

# Acute complications of percutaneous transluminal coronary angioplasty for total occlusion

The incidence of major complications after percutaneous coronary angioplasty (PTCA) of a totally occluded artery was assessed retrospectively. A total of 1649 PTCA procedures were analyzed. After exclusion of procedures for acute myocardial infarction or total occlusion that resulted from restenosis, 90 patients were selected. Forty-four patients (49%) had stable angina and 46 (51%) had unstable angina. The estimated duration of occlusion was  $87 \pm 78$  days in patients with stable angina, as compared with  $10 \pm 8$  days in patients with unstable angina ( $p < 0.001$ ). Abrupt vessel closure during PTCA occurred only in patients with unstable angina (0% versus 17%,  $p < 0.05$ ). The major complication rate was 2.5% in the stable angina group, and 20% in unstable angina group ( $p < 0.01$ ). This rate was also significantly higher than the complication rate of 8% observed in 442 procedures that were performed during the same period in patients with the unstable angina and nonocclusive stenosis ( $p < 0.01$ ). Patients with unstable angina who undergo PTCA of a totally occluded artery represent a subset at high risk for major complications. (AM HEART J 1991;121:417.)

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Improvements in technology and operator experience have led to a greater use of percutaneous transluminal coronary angioplasty (PTCA) for chronically occluded coronary arteries, which now accounts for up to 10% of the total number of procedures that are performed in large centers.<sup>1</sup> Percutaneous recanalization of an occluded vessel followed by balloon dilatation constitutes a reasonable therapeutic alternative to coronary artery bypass surgery (CABG) and appears to be a challenging and attractive approach in patients with persistent ischemia in spite of an optimal drug regimen, especially in the presence of single-vessel coronary artery disease.

From a practical standpoint, coronary artery occlusion has been traditionally divided into functional occlusion and total occlusion.<sup>2</sup> Functional occlusion,

which is defined as a faint, late anterograde opacification of the vessel lumen distal to the obstruction, may rather represent an extremely severe stenosis, which has a higher primary success rate of angioplasty, as compared with total occlusion.<sup>3-5</sup> In spite of a lower primary success rate, PTCA of a total coronary occlusion (not associated with acute myocardial infarction [MI]) has often been considered a relatively safe and low-risk procedure.<sup>3-11</sup> The primary success rate is mainly determined by the duration of occlusion.<sup>3-9</sup> The longer the duration, the more the lesion is organized and the less is the likelihood of recanalization. In relation to the underlying pathophysiology of unstable angina pectoris,<sup>12, 13</sup> it seems conceivable that total occlusion in patients with unstable angina may be of shorter duration and thus easier to recanalize. On the other hand, the rate of major in-hospital events (MI, emergency revascularization either by repeat PTCA or CABG, and in-hospital death) has been shown to be higher in patients who undergo PTCA for unstable angina pectoris.<sup>14-19</sup> Patients with unstable angina who present with a totally occluded ischemia-related artery at the time of the procedure may even represent a subgroup at higher risk for acute complications, since intracoro-

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nary instrumentation in this particular situation may easily result in fragmentation and dislodgement of an occlusive intraluminal thrombus.

Therefore this retrospective study was undertaken to assess the incidence of major procedure-related complications in patients who underwent PTCA of a totally occluded vessel, with a special emphasis on patients who present with unstable angina pectoris at the time of the procedure.

## METHODS

**Study population.** From January 1986 to December 1988, 1649 PTCA procedures were performed at our institution. Angioplasty procedures that were attempted on occluded native coronary arteries were retrospectively identified from the catheterization laboratory computer data base and the corresponding cineangiographic films, and reports were reviewed. Total occlusion was defined as complete absence of antegrade contrast filling of the involved coronary artery beyond the site of obstruction. According to this definition, 153 procedures that were attempted on totally occluded coronary arteries were initially identified. Of these, 63 procedures performed in the setting of acute MI or total occlusion that resulted from a previous procedure (restenosis) were excluded from the study. Thus 90 procedures for total occlusion, which were attempted in 90 patients, were selected and constituted our study group. This group was then subdivided into a group with stable angina and a group with unstable angina, according to the information that was obtained by review of medical records. Unstable angina pectoris was defined as progressive angina, angina at rest, or early postinfarction angina, as proposed by de Feyter.<sup>18</sup> Accordingly, 44 patients (49%) were assigned to the stable angina group and 46 (51%) to the unstable angina group. Of the 46 patients with unstable angina, the great majority (36 patients; 78%) had either angina at rest or postinfarction angina, whereas the remaining 10 patients had progressive angina (new onset angina of a progressive nature or sudden worsening of preexisting stable angina).

