Efficacy of Coronary Revascularization in Patients With Acute Chest Pain Managed in a Chest Pain Unit

JUAN SANCHIS, MD, FESC; VICENT BODÍ, MD, FESC; JULIO NÚÑEZ, MD; LUIS MAINAR, MD;
EDUARDO NÚÑEZ, MD; PILAR MERLOS, MD; EVA RÚMIZ, MD; GEMA MIÑANA, MD;
XAVIER BOSCH, MD, FESC; AND ANGEL LLÁCER, MD, FESC

OBJECTIVE: To investigate the safety of discharge of patients deemed at low risk of cardiac events after evaluation in a chest pain unit and to determine the prognostic effect of revascularization of patients deemed at high risk.

PATIENTS AND METHODS: The study population consisted of 1088 patients presenting at the emergency department from January 15, 2001, to September 1, 2006, with chest pain but without ischemia on electrocardiography or troponin elevation. Patients were managed by a chest pain unit protocol that included early exercise testing. Three groups of patients were distinguished: (1) those discharged after exercise testing (424 [39%]); (2) those in whom unstable angina was ruled out after in-hospital evaluation (208 [19%]); and (3) those in whom unstable angina was confirmed or not ruled out (456 [42%]). Of the 456 patients in group 3, 183 (40%) were revascularized at the index episode. The primary end point was the occurrence of myocardial infarction or death within 1 year. Adjustments were made for patient characteristics and a propensity score for revascularization (*c* statistic [0.83]).

RESULTS: Groups 1 and 2 showed lower rates of the primary end point than group 3 (group 1: 7 [1.7%]; group 2: 1 [0.5%]; group 3: 62 [13.6%]; *P* = .001). In group 3, revascularization at the index episode did not reduce the primary end point in the univariate (22 [12%] vs 29 [11%]; *P* = .80) and multivariate (hazard ratio, 1.4; 95% confidence interval, 0.7-2.5; *P* = .40) analyses. In-hospital revascularization decreased the need for postdischarge revascularization (hazard ratio, 0.3; 95% confidence interval, 0.1-0.7; *P* = .01).

CONCLUSION: Chest pain unit protocols are associated with safe patient discharge. Although early revascularizations may decrease the need for postdischarge revascularizations, they may not improve 1-year outcomes by reducing the number of myocardial infarctions or deaths.

Mayo Clin Proc. 2009;84(4):323-329

CI = confidence interval; HR = hazard ratio

Making decisions for the care of patients presenting at the emergency department with chest pain of uncertain origin is challenging.¹ Physicians risk incorrectly discharging patients with acute coronary syndrome or inappropriately hospitalizing patients without ischemic heart disease. The cardiac troponins, which are markers of acute myocardial infarction, permit diagnosis with high sensitivity and specificity.² In addition, the implementation of chest pain unit protocols incorporating early exercise testing allows the evaluation of patients with nondiagnostic findings on electrocardiography and normal troponin levels.³ Noninvasive imaging techniques complete

the triage process in instances in which patients are unable to exercise.⁴⁻⁶

This exhaustive evaluation reveals a number of patients with significant coronary artery stenosis despite the absence of evidence of ischemia on initial electrocardiography and normal levels of troponin markers. In these cases, unstable angina is usually diagnosed, which is then treated with a revascularization procedure. The outcome of prompt revascularization in such patients is uncertain. Subgroup analysis in acute coronary syndrome trials has not shown a benefit of invasive management in patients without ST-segment deviation or troponin elevation.^{7,8} These trials involved a broad spectrum of patients, including those with non-ST-segment elevation acute myocardial infarction, and did not represent the chest pain unit population.

The current study examined a series of consecutive patients presenting at an emergency department with chest pain without ST-segment deviation or troponin elevation. The patients were managed by a chest pain unit protocol. The aim of the study was to investigate the safety of the decision to discharge patients deemed at low risk of cardiac events and to determine the effect of early revascularization on the prognosis of patients deemed to have unstable angina or to be at high risk of cardiac events at the index episode.

PATIENTS AND METHODS

The study group included 1088 consecutive patients presenting at the emergency department from January 15, 2001, to September 1, 2006, with chest pain considered by the cardiologist on duty to be of possible coronary origin. A noncardiologist assessed the eligibility of patients for the

From the Servei de Cardiologia, Hospital Clínic Universitari, Universitat de València, València, Spain (J.S., V.B., J.N., L.M., E.N., P.M., E.R., G.M., A.L.) and Servei de Cardiologia, Hospital Clínic i Provincial, Barcelona, Spain (X.B.).

