Immediate vs Delayed Intervention for Acute Coronary Syndromes: A Randomized Clinical Trial

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Immediate vs Delayed Intervention for Acute Coronary Syndromes

A Randomized Clinical Trial

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Context International guidelines recommend an early invasive strategy for patients with high-risk acute coronary syndromes without ST-segment elevation, but the optimal timing of intervention is uncertain.

Objective To determine whether immediate intervention on admission can result in a reduction of myocardial infarction compared with a delayed intervention.

Design, Setting, and Patients The Angioplasty to Blunt the Rise of Troponin in Acute Coronary Syndromes Randomized for an Immediate or Delayed Intervention (ABOARD) study, a randomized clinical trial that assigned, from August 2006 through September 2008 at 13 centers in France, 352 patients with acute coronary syndromes without ST-segment elevation and a Thrombolysis in Myocardial Infarction (TIMI) score of 3 or more to receive intervention either immediately or on the next working day (between 8 and 60 hours after enrollment).

Main Outcome Measures The primary end point was the peak troponin value during hospitalization; the key secondary end point was the composite of death, myocardial infarction, or urgent revascularization at 1-month follow-up.

Results Time from randomization to sheath insertion was 70 minutes with immediate intervention vs 21 hours with delayed intervention. The primary end point did not differ between the 2 strategies (median [interquartile range] troponin I value, 2.1 [0.3-7.1] ng/mL vs 1.7 [0.3-7.2] ng/mL in the immediate and delayed intervention groups, respectively; $P=.70$). The key secondary end point was observed in 13.7% (95% confidence interval, 8.6%-18.8%) of the group assigned to receive immediate intervention and 10.2% (95% confidence interval, 5.7%-14.6%) of the group assigned to receive delayed intervention ($P=.31$). The other end points, as well as major bleeding, did not differ between the 2 strategies.

Conclusion In patients with acute coronary syndromes without ST-segment elevation, a strategy of immediate intervention compared with a strategy of intervention deferred to the next working day (mean, 21 hours) did not result in a difference in myocardial infarction as defined by peak troponin level.

Trial Registration clinicaltrials.gov Identifier: NCT00442949

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THE OPTIMAL INTERVENTION IN the treatment strategy of patients presenting with acute coronary syndromes without ST-segment elevation (NSTE-ACS) has been debated for years. Numerous studies, randomized trials, and meta-analyses have investigated the potential benefits of invasive over conservative strategies, and most have suggested a prolonged advantage of an invasive approach for the prevention of death or myocardial infarction (MI), particularly among high-risk patients.[1-14]

If an invasive strategy is generally accepted to be the best option and is currently recommended in high-risk patients, little information is available regarding the optimal timing of coronary angiography and intervention.[15,16] Only 2 randomized studies evaluated the timing of intervention (early vs late) with patients in the 2 study groups receiv-

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ing comparable antithrombotic and invasive therapy.[10,12] The Intracoronary Stenting With Antithrombotic Regimen Cooling Off (ISAR-COOL) study showed that early angiography (mean time to catheterization, 3 hours) was superior to delayed angiography (4 days) in preventing death or MI at 1-month follow-up. In contrast, the recent Timing of Intervention in Patients With Acute Coronary Syndromes (TIMACS) study showed no advantage of early catheterization (14 hours) over late catheterization (50 hours) to prevent death, MI, or stroke at 6-month follow-up. The ISAR-COOL study had a long waiting period for catheterization in the control group, which is probably not fully representative of contemporary practice in high-volume centers with expedited care, whereas the "early" group in the TIMACS study had a longer delay to angiography than those in previous studies that also investigated a rapid invasive approach.[8,10,11]

Most high-volume centers have primary percutaneous coronary intervention (PCI) programs for acute ST-segment elevation myocardial infarction, a strategy that has been associated with improved outcome in these patients.[17] The same centers usually perform rapid catheterization for NSTE-ACS, in general on the day following admission. Whether further reduction in the time to intervention could reduce the occurrence of ischemic events is an attractive hypothesis but is so far unverified. In this study, we compared a strategy of immediate intervention mimicking a primary PCI approach to NSTE-ACS with a strategy of intervention scheduled on the next working day.