All patients had clinical evidence of myocardium viability in the region of distribution of the occluded vessel, as documented by ischemic ECG modifications during chest pain at rest, exercise test, or thallium-201 scintigraphy and/or on the basis of regional wall motion analysis (echocardiography, left ventricular angiography). Patients with stable angina were referred for elective PTCA because of the persistence of anginal complaints in spite of optimal medical treatment. Patients who presented with unstable angina were routinely receiving antiplatelet and heparin therapy in addition to their antianginal treatment.

**Angioplasty procedure.** PTCA was carried out with a preformed 8F guiding catheter, a steerable dilatation system, and a pneumatic inflation device. A 7F pacing electrode was positioned in the right atrium. Before the procedure, 10,000 IU of heparin and 250 mg of aspirin were administered intravenously. Four ECG leads (I, II, III and V<sub>2</sub> for a left anterior descending artery lesion; leads I, II, III and V<sub>5</sub> for a circumflex artery lesion; and leads I, II, III and

V<sub>5</sub> for a right coronary artery lesion) and aortic pressure were monitored continuously. Recanalization was first attempted by probing the occluded segment with a standard soft-tipped guide wire, and if this approach failed, a stiffer guide wire was used. "Splinting" of the guide wire with the dilatation catheter or a perfusion catheter could also be attempted to improve its axial strength. After successful recanalization of the occluded segment and appearance of the guide wire in the downstream vessel, the intraluminal position of the guide wire was generally confirmed by its easy mobility or its course in the distal vessel, as seen by antegrade contrast flow around the guide wire or through collaterals. Thereafter, the dilatation catheter was advanced and positioned across the lesion. Depending on the situation, contrast injections through the dilatation catheter could also be performed to visualize the distal vessel lumen beyond the stenosis. Balloon inflation pressure varied from 2 to 12 atm, and the inflation period ranged from 30 to 180 seconds. The procedure was carried out with a cardiac surgical team on standby. Acute coronary closure that was presumably caused by thrombus formation, distal embolization, and residual thrombus at the site of dilatation were usually managed with intracoronary thrombolytic therapy.

After angioplasty, arterial and venous sheaths were usually left in place, and adequate anticoagulation with intravenous heparin infusion was continued for 24 hours. Patients were monitored for 24 hours, and serial ECGs and cardiac enzyme levels were obtained. Aspirin (500 mg daily) and nifedipine (40 to 60 mg daily) were given after the procedure.

In patients who underwent multivessel PTCA, the occluded vessel was usually attempted first. When a coronary artery that supplies collaterals had to be dilated, this was always performed after an attempt had been made on the totally occluded vessel. In patients with unstable angina pectoris and multivessel disease, PTCA was usually attempted on the ischemia-related vessel only.<sup>18</sup> The ischemia-related vessel was identified by the correlation of ischemic ECG modifications with angiographic findings. The totally occluded segment was found to represent the culprit lesion in all cases.

**Baseline characteristics.** The two groups were compared for age, gender, history of previous MI in the region of distribution of the occluded vessel, and estimated maximal duration of total occlusion. The maximal duration of total occlusion was estimated on the basis of the available clinical and angiographic information. For instance, in patients without a previous angiogram or in patients in whom a previous angiogram documented a complete occlusion, the maximal potential duration of occlusion was estimated as the time interval (in days) between a major change in anginal symptoms (or the occurrence of MI) and the date of the procedure. In patients with a previous angiogram that showed a nonoccluded segment, the maximal potential duration of occlusion was calculated as the time elapsed between the date of coronary angiogram and the date of PTCA, provided that no clinical events had occurred in the meantime. In three patients, the duration of occlusion could not be estimated.

