reported to be rare.

Since the ultimate efficacy of reperfusion to salvage myocardium is related to the severity of the residual stenosis, the latter holds the key to outcome in the long term. Animal experiments have shown that ischemia continues when flow remains restricted. In fact, ventricular function continues to deteriorate when coronary blood flow falls below a critical threshold [71-73]. It was also shown that recovery of regional left ventricular function is greatest when the remaining stenosis after intervention either with thrombolytic agents alone or combined with PTCA is minimal [74-76]. Furthermore, in a recent randomized study in a small group of patients comparing intracoronary streptokinase versus direct angioplasty, it was demonstrated that angioplasty was significantly more effective in alleviating the underlying coronary stenoses. It resulted in less peri-infarction angina and ischemia, and improved left ventricular function [61]. In another

Table 3. Immediate (or early) coronary angioplasty after initial thrombolysis (i.c. or i.v.)

ADVANTAGES
More gradual reperfusion: O_2 and Ca^{2+} paradox less likely
Better delineation of stenotic lesion: known distal vessel, proper size of balloon
Extent of intervention based on knowledge of severity of residual stenoses
DISADVANTAGES
Delay in achievement of optimal antegrade flow
Dilatation of a "recanalized" lesion may be complicated by a total occlusion
Uncertainty as to the degree of completion of the lytic process
Loss of time and money since therapeutic equipment for angioplasty must be inserted after removal of infusion catheter
Requires staffing and maintenance of an interventional laboratory around-the-clock.

Table 4. Delayed coronary angioplasty after lysis

ADVANTAGES
Elective procedure in optimal conditions after more comprehensive clinical assessment
Availability of surgical backup on a nonemergency basis
Persistent lytic state may have resulted in fufther (and even complete) thrombolysis
DISADVANTAGES
Potential for intercurrent reocclusion higher
Additional cost and patient discomfort due to need for a second procedure

Table 5. Success rate of coronary angioplasty in evolving myocardial infarction

AUTHOR	NO. PATIENTS	SUCCESS RATE %
Immediate coronary angioplasty without thrombolysis		
Pepine 1984 [57]	8	100
Holmes 1985 [58]	26	85
Linnemeier 1985 [60]	31	87
O'Neill 1986 [61]	29	83
Rutherford 1986 [62]	222	91
Topol 1986 [63]	29	83
Marco 1987 [59]	43	95
IMMEDIATE CORONARY ANGIOPLASTY AFTER SUCCESSFUL LYSIS		
Meyer 1982 [52]	21	81
Serruys 1983 [54]	18	100
Gold 1984 [64]	12	75
Papietro 1985 [65]	11	82
Erbel 1985 [66]	117	69
Holmes 1985 [58]	15	73
Thoraxcenter 1987*	115	88
Topol 1986 [63]	31	96
Kitazume 1986 [68]	16	88
IMMEDIATE CORONARY ANGIOPLASTY AFTER FAILED LYSIS		
Gold 1984 [64]	16	69
Holmes 1985 [58]	14	71
Papietro 1985 [65]	7	57
Prida 1986 [67]	18	83
Kitazume 1986 [68]	6	83

*Not published

randomized study, it was shown that coronary angioplasty immediately after combined i.v. or i.c. streptokinase (STK), compared to early combined i.v. or i.c. STK, was followed by an improvement in the regional left ventricular function in patients with anterior wall infarction only [77]. These results seem to justify early coronary angioplasty after thrombolytic treatment in cases with severe residual stenosis.

Reocclusion after initially successful thrombolytic therapy continues to be a significant problem. Angiographically verified reocclusion may occur in up to 25% of patients [78, 79]. It is generally accepted that rethrombosis and reinfarction are more likely to occur in the presence of a severe residual stenosis [54, 80], and certain characteristics of the geometry of the stenosis predict that rethrombosis will take place [80]. In a few nonrandomized studies [54, 74], it has been demonstrated that in subgroups of patients treated by the combination of thrombolytic agents and coronary angioplasty, the reocclusion and reinfarction rate is lower. In fact, angiographically established reocclusion rates after initially successful thrombolysis followed by successful coronary angioplasty varies from 3% to 18%, while in-hospital clinical reinfarction ranges between 11% and 18% [52, 58, 65]. In a recently conducted randomized study, the effect of coronary angioplasty following immediately after successful thrombolytic therapy demonstrated a lower incidence of reocclusion (14%), although this was not statistically significantly different (20%) from those treated with lysis alone [77]. However, the number of patients studied were small.

At present, while many questions are not yet answered, we propose the following practical scheme for the management of patients with an acute myocardial infarction (Figure 2). Thrombolytic treatment should begin as soon as possible, preferably out of the hospital, in patients who present with chest pain within 4 hours of onset of symptoms. Immediate coronary evaluation should be undertaken while the perfusion of the thrombolytic agent is maintained. In case of complete occlusion, mechanical perforation and dilatation should be immediately performed. With a severe remaining stenosis, angioplasty should be performed, but not in cases with minor or moderate stenosis.