METHODS

Study Population

The Angioplasty to Blunt the Rise of Troponin in Acute Coronary Syndromes Randomized for an Immediate or Delayed Intervention (ABOARD) study, conducted from August 2006 through September 2008, enrolled patients with NSTE-ACS admitted at 13 high-volume centers in France with 24-hour facilities for treatment of primary PCI. The protocol was approved by the Comité de Protection des Personnes Ile-de France IV. The trial was led by the Academic Research Organization ACTION, the coordinating center being the Institut de Cardiologie at Pitié-Salpêtrière Hospital. Data management and statistical analyses were under the responsibility of the Unité de Recherche Clinique at Lariboisière Hospital. The trial was sponsored by the Direction de la Recherche Clinique at Assistance Publique-Hôpitaux de Paris (AP-HP) and mainly funded by a public grant from the Programme Hospitalier de Recherche Clinique.

Non–ST-segment elevation ACS was defined by the presence of at least 2 of the following criteria: (1) symptoms of myocardial ischemia, (2) electrocardiographic ST-segment abnormalities (depression or transient elevation of at least 0.1 mV) or T-wave inversion in at least in 2 contiguous leads, or (3) an elevated cardiac troponin I value (above the upper limit of normal). Eligible patients had to have also a Thrombolysis in Myocardial Infarction (TIMI) score of 3 or greater and an indication for coronary angiography. Main exclusion criteria were age younger than 18 years; refractory ischemia, major arrhythmias, or hemodynamic instability requiring immediate catheterization; ongoing treatment with warfarin, fibrinolysis, or glycoprotein IIb/IIIa inhibitor; and contraindications to abciximab. All patients provided written voluntary informed consent.

Randomization and Interventions

At admission, patients were centrally randomized with the use of a telephone Interactive Voice Randomization System to undergo an immediate invasive strategy or an invasive strategy scheduled on the next working day. Next working day was defined by a time window of 8 to 60 hours after enrollment, so that catheterization could be scheduled on the next calendar day for weekday admissions and on Mondays for weekend admissions. Decisions regarding the method for revascularization were left to the discretion of the investigators. In the 2 groups, when PCI was believed appropriate on the basis of the coronary angiogram, the investigators were asked to perform culprit vessel PCI in the same setting. In case of multivessel PCI, nonculprit vessels could be revascularized in the same setting or in a staged fashion, according to investigator preferences. In the 2 groups, when PCI was decided, abciximab treatment had to be started before wire-crossing of the lesion, using specific trial-labeled abciximab. When revascularization with coronary artery bypass graft (CABG) surgery was preferred, it was to be performed as soon as possible during the initial hospitalization period, regardless of randomized group.

Medical Therapy and Follow-up

Antithrombotic treatments respected local practice of the participating centers but were to be identical in the 2 study groups. Aspirin was recommended with an initial high loading dose of up to 500 mg, followed by 75 mg once daily. A high clopidogrel loading dose of more than 300 mg was also recommended, followed by 75 to 150 mg once daily. Choice and dose of anticoagulant were left to the discretion of the investigators. In patients undergoing PCI, abciximab was started just before intervention, with a 0.25-mg/kg intravenous bolus immediately followed by a 0.125-μg/kg per minute (to a maximum of 10 μg/min) continous intravenous infusion for 12 hours after completion of PCI. β-Blockers, statins, and angiotensin-converting enzyme inhibitors were strongly recommended as concomitant treatments. Patients underwent 12-lead electrocardiography before and after revascularization. Blood samples were taken every 6 hours before and after intervention (up to 24 hours after intervention or discharge) for measurement of troponin I and creatine kinase or creatine kinase MB values. Blood sampling was repeated in case of recurrent ischemic episode during hospitalization. Measurements were per-

formed locally, and the centers were requested to provide their value for the 99th percentile of the distribution curve of values obtained in a healthy population, as has been advocated for several years.[18] All biomarker values collected in each randomized patient were entered in a computer database for further analysis. One-month follow-up data were collected through a patient visit or, if not possible, by telephone interview.