A consensus by two experienced angiographers was used to evaluate angiographic cinefilms. Angiographic success was defined as a residual stenosis less than 50%, as determined by visual assessment. At the time of angiographic cinefilm review, the two angiographers were not aware of the anginal status and the clinical evolution of the patients. In the few cases in which there was no consensus between the two observers, the opinion of a third angiographer was solicited. The two subgroups were compared for (1) left ventricular ejection fraction, (2) extent of coronary artery disease, (3) site of occlusion, (4) estimated length of the occluded segment, and (5) angiographic evidence of intraluminal thrombus. Ejection fraction was calculated from a 30-degree right anterior oblique cineangiogram of the left ventricle. The extent of coronary artery disease was defined as the total number of epicardial vessels (or their major branches) that contained a visually assessed luminal diameter narrowing greater than 50%. An attempt was made to quantify the length of the nonvisualized coronary segment in patients in whom the distal extremity of the occlusion could be clearly defined by collateral contrast filling of the involved epicardial vessel. This estimation was made from the projection most perpendicular to the direction of contrast flow to minimize the effects of foreshortening. The diameter of the 8F guiding catheter was used as a reference for measurement. According to the value obtained, the estimated length was categorized as  $\leq 1$  cm, 1 to 2 cm, or  $\geq 2$  cm. This measurement could not be obtained in 23 cases (26%), mainly because of poor visualization of the distal vessel lumen. The angiographic criteria for the presence of intraluminal thrombus included an intraluminal central filling defect or lucency surrounded by contrast material, that was seen in multiple projections, and contrast staining within the lumen or at the site of occlusion.

**Angiographic complications.** The occurrence of the following angiographic complications was also evaluated to obtain a possible association with in-hospital events: (1) visible embolization, (2) coronary intimal dissection, (3) abrupt vessel reocclusion during PTCA, and (4) dilatation-induced occlusion of side branches. Embolization was defined as an intraluminal central filling defect surrounded by contrast material downstream to the site of angioplasty. Abrupt cutoff of contrast medium observed in the distal epicardial vessel or distal side branches was also considered to be consistent with embolization. Coronary intimal dissection, defined according to the National Heart, Lung, and Blood Institute PTCA Registry,<sup>20</sup> was categorized as minor or severe. Minor dissection was defined as a linear filling defect that did not compromise vessel lumen and did not result in delayed runoff of contrast in the antegrade flow. Severe dissection was defined as contrast staining within the vessel wall, contrast extravasation, extensive luminal or spiral-shaped filling defect ( $\geq 1$  balloon length) with delayed runoff of contrast material in the distal vessel, or dissection that resulted in occlusion of the dilated vessel. As suggested by Meier et al.,<sup>21</sup> dilatation-induced occlusion of side branches was defined as disappearance of side branches, stagnation of contrast flow, and/or occurrence of filling by collaterals. All angiographically visible proximal and involved side branches were in-

cluded. A side branch was considered to be involved in the lesion if its origin was situated in the immediate vicinity of the obstruction or if the side branch was subjected to temporary occlusion while the balloon was inflated.

**In-hospital events.** Clinical success was defined as an angiographically successful PTCA without any major procedure-related complication or recurrence of ischemic symptoms during hospitalization. The following in-hospital events were considered to be major procedure-related complications: (1) periprocedural MI, (2) emergency revascularization (either repeat PTCA or CABG), and (3) in-hospital death. The diagnosis of a periprocedural MI was determined by the development of new pathologic Q waves on a 12-lead ECG or a typical increase in serum cardiac enzymes (more than twice the normal level). Emergency PTCA was defined as a second procedure during the same hospitalization for the occurrence of acute ischemia that suggested abrupt vessel closure after a previously successful procedure. Abrupt closure that occurred during the initial PTCA session was not considered to be a major complication if it was successfully managed by repeat dilatation with or without intracoronary infusion of thrombolytic agents and if it did not result in myocardial necrosis. CABG, when performed during the same hospitalization after failed attempt of recanalization but otherwise uncomplicated procedure, was not considered to be a procedure-related complication.

**Statistical analysis.** Data are presented as mean  $\pm$  standard deviation. Categorical variables were analyzed with the chi-square test or Fisher's exact test, as appropriate. Continuous variables were analyzed with the unpaired Student's *t* test. A *p* value of less than 0.05 was considered statistically significant.

## RESULTS

**Baseline characteristics.** As shown in Table I, the two groups were similar for age, gender, and history of previous MI in the region of distribution of the occluded vessel. The estimated maximal duration of occlusion was shorter in patients with unstable angina than in patients with stable angina ( $10 \pm 8$  days vs  $87 \pm 78$  days,  $p < 0.001$ ). No statistically significant difference was observed between the two groups with respect to left ventricular ejection fraction, extent of coronary artery disease, site of the occluded segment, estimated length of occlusion, and angiographic evidence for intraluminal thrombus.

**Angiographic complications.** The occurrence of visible embolization, coronary intimal dissection, acute reocclusion during PTCA, and occlusion of side branches was observed more frequently in patients with unstable angina (Table II). However, the only significant difference was observed in the frequency of abrupt vessel reocclusion during PTCA, which occurred only in the subgroup of patients with unstable angina (0% versus 17%,  $p < 0.05$ ).