Conclusion

In the absence of a cure, the physician's objective is to palliate and protect the individual patient as much as possible and at the lowest possible risk. Aggressive intervention with thrombolytic therapy is the current preferred means of managing patients with evolving myocardial infarction, provided therapy can begin within 4 hours after the onset of symptoms. Currently, the available data on the use of PTCA following thrombolysis are limited and conflicting, and no clear answers have as yet emerged about the additional effects of PTCA on left ventricular ischemia, preservation of left ventricular function, or prevention of reocclusion. We therefore feel that, at present, PTCA following thrombolysis should not be recommended as a routine procedure for all patients, but should be restricted to those with a remaining severe stenosis or those with failed thrombolysis. The end goals are a stable clinical state, preservation of myocardial function, and consequent improvement of morbidity and mortality. These need to be balanced against potential adverse effects of the intervention. One thing has become clear: The intervention should be instituted as soon as possible after the onset of symptoms to confer maximum benefits, and large, usually anterior, infarcts show the greatest gains.

Unstable angina should also be managed with haste, initially with stepwise intensification of pharmacological therapy to produce a stable state. Early angiography is indicated if this approach fails, and coronary angioplasty should be performed when a stenosis technically suitable for dilatation and responsible for the unstable state is found. The decision in favor of dilatation in single-vessel disease is easy to make. In the presence of multivessel disease, in some patients uncertainty remains. Dilatation of the ischemia-related vessel only, as opposed to total revascularization by multiple dilatations or bypass surgery, is currently preferred, but remains to be solved on the basis of more study.

Improvements in the equipment used for coronary angioplasty, such as steerable systems and low-profile balloons, have enhanced the success rates of this approach. Further refinements, including soft-tip guiding catheters, antegrade perfusion catheters, of laser techniques, should lead to even better results and higher safety of the procedures. Restenosis and reocclusion rates remain disappointingly high and pose a serious problem that needs to be resolved, either by better pharmacological approach or by prosthesis such as intravascular stents.

Coronary angioplasty has now reached a definitive place in the treatment of acute myocardial ischemia and infarction. Research should be increased to improve the technique, to accurately define the indications for its use, and to study the timing of dilatation in this group of acutely ill patients.

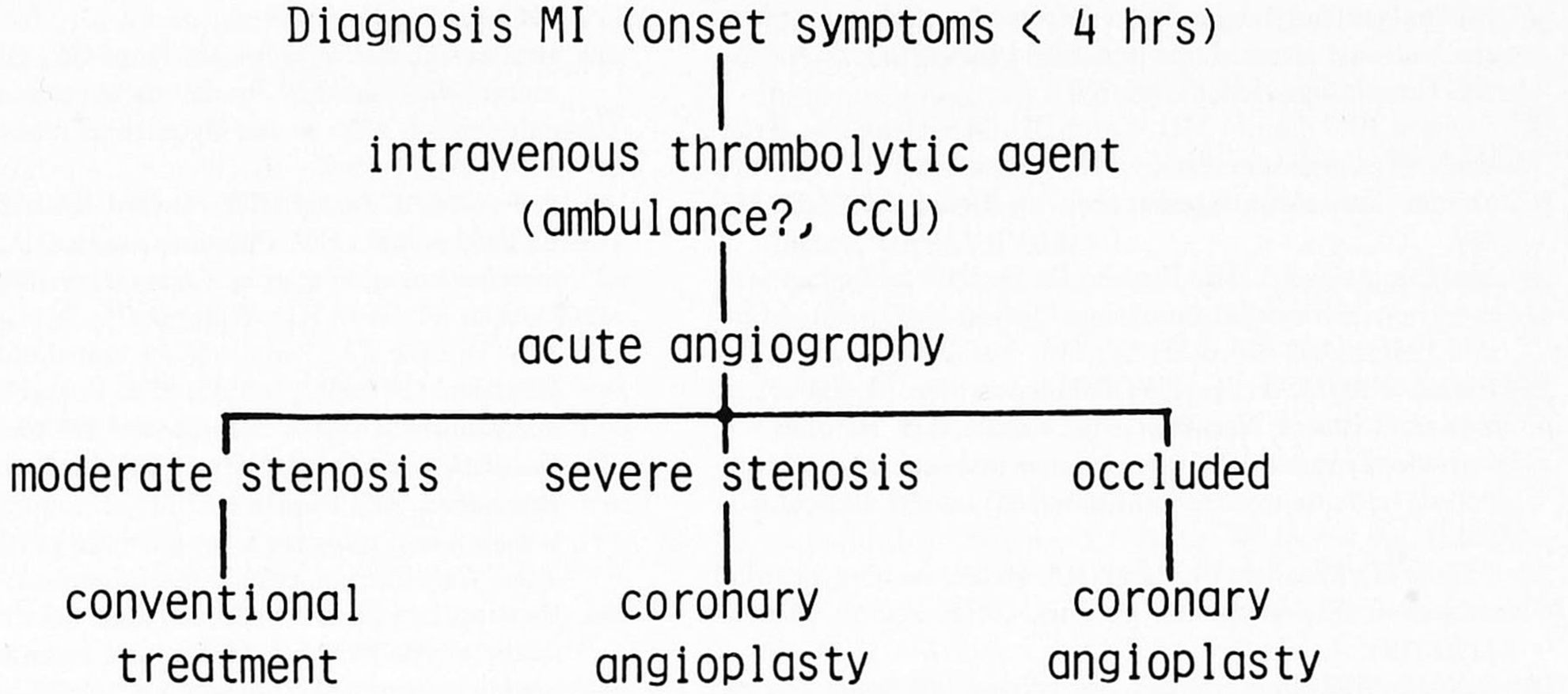

Fig. 2. Proposed management for patients with evolving myocardial infarction. MI: myocardial infarction; CCU: coronary care unit.

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