Outcome Measures

The primary end point was the peak troponin I value during hospitalization for each patient. The key secondary end point was a composite of death, MI, or urgent revascularization at 1-month follow-up. Death was defined as death from any cause. Myocardial infarction was defined as any recurrent myocardial necrosis occurring either spontaneously or in the setting of revascularization. Recurrent myocardial necrosis was defined by the occurrence of any of the following: new Q waves in 2 or more contiguous electrocardiographic leads; spontaneous or post-PCI elevation of levels of creatine kinase and its MB isoenzyme to at least 2 times the upper limit of normal, with an increase of 50% or more over the previous value (if only creatine kinase values were available, the same rule applied, but a simultaneous increase in troponin I level was required); post-CABG elevation of levels of creatine kinase and its MB isoenzyme to at least 5 times the upper limit of normal, with an increase of 50% or more over the value obtained before operation (if only creatine kinase values were available, the same rule applied but a simultaneous increase in troponin level was required).

Major bleeding included spontaneous, PCI-related, or CABG-related bleeding. Major bleeding was defined according to the STEEPLE definitions,[19] by the presence of at least 1 of the following: bleeding resulting in death; retroperitoneal bleeding (confirmed by ultrasound, magnetic resonance imaging, computed tomography, surgery, or autopsy), intracranial bleeding (documented with magnetic resonance imaging, computed tomography, any other examination or autopsy), or intraocular bleeding; bleeding with hemodynamic compromise requiring specific treatment (inotropic drugs, administration of fluid or macromolecules); bleeding requiring surgical intervention or decompression of a closed space to stop or control the event (vascular surgery, drainage of cardiac tamponade); any transfusion of at least 1 unit of red blood cells or whole blood; or clinically overt bleeding resulting in a 3-g/dL decrease in hemoglobin value (or, when hemoglobin values were not available, a 10% decrease in hematocrit). Thrombocytopenia was defined as a platelet count less than 50000 cells/μL or a decrease of more than 50% from the admission value. End points were adjudicated by a central committee unaware of the treatment assignments of the patients.

Statistical Analysis

We calculated that a sample size of 176 in each group would ensure a power of at least 80% to detect a difference in peak troponin I values between the 2 strategies if the effect size (ratio of difference to standard deviation) was 0.3, using a *t* test, with a bilateral risk set at 5%. On this basis, the trial enrolled 352 patients. Analysis was by intention-to-treat. In case of missing values, a sensitivity analysis was carried out to check the robustness of the conclusions. Since the statistical distribution of the main criterion was found to be non-gaussian (tested by Shapiro-Wilk test), the Mann-Whitney test was used to compare the 2 strategies, and median differences associated to Hodges-Lehman 95% confidence interval (CI) were used to estimate differences between strategies for the whole population and for subgroups. All secondary end points were qualitative variables, and differences were tested by χ^2 or by Fisher exact probability tests if the validity criteria for the χ^2 test were not fulfilled. All tests were 2-sided, with a significance level fixed at 5%. All analyses were performed using SAS version 9.2 (SAS Institute Inc, Cary, North Carolina).