**Success rate and in-hospital events.** A residual sig-

**Table I.** Baseline characteristics

	Stable angina [n (%)]	Unstable angina [n (%)]	p Value
No. of patients	44	46	
Age (yr)	56.2 ± 9.9	56.7 ± 9.5	NS
Gender (male)	35 (79.5)	31 (67.5)	NS
Previous MI*	22 (41)	19 (40)	NS
Estimated duration of occlusion (days)	87 ± 78 (range: 10-478)	10 ± 8 (range: 1-33)	<i>p</i> < 0.001
Ejection fraction	0.58 ± 0.11	0.57 ± 0.14	NS
Extent of coronary artery disease			
1-vessel	20 (45.5)	27 (58.5)	
2-vessel	20 (45.5)	15 (32.5)	NS
3-vessel	4 (9)	4 (9)	
Site of occluded segment			
RCA	20 (45.5)	19 (41)	
LAD	13 (29.5)	20 (44)	NS
LCX	11 (25)	7 (15)	
Estimated length of occlusion			
≤1 cm	17 (39)	23 (50)	
1-2 cm	16 (36)	9 (20)	NS
≥2 cm	1 (2.5)	1 (2)	
Unknown	10 (22.5)	13 (28)	
Intraluminal thrombus	2 (5)	6 (13)	NS

LAD, Left anterior descending coronary artery; LCX, left circumflex coronary artery; MI, myocardial infarction; NS, not significant; RCA, right coronary artery.

\*Previous myocardial infarction in the flow region of the occluded vessel.

**Table II.** Angiographic complications\*

	Stable angina [n (%)]	Unstable angina [n (%)]	p Value
No. of patients	44	46	
Visible embolization	2 (9)	8 (23)	NS
Intimal dissection			
Minor	7 (16)	12 (26)	NS
Severe	3 (7)	5 (11)	NS
Acute reocclusion during PTCA	0	6 (17)	<i>p</i> < 0.05
Occlusion of side branches†			
Proximal	1/22 (4.5)	3/18 (17)	NS
Involved	3/31 (10)	5/23 (22)	NS

PTCA, percutaneous transluminal coronary angioplasty; other abbreviations as in Table I.

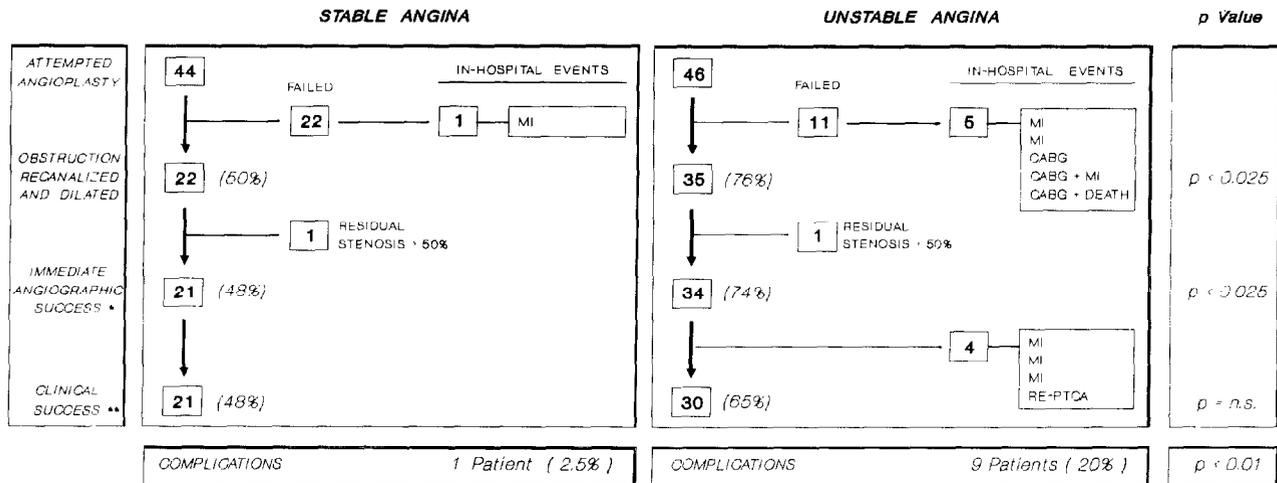
\*See text for definitions.