This work was supported by a HERACLES grant (Instituto de Salud Carlos III, Madrid, Spain). Drs Sanchis, Bodí, Núñez, Mainar, and Llacer were also supported by grant FIS PI070640 (Instituto de Salud Carlos III, Madrid, Spain), and Dr Bosch was also supported by grant FIS PI0500120 (Instituto de Salud Carlos III, Madrid, Spain).

Individual reprints of this article are not available. Address correspondence to Juan Sanchis, MD, FESC, Servei de Cardiologia, Hospital Clínic Universitari, Blasco Ibáñez 17, 46010 València, Spain (sanchis_juafor@gva.es).

© 2009 Mayo Foundation for Medical Education and Research

study by determining whether their chest pain was of coronary origin, and a cardiologist performed a second evaluation and confirmed the diagnosis. The exclusion criteria were ST-segment deviation of 1 mm or greater on initial electrocardiography, troponin I elevation at any determination, or known prior nonischemic heart disease (valvular heart disease or cardiomyopathy). Troponin I was measured at admission and at 12 hours from the onset of chest pain. Two different troponin I assays were used: the Immulite assay (Diagnostic Products Corporation, Los Angeles, CA) until October 1, 2003, and, after that date, the Dimension assay (Dade Behring, Newark, DE). Positive and negative values for myocardial infarction were assigned according to the minimal troponin threshold measured with a coefficient of variation less than 10% in each assay, as indicated by the manufacturer. The precision of the troponin threshold measurements was confirmed by our laboratory. For commercially available troponin assays, the less than 10% imprecision cutoff value has been recommended for clinical purposes.⁹

MANAGEMENT

All patients were evaluated by a chest pain unit protocol, which included a clinical history and early (<24 h after admission) exercise testing in patients able to exercise.¹⁰⁻¹³ A complete clinical history was recorded, including symptoms at presentation, coronary risk factors, history of ischemic heart disease, and extracardiac vascular disease (peripheral arterial disease, prior stroke, or renal failure defined by a creatinine level ≥ 1.4 mg/dL [to convert to $\mu\text{mol/L}$, multiply by 88.4] at admission). Data on the characteristics of chest pain at presentation were collected using a predefined questionnaire introduced by Geleijnse et al,¹⁴ which evaluates pain location, radiation, characteristics, severity, influences, associated symptoms, and history of exertional angina. Points were assigned according to the presence or absence of these diagnostic features. Typical chest pain was defined by a total score of 10 points or greater.

A symptom-limited Bruce protocol was used in the exercise test. Patients who were unable to exercise or who had positive findings on the exercise test were hospitalized for further evaluation, whereas patients with negative findings on the exercise test were discharged. If the exercise test was inconclusive, the final decision to hospitalize or discharge the patient was at the discretion of the attending physician.

STUDY GROUPS

The patient population was divided into 3 groups: group 1 (424 [39%]) included patients discharged after the exercise test; group 2 (208 [19%]), those initially hospitalized but in whom unstable angina was ruled out after further evaluation; and group 3 (456 [42%]), those in whom unstable

angina was confirmed or could not be ruled out after hospitalization at the index episode. In group 3, revascularization at the index hospitalization was performed in the case of substantial coronary artery stenosis that was deemed amenable to revascularization.

Figure 1 summarizes in-hospital management and study groups. Group 1 patients were discharged early: 392 (92%) after negative findings on an exercise test and 32 (8%) after an inconclusive exercise test. However, 664 (61%) of the study patients were hospitalized: 134 (20%) after positive findings on an exercise test, 97 (15%) after an inconclusive test, and 433 (65%) who were unable to exercise. In patients who were unable to exercise, the extent of the in-hospital evaluation was determined by the treating cardiologist, who had the options of cardiac magnetic resonance imaging with dipyridamole, coronary angiography, or medical treatment without further study.¹⁵

Among hospitalized patients, group 2 patients had no evidence of unstable angina (208 patients [31%]), as determined by normal findings on cardiac magnetic resonance imaging with dipyridamole in 94 patients (45%) and by normal findings on coronary angiography in 114 patients (55%). Group 3 comprised the remaining 456 patients, in whom unstable angina was diagnosed or could not be eliminated as the diagnosis. Of the 292 patients (64%) in group 3 who underwent coronary angiography that revealed substantial coronary artery stenosis, 190 (65%) were revascularized (134 underwent coronary angioplasty and 56 had bypass surgery). The remaining 164 patients (36%) in group 3 were conservatively managed.

END POINTS

The primary end point was acute myocardial infarction or all-cause mortality at 1-year follow-up. The secondary end point