RESULTS

Patient Characteristics

Three hundred fifty-two patients were randomly assigned to undergo immediate or delayed intervention at 13 French centers with primary PCI facilities. Baseline characteristics were well balanced between treatment groups (TABLE 1). As expected from the enrollment criteria, many patients presented with comorbid conditions (95 [27%] with diabetes, 261 [74%] with elevated troponin I level, and 94 [27%] with TIMI score ≥5 on a maximum scale of 7). The patients received optimal medical therapy, which was similar in the 2 study groups, including statins in 333 (95%), β-blockers in 303 (86%), angiotensin-converting enzyme inhibitors in 289 (83%), and intense antiplatelet therapy as shown by high doses of clopidogrel and abciximab in 221 (99%) of patients undergoing PCI. Low-molecular-weight heparin was the most common anticoagulation prescribed. One-month follow-up was obtained in all patients.

Procedure Characteristics

Median time from randomization to sheath insertion was 70 (interquartile range [IQR], 0.51-123) minutes in the immediate intervention group, reflecting a primary PCI approach, compared with 21 (IQR, 18-25) hours in the delayed intervention group, confirming that intervention in this group was most often performed on the day following randomization. A coronary angiogram was obtained in all but 1 patient (FIGURE 1). Arterial access was radial in 296 patients (84%), multivessel disease was present in 178 patients (60%), and the left anterior descending artery was most frequently identified as the culprit artery. Percutaneous coronary intervention was performed in 222 (75%) and CABG in 33 (11%) patients with significant lesions on the coronary angiogram; on average, patients undergoing PCI received 1.2 (SD, 0.9) stents, of which 51% were drug-eluting stents (TABLE 2).

Main Outcome

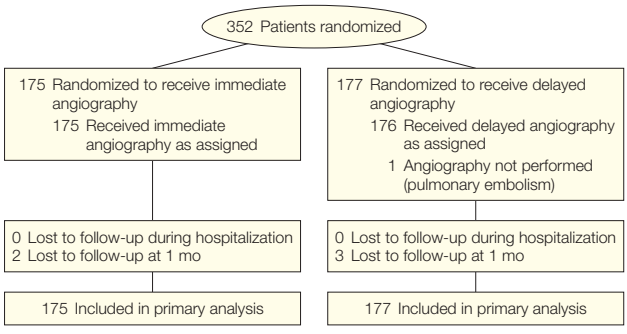
Troponin I release, as reflected by peak value collected during hospitalization,

Table 1. Baseline Patient Characteristics

Characteristic	Intervention Strategy, No. (%)	
	Immediate (n = 175)	Delayed (n = 177)
Age, mean (SD), y	65 (12)	65 (12)
Women	48 (27.4)	52 (29.4)
Weight, mean (SD), kg	77 (16)	76 (15)
Medical history		
Current smoking	56 (32.0)	60 (33.9)
Diabetes mellitus	38 (21.7)	57 (32.2)
Dyslipidemia	100 (57.1)	102 (57.6)
Hypertension	115 (65.7)	108 (61.0)
Previous CABG	9 (5.1)	12 (6.8)
Previous MI	29 (16.6)	33 (18.6)
Previous PCI	43 (24.6)	54 (30.5)
Previous PAD	18 (10.3)	25 (14.1)
Previous stroke	9 (5.1)	8 (4.5)
Previous cancer	7 (4.0)	11 (6.2)
Respiratory insufficiency	10 (5.7)	10 (5.6)
Cardiac insufficiency	7 (4.0)	7 (4.0)
Entry criteria		
Ischemic symptom	172 (98.3)	173 (97.7)
ST-T segment changes	122 (69.7)	136 (76.8)
Elevated troponin I	132 (75.4)	129 (72.9)
TIMI score		
≥3	167 (95.4)	169 (95.5)
≥5	40 (22.9)	54 (30.5)
Treatments during hospitalization		
Aspirin	173 (99.4)[a]	177 (100)
Clopidogrel	168 (96.6)[a]	175 (98.9)
Loading dose, mean (SD), mg	660 (268)	663 (267)
Maintenance dose, mean (SD), mg	111 (39)	111 (40)
Abciximab	114 (65.1)	101 (57.4)[a]
Unfractionated heparin only	9 (5.1)[a]	6 (3.4)
LMWH only	120 (68.6)[a]	119 (67.2)
Both unfractionated heparin and LMWH	40 (22.9)[a]	51 (28.8)
Neither unfractionated heparin nor LMWH	5 (2.9)[a]	1 (0.6)
β-Blocker	152 (87.4)[a]	151 (85.3)
Statin	164 (94.3)[a]	169 (95.5)
ACE inhibitor or ARB	147 (84.5)[a]	142 (80.2)[a]
Insulin	36 (20.7)[a]	54 (30.5)