†The percentage (in parentheses) represents the number of cases in which side-branch occlusion was observed divided by the number of cases in which side branches were present.

nificant stenosis remained after PTCA in one patient of each group. As shown in Fig. 1, the immediate angiographic success rate was 48% in patients with stable angina, as compared with 74% in the unstable angina group (*p* < 0.025). One major procedure-related complication (MI) was observed in the stable angina group after a failed recanalization, which

leads to a major complication rate of 2.5%. Conversely, 11 in-hospital events occurred in nine patients (20%) in the unstable angina group (*p* < 0.01). This was observed in five of 11 patients whom attempted recanalization failed, and in four of 34 patients after an angiographically successful procedure. Interestingly, procedure-related complications in patients with unstable angina were observed only in those who had angina at rest or early postinfarction angina. The clinical success rate was 48% in the stable angina group and 65% in the unstable angina group (*p* = 0.09).

Table III provides additional information on patients who sustained in-hospital complications. After unsuccessful attempts on the occluded vessel, two patients (no. 2 and no. 5) had PTCA of another vessel that supplies collaterals to the occluded one. In these patients, complications were not directly related to attempted recanalization of the total occlusion. However, they were not excluded from the analysis since in this particular situation, failure to recanalize the occluded segment might have influenced patient outcome. Nevertheless, the exclusion of those two cases from the study would result in a complication rate of 16% in the unstable angina group (seven of 44 patients), which would remain significantly higher than in patients with stable angina (*p* < 0.05).



**Figure 1** Immediate angiographic and clinical success rates and major procedure-related complications in patients with stable and unstable angina pectoris who underwent coronary angioplasty of a totally occluded artery. \*Defined as a residual stenosis less than 50%, as determined by visual assessment. \*\*Defined as angiographically successful dilatation without major procedure-related complication or recurrence of ischemic symptoms during hospitalization. CABG, emergency coronary artery bypass surgery; MI, periprocedural myocardial infarction; RE-PTCA, emergency coronary angioplasty.

**DISCUSSION**

**Safety and efficacy of the procedure.** During the first years of PTCA, total coronary occlusion was regarded as a relative contraindication to the technique. With advances in technology and operator experience, several groups have reported favorable results, especially when the duration of occlusion was estimated to be less than 2 months.<sup>3-6, 8, 9</sup> Even if the primary success rate is lower than for nonocclusive stenoses, balloon angioplasty of a totally occluded coronary artery has been regarded as a relatively safe procedure with a low complication rate.<sup>3-9</sup> Nevertheless, our observations suggest that this rate may not be accurate for patients with unstable angina pectoris.

**PTCA and unstable angina.** Many reports have already shown that the performance of PTCA in patients with unstable angina pectoris carries a higher risk of acute complications.<sup>14-19</sup> The reasons for this high complication rate appear to be related to the underlying pathophysiology. In addition to the high-grade fixed coronary stenosis that is present in almost all patients with unstable angina,<sup>22, 23</sup> other dynamic conditions play a role including plaque fissuring with platelet aggregation; increased vasomotor tone; and formation of intraluminal thrombus.<sup>12, 13, 24-30</sup> There is well-established evidence for the rapid development and ubiquity of intraluminal thrombosis, which has been derived from angiographic,<sup>31, 32</sup> angioscopic,<sup>33</sup> and histopathologic observations.<sup>12, 13</sup> It has been demonstrated that the presence of preexisting intraluminal thrombus at

angiography constitutes a risk factor for acute complications during or shortly after PTCA,<sup>34, 35</sup> which is supported by the high rate of abrupt vessel closure and major complications that was observed in this series in patients with unstable angina. Experimental studies have also shown that endothelial denudation, platelet adhesion, mural thrombus, and localized vasoconstriction at the site of dilatation may all result from PTCA.<sup>36-38</sup> Thus if performed in the setting of unstable angina, it seems conceivable that balloon dilatation itself may cause further injury to the already ulcerated intima and intensify the ongoing thrombogenic process.

As stated previously, in-hospital complications that were observed in our group of 46 patients with unstable angina occurred only among those who had angina at rest or early postinfarction angina. This observation is in agreement with the findings of Black et al.<sup>39</sup> who showed, in a large series, that short duration of symptoms, angina at rest, and urgent PTCA for intractable angina were risk factors for the development of ischemic complications after PTCA.