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; CABG, coronary artery bypass graft; LMWH, low-molecular-weight heparin; MI, myocardial infarction; PAD, peripheral arterial disease; PCI, percutaneous coronary intervention; TIMI, Thrombolysis in Myocardial Infarction.
[a]Missing value for 1 patient.

Figure 1. Trial Flow



did not differ between the 2 strategies (median, 2.1 [IQR, 0.3-7.1] ng/mL vs 1.7 [IQR, 0.3-7.2] ng/mL in the immediate and delayed intervention groups, respectively; $P=.70$). The probability of MI as measured by the curves of troponin peak values was similar with either strategy (FIGURE 2). Consistent results were found across all major subgroups (FIGURE 3). In the subset of revascularized patients, the proportion of peak troponin values occurring before the procedure was 109 (43.4%; 95% CI, 37.3%-49.6%), whereas the proportion of peak troponin values occurring after the procedure was 142 (56.6%; 95% CI, 50.4%-62.7%).

Secondary Outcomes

The key secondary end point combining death, MI, or urgent revascularization at 1-month follow-up occurred in 13.7% (95% CI, 8.6%-18.8%) of patients with the immediate strategy and 10.2% (95% CI, 5.7%-14.6%) of patients with the delayed strategy ($P=.31$). Because 5 patients (2 in the immediate group and 3 in the deferred group) did not come for the 1-month visit, we checked that similar conclusions were drawn when the secondary end points for these patients were considered not reached (TABLE 3) or reached (data not shown).

The incidence of the 3 components taken individually through 30 days was not significantly different between the 2 groups (Table 3). Of the 24 MIs, 9 occurred before and 15 after catheterization. When a different definition of MI was tested, using 5 times the upper limit of normal of creatine kinase MB with an increase of 50% or more over the previous value, no significant difference was observed between the 2 strategies (n=7 [4%] vs n=3 [1.7%], $P=.22$). The neutral effect of intervention observed overall for the key secondary end point was also consistent across all major subgroups. When the analyses were restricted to revascularized patients, no significant difference was observed between the 2 strategies for both the primary and secondary end points. To exclude that long delays to the catheterization labo-

ratory would bias the results toward the negative, we performed a sensitivity analysis confirming that results and conclusions reported in Table 3 were similar when patients of the deferred group with a time to the catheterization laboratory in the greater than 75th percentile were excluded.

Recurrent ischemia was not significantly lower with the immediate strategy than with the delayed approach (12.0% [95% CI, 7.2%-16.8%] vs 18.6% [95% CI, 12.9%-24.4%], respectively; $P=.08$), and the composite quadruple end point of death, MI, urgent revascularization, or recurrent ischemia occurred in 21.1% (95% CI, 15.1%-27.2%) and 21.5% (95% CI, 15.4%-27.5%) of patients, respectively ($P=.94$).

Hospital stay was significantly reduced with the immediate strategy compared with the delayed intervention strategy (median, 55 [IQR, 30-98] hours vs 77 [IQR, 49-145] hours, respectively; $P<.001$).