**Unstable angina and total coronary occlusion.** Although no attempt was made to quantify angiographically the volume of intraluminal thrombus, a plausible reason for the high complication rate that is observed in patients with unstable angina could be related to this variable. In addition to the risk of abrupt vessel reocclusion, large intraluminal thrombi may lead to an increased risk of embolization. Once a complicated coronary lesion has progressed to

**Table III.** Description of major procedure-related complications observed in patients with total coronary occlusion

Patient	Age (yr)	Gender	Anginal status	Site of occlusion	Estimated duration (days)	In-hospital event(s)	Comment
1	60	F	Stable	LAD	20	MI	Occlusion of involved diagonal branch during attempted recanalization. Elective bypass surgery 19 days later.
2	53.6	M	Unstable	LAD	5	MI	Unsuccessful attempt on occluded LAD. Occlusion marginal branch after PTCA or LCX.
3	64.7	M	Unstable	RCA	3	MI	Occlusion of proximal right ventricular branch resulting in loss of collaterals. VF → Successful reanimation.
4	55.7	M	Unstable	LAD	21	CABG	Jeopardized diagonal branch during intracoronary instrumentation. Dissection in proximal LAD.
5	65	F	Unstable	RCA	8	CABG MI	Unsuccessful recanalization of RCA. Successful PTCA of LCX but abrupt closure 7 hours later. Failed re-PTCA → CABG.
6	39.2	M	Unstable	LAD	10	CABG Death	Attempted PTCA of proximal occluded LAD. Dissection and visible thrombus in LCX. BP drop. Death in OR. Massive MI.
7	54.4	M	Unstable	LAD	8	MI	Dissection and distal embolization after first dilatation. Satisfactory results after intracoronary SK and distal PTCA.
8	62.7	F	Unstable	RCA	3	MI	Severe fall in BP and HR during PTCA after reocclusion of RCA. IV atropine, dopamine, and colloids. Successful redilatation.
9	65.5	M	Unstable	LAD	6	MI	Occlusion of diagonal branch involved in the occluded segment. Normal runoff of distal LAD after PTCA.
10	69.2	F	Unstable	RCA	5	re-PTCA	Abrupt closure (chest pain, elevated ST segment) 19 hours after PTCA. Satisfactory results after emergency angioplasty.

BP, Blood pressure; CABG: emergency coronary artery bypass surgery; F, female; →, subsequent; IV, intravenous; M, male; OR, operating room; re-PTCA, emergency coronary angioplasty; SK, streptokinase; VF, ventricular fibrillation; other abbreviations as in Tables I and II.

complete occlusion, intraluminal thrombus may propagate beyond the site of obstruction.<sup>40</sup> After recanalization and dilatation, the restored antegrade blood flow may "flush" poststenotic thrombotic material toward the distal vascular bed, which may ultimately lead to myocardial necrosis.

Such a high complication rate in patients with unstable angina may also be related to inadequate collateral blood supply in the flow region of the occluded artery. Patients with unstable angina who present with a totally occluded ischemia-related artery might have poorer myocardial perfusion of the involved flow region as compared to those with persistent antegrade coronary flow. This would potentially lead to an increased vulnerability for myocardial necrosis after an ischemic insult such as side-branch occlusion

or distal embolization. Although this study was not aimed at assessment of the collateral supply, adequate visualization of the distal extremity of the occluded segment by collateral contrast opacification was observed in 33 of the 46 patients with unstable angina. Of these 33 patients, six sustained acute complications (18%), in comparison to three of the remaining 13 patients with unstable angina (23%) with poor or absent collateral filling (*p* value was not significant). Although the number of patients may be not sufficient to draw meaningful conclusions, this does not support the assumption that absence of angiographically visible collaterals was associated with an increased risk of complications.

Nevertheless, other possible mechanisms that are not detectable with conventional coronary angiogra-

phy may play a role. Pathologic studies in patients with unstable angina who died have demonstrated that spontaneous embolization of platelet aggregates can cause microinfarcts in small intramyocardial arteries.<sup>13</sup> Furthermore, in situ coronary thrombi may contain degranulating platelets, which release vasoconstrictors such as thromboxane A<sub>2</sub> and serotonin.<sup>41-43</sup> Leukocytes contained within recent thrombi can also produce leukotrienes, which constitute potent microvascular vasoconstrictors.<sup>44-47</sup> Wilson et al.<sup>48</sup> have recently described a syndrome of intense microvascular constriction after PTCA of acute thrombotic coronary lesions, which was attributed to the release of potent vasoconstrictors from intraluminal thrombus. In the presence of large, occlusive intraluminal thrombus, it seems conceivable that mechanical disruption of the clot induced by PTCA may further potentiate microembolization or induce considerable release of potent vasoconstrictors. However, it should be noted that in all patients with total coronary occlusion in whom a major complication occurred, a plausible "angiographic" explanation could be provided, such as abrupt closure, occlusion of side branches, or visible embolization. The assumption that the above mentioned pathophysiologic mechanisms were involved or superimposed remains purely speculative, and the assessment of such processes at the microvascular level was beyond the scope of this retrospective clinical study.

**Comparison with nonocclusive stenosis** (Table IV). During the study period, 1079 PTCA procedures were performed on native coronary arteries with nonocclusive stenoses (with the exclusion of left main PTCA and repeat procedures for restenosis). With the same criteria, the major complication rate that was observed in 637 elective procedures that were performed in patients with stable angina was 4% (26 patients), which is similar to the rate of 3% to 4% reported in other series of PTCA in patients with stable angina.<sup>1, 49, 50</sup> However, in-hospital events occurred in 8% of 442 PTCA procedures that were performed on nonocclusive coronary stenoses in patients with unstable angina ( $p < 0.005$ ). Although this is consistent with our previous observations and with the major complication rates of 3% to 12% reported by other investigators,<sup>14-19</sup> this rate remains significantly lower than the rate of 20% observed in the subgroup of unstable patients who presented with a total coronary occlusion at the time of the procedure ( $p < 0.025$ ).

**Comparison with previous reports.** Many reports have demonstrated that the performance of PTCA of a total coronary occlusion carries a low risk of acute complications,<sup>3-10</sup> even if the primary success rate is

**Table IV.** Rate of major complications in 1169 PTCA procedures according to the anginal status and the severity of coronary stenosis (from January 1986 to December 1988)

	Total occlusion	Non-occlusive stenosis	Total number	p Value†
<b>Stable angina</b>				
No. of patients	44	637	681	$p = \text{NS}$
with in-hospital events	1 (2.5%)	26 (4%)	27 (4%)	
<b>Unstable angina</b>				
No. of patients	46	442	488	$p < 0.025$
with in-hospital events	9 (20%)	36 (8%)	45 (9%)	
Total no. of procedures	90	1079	1169	
p Value‡	$p < 0.01$	$p < 0.005$	$p < 0.0005$	

\*Excluding coronary angioplasty of saphenous bypass graft, left main coronary artery, and for restenosis.

†Comparison of major complications rates between total occlusion and nonocclusive stenosis in patients with stable and unstable angina.

‡Comparison of major complication rates between patients with stable and unstable angina for total occlusion, nonocclusive stenosis, and total number of patients.

less favorable than the rate achieved in nonocclusive stenosis. Although there was a great variation in inclusion criteria and definitions of coronary occlusion, the majority of patients in these previous reports underwent PTCA for "chronic" total occlusion on an elective basis. The complications rate of 2.5% that was observed in the present series in patients with stable angina is in concordance with previous reports.

However, our observations differ from previous series with respect to the number of patients with unstable angina, which may explain, in part, the high rate of acute complications. In fact, 46 patients (51%) had PTCA in the setting of unstable angina.

**Clinical implications.** Since thrombolytic therapy combined with PTCA has been widely and safely used in the setting of acute MI, it may seem justified to apply this strategy to patients with unstable angina and total occlusion. We have used thrombolytic therapy in our institution as a "bail out" procedure during angioplasty to manage acute coronary closure, which was presumably caused by thrombus formation.<sup>51</sup> However, administration of a thrombolytic agent before attempted mechanical recanalization of a total occlusion in a patient with unstable angina might represent a rational approach. Although the role of thrombolytic therapy in unstable angina pectoris remains uncertain,<sup>52, 53</sup> patients with total coronary occlusion may represent a subgroup that could potentially benefit the most from a strategy of pretreatment with thrombolytic agents in an attempt to reduce the amount of intraluminal throm-

bus, stabilize the coronary lesion, and eventually decrease the risk of distal embolization or abrupt vessel closure. In fact, de Zwaan et al.<sup>53</sup> showed that the effect of thrombolytic therapy in patients with unstable angina was most marked in totally occluded or severely narrowed vessels, as assessed by quantitative angiographic analysis.

The ability of thrombolytic agents to dissolve intracoronary thrombus is expected to decrease as the duration of occlusion increases and as organization occurs. However, there is some evidence that thrombolysis might be effective in coronary occlusions of longer duration. Prolonged selective infusion of urokinase has been used successfully in small series to recanalize totally occluded coronary arteries and aortocoronary bypass grafts with documented thrombosis of 2 to 8 weeks' duration.<sup>54, 55</sup> However, the value of such an approach in patients with unstable angina who undergo PTCA of a totally occluded ischemia-related artery has to be determined by further prospective clinical trials.