Safety Outcomes

There was no difference in major bleeding between the 2 groups (Table 3). Nineteen patients presented with major bleeding, CABG or non-CABG related, with or without transfusion. The most frequent overt bleeding complications were gastrointestinal tract (n=4) and puncture-related (n=4, all groin hematomas) bleeding; other bleeding complications were hemopericardium (n=2), intracranial (n=1), epistaxis (n=1), and non-access site–related hematoma (n=1). One of these patients had 2 bleeding events. Seven more patients had no clinical evidence of bleeding but presented either a decrease in hemoglobin level during hospitalization or had anemia on admission motivating a transfusion; these patients were then counted as having major bleeding.

COMMENT

This study demonstrates the feasibility of immediate catheterization and revascularization in patients who present with NSTE-ACS but does not show that this strategy is superior to catheterization scheduled on the next working day. The hypothesis that reducing the waiting period for revascularization to a delay of primary PCI would reduce MI is not confirmed. To our knowledge, the mean time to catheterization in our delayed intervention group is also the shortest time to catheterization ever reported in the conservative group of randomized studies, but we believe it accurately reflects current practice in high-volume centers performing expedited care for patients with NSTE-ACS. There was no suggestion of a possible benefit with the strategy of immediate catheterization in any subgroup, including the highest-risk subgroups.

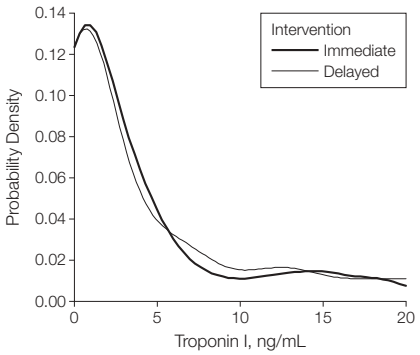
One concern with studies comparing different strategies of intervention

Table 2. Delays and Results of Cardiac Procedures

Delays, Median (IQR), h	Intervention Strategy: Immediate (n = 175)	Intervention Strategy: Delayed (n = 177)
Delays		
Time from admission to randomization, median (IQR), hr.min	1.07 (0.33-2.21)	1.11 (0.28-2.20)
Time from randomization to sheath insertion, median (IQR), hr.min	1.10 (0.51-2.03)	20.48 (17.30-24.36)
Time from sheath insertion to end of procedure, median (IQR), hr.min[a]	0.45 (0.35-0.60)	0.47 (0.34-0.65)
Arterial access, No. (%)[b]		
Radial	152 (87.4)	144 (81.8)
Femoral or brachial	21 (12.1)	29 (16.5)
Multiple	1 (0.6)	3 (1.7)
Angiographic findings, No./total (%)		
Significant lesion(s)	146 (83.4)	151 (85.3)
Left main trunk disease	9/146 (6.2)	17/151 (11.3)
Single-vessel disease	63/146 (43.2)	51/151 (33.8)
Double-vessel disease	48/146 (32.9)	54/151 (35.8)
Triple-vessel disease	32/146 (21.9)	44/151 (29.1)
CABG disease	6/146 (4.1)	7/151 (4.6)
Culprit artery, No./total (%)		
Left main trunk	6/146 (4.1)	11/151 (7.3)
Left anterior descending artery	71/146 (48.6)	68/151 (45.0)
Circumflex artery	36/146 (24.7)	44/151 (29.1)
Right coronary artery	36/146 (24.7)	38/151 (25.2)
Coronary bypass graft	3/146 (2.1)	3/151 (2.0)
Revascularization		
Percutaneous coronary intervention, No./total (%)	117/146 (80.1)	105/151 (69.5)
Stent (at least 1), No./total (%)	110/117 (94.0)	101/105 (96.2)
Drug-eluting stent (at least 1), No./total (%)	56/117 (47.9)	58/105 (55.2)
Number of stents/patient, mean (SD)	1.2 (0.9)	1.2 (1.0)
CABG surgery, No./total (%)	16/146 (11.0)	17/151 (11.3)