**Limitations of the study.** This retrospective study has several limitations. Coronary angiography is the only clinical available method to detect the presence of intracoronary thrombus, and its sensitivity appears to be low in comparison with angioscopic and histopathologic observations. Even if the presence of intraluminal thrombus is highly suspected in the setting of recent coronary occlusion, angiographic criteria probably underestimate its frequency to a considerable degree. This may explain why intracoronary thrombus was identified in only 13% of our patients who had unstable angina before PTCA. Angiographic estimation of the length of the nonvisualized segment may also lack accuracy and lead to overestimation in some cases. Furthermore, the inability to estimate this variable in 23 cases (26%) may have resulted in erroneous inferences in the study group.

Additionally, determination of the duration of total occlusion on the basis of available clinical and angiographic information constitutes a rough estimate of the actual time interval. Although the duration is expected to be shorter in patients with unstable angina, one cannot be certain that the "age" of occlusion is equivalent to the duration of patients symptoms.

Finally, the relatively small number of patients that was included in this study may introduce the possibility of a type II error (failure to demonstrate a statistically significant difference when it exists). For instance, the observed frequency of visible embolization after PTCA was higher in patients with unstable angina (9% vs 23%), but no statistical dif-

ference could be demonstrated. This may also explain why the difference in the clinical success rate between the two subgroups (48% vs 65% in patients with unstable angina did not reach the level of statistical significance.

**Conclusions.** In spite of these limitations, we believe that the occurrence of such a high rate of acute complications in patients with unstable angina pectoris (especially in those with angina at rest or postinfarction angina) who undergo PTCA of a total coronary occlusion should be emphasized. Even if recent coronary occlusions have a higher likelihood of recanalization, this may be regarded as a "double-edged sword" in patients with unstable angina. This may be related to the volume of intraluminal thrombus, which in turn may lead to an increased risk of embolization or abrupt vessel closure. The major complication rate of 20% that was observed in patients with unstable angina was much higher than the complication rate of 2.5% in patients with stable angina. This rate was also significantly higher than the complication rate of 8% that was observed in patients with unstable angina who underwent PTCA of nonoccluded vessels during the same period. Patients with unstable angina who present with a totally occluded ischemia-related artery may constitute a subset that could potentially benefit from a strategy of pretreatment with thrombolytic agents. Further prospective trials are needed to effectively assess the usefulness and safety of this approach.

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## The combined antiischemic effects of the thromboxane receptor antagonist SQ 30,741 and tissue-type plasminogen activator

The thromboxane-receptor antagonist, SQ 30,741, may be used as adjuvant therapy for thrombolysis and has also been shown to have antiischemic activity that is independent of its thrombolytic activity. Since tissue-type plasminogen activator (t-PA) and SQ 30,741 may be administered simultaneously, we determined whether the antiischemic effects of SQ 30,741 can be potentiated by t-PA. This was accomplished by combining doses of t-PA and SQ 30,741, which alone were not cardioprotective. Anesthetized dogs were subjected to left circumflex coronary artery occlusion for 90 minutes and reperfusion for 5 hours. The dogs were treated during reperfusion with a dose of t-PA that caused approximately a 30% reduction in plasma fibrinogen alone or in combination with 1.5 mg/kg + 0.4 mg/kg/hr SQ 30,741, which started 10 minutes after initiation of ischemia. At these doses, neither t-PA nor SQ 30,741 alone significantly reduced infarct size (57% ± 6%, 50% ± 10%, 57% ± 6% of the left ventricular area at risk for vehicle controls, t-PA, and SQ 30,741 respectively); however, combination treatment resulted in a significant reduction in infarct size (37% ± 5% of the left ventricular area at risk). Higher doses of t-PA and SQ 30,741 alone significantly reduced infarct size. The protective effects of t-PA and SQ 30,741 occurred without altering peripheral hemodynamic status. No differences in collateral or reperfusion blood flow were observed between groups. Thus although SQ 30,741 may act to improve the efficacy of thrombolysis, t-PA may in turn enhance the antiischemic activity of SQ 30,741 or at least reduce the threshold dose. (*AM HEART J* 1991;121:426.)

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Reperfusion of myocardial tissue after acute myocardial ischemia or infarction has become a clinical reality, in part, because of the use of effective thrombolytic agents. Several thrombolytic agents have shown efficacy, and among the most interesting are activators of plasminogen. One such agent is tissue-