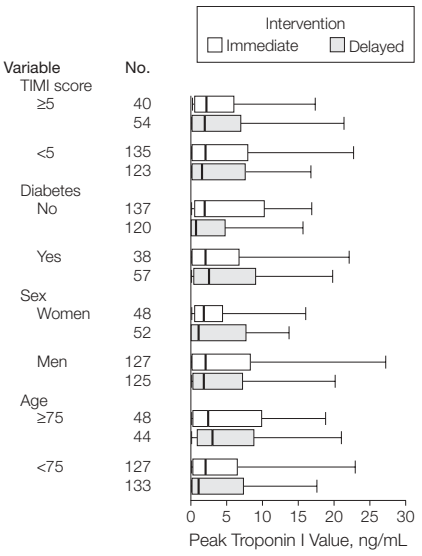
Abbreviations: CABG, coronary artery bypass graft; IQR, interquartile range; PCI, percutaneous coronary intervention.
[a] Angiography with PCI.
[b] Missing value for 1 patient in each group.

Figure 2. Peak Troponin I Values (Primary End Point) in Groups Receiving Immediate and Delayed Invasive Intervention



Curves represent probability density function of the peak troponin value (for each value x of troponin, density is the probability for troponin value to be in the interval [x, x + dx]).

Figure 3. Primary End Point (Peak Troponin I Value) in Relevant Subgroups



Boxes indicate median (interquartile range); whiskers, 10th and 90th deciles. TIMI indicates Thrombolysis in Myocardial Infarction.

in NSTE-ACS is the frequent imbalance in rates of catheterization, revascularization, and medications used. Moreover, rapid percutaneous revascularization may expose stented patients to ineffectiveness of some medications that have a slow onset of action. These limitations may not apply to our study, because all patients in the 2 groups underwent catheterization, leading to comparable rates of revascularization. In all patients, we used high loading doses of clopidogrel, reducing its slow onset of action; when PCI was performed, immediate and strong platelet inhibition was provided with the administration of abciximab, a strategy of intense antiplatelet therapy comparable to what is recommended in primary PCI and what has been shown effective in treatment of high-risk NSTE-ACS.[20] A recent study has confirmed that glycoprotein IIb/IIIa inhibitors should not be routinely administered at admission in NSTE-ACS but rather initiated after angiography, a strategy applied in our study.[21]

The benefit of early intervention in NSTE-ACS relates directly to the patient's level of risk as evaluated by the Global Registry of Acute Coronary Events (GRACE) score in TIMACS, the TIMI score in our study, and more intuitively in ISAR-COOL.[10,12] The magnitude of clinical benefit in these studies also correlates with the difference in time to catheterization between the 2 strategies—long in ISAR-COOL (83 hours), intermediate in TIMACS (36 hours), and short in ABOARD (19 hours). According to all 3 studies, an early invasive approach is no better than a delayed approach at preventing death; it also has little effect on MI, while there is a modest reduction in episodes of refractory ischemia. Thus, rapid or urgent catheterization appears preferable in high-risk or unstable patients, while the benefit in other situations may be limited to practicality and length of hospital stay.

Many different definitions of MI have been used in prior studies, using different cutoff levels of creatine kinase MB: the upper limit of normal,[4,5] greater than 2 times the upper limit of normal,[9,22] or greater than 3 times the upper limit of normal.[7] The upper limit of normal of troponin I level has also been used in the definitions of MI in more recent recent trials.[23] We designed our study following the recommendations of the European Society of Cardiology,[18] with a definition of MI based on troponin value for the primary end point, a recommendation confirmed during the study by the publication of the Joint Task Force for the Redefinition of Myocardial Infarction.[24] We used the peak troponin value during hospitalization, occurring before or after revascularization, knowing that periprocedural myonecrosis and spontaneous or recurrent myonecrosis both have prognostic implications.[25-27] The peak troponin value is also rarely missed in patients with NSTE-ACS and is certainly a better end point in this study than the area under

Table 3. Study End Points

End Point	Intervention Strategy, No. (%)		*P* Value
	Immediate (n = 175)	Delayed (n = 177)	
Peak troponin I during index hospitalization, median (IQR), ng/mL (primary end point)	2.1 (0.3-7.1)	1.7 (0.3-7.2)	.70
Death, MI, or urgent revascularization at 1 mo, (key secondary end point)	24 (13.7)	18 (10.2)	.31
Death (all-cause)	5 (2.9)	2 (1.1)	.28
MI	16 (9.1)	8 (4.5)	.09
Non–CABG-related	15 (8.6)	8 (4.5)	.12
Post-CABG	1 (0.6)	0 (0)	.50
Urgent revascularization	6 (3.4)	10 (5.6)	.32
PCI	5 (2.9)	7 (4.0)	.57
CABG	1 (0.6)	3 (1.7)	.62
Death, MI, urgent revascularization, or recurrent ischemia at 1 mo	37 (21.1)	38 (21.5)	.94
Recurrent ischemia with or without urgent revascularization at 1 mo	21 (12.0)	33 (18.6)	.08
Major bleeding at 1 mo	7 (4.0)	12 (6.8)	.25
Non–CABG-related	4 (2.3)	9 (5.1)	.26
CABG-related	3 (1.7)	3 (1.7)	>.99
Transfusion ≥2 units	6 (3.4)	10 (5.6)	.32
Transfusion ≥5 units	2 (1.1)	2 (1.1)	>.99
Thrombocytopenia	5 (2.9)	8 (4.5)	.41
Non-CABG	4 (2.3)	7 (4)	.54
Post-CABG	1 (0.6)	1 (0.6)	>.99

Abbreviations: CABG, coronary artery bypass graft; IQR, interquartile range; MI, myocardial infarction; PCI, percutaneous coronary intervention.

the curve, which is directly affected by the delay to catheterization. Using intense antiplatelet therapy and comparing immediate to delayed intervention, we could not demonstrate a significant difference in MI, regardless of the definition of MI based on peak troponin (primary end point) or peak creatine kinase MB (secondary end point) values. Recurrent ischemia as well as urgent revascularization was numerically lower with the immediate strategy, but these differences did not reach statistical significance. Such favorable trends with early intervention are consistent with those from other studies, which had different timings for revascularization.[10,12]

The safety of immediate intervention was not different from that of delayed intervention. We used the STEEPLE definitions of major bleeding, because they are more sensitive than other bleeding definitions and are more adapted to percutaneous intervention. The predominant use of radial access in our multicenter intervention study limited the number of access-site complications.[28,29] Gastrointestinal tract bleeding was the most frequent complication and was possibly underestimated, because occult gastrointestinal tract bleeding also may have occurred in some of the 7 patients who had anemia or a decrease in hemoglobin level without overt bleeding.

The use of optimal medical therapy was higher in our study than that reported in registries, which may appear as a limitation and could influence effectiveness in clinical practice. Additionally, the study sample size, like that in other studies, limited the ability to arrive at a definite conclusion regarding a difference in clinical events.[6,8,10,11,30] Nevertheless, the strategy of immediate intervention does not appear to provide any benefit or harm in comparison with an intervention postponed to the next working day; it was, however, associated with a significantly shorter hospital stay. A large majority of patients with NSTE-ACS remain free of complications, and after successful percutaneous revascularization, nothing should hamper hospital discharge. In general, conservative strategies consume considerable resources, drugs, and physician and nursing time, and this shortening in hospital stay may appear to be a practical and economic advantage in high-volume centers with a rapid turnover, especially when the patients present during daytime and catheterization rooms are already activated. However, further economic analyses would be required to assess the cost-effectiveness of such strategy in various health care systems.

In patients with moderate- to high-risk NSTE-ACS, a strategy of immediate intervention compared with a strategy of intervention deferred to the next working day (mean, 21 hours) did not result in a difference in MI as defined by peak troponin level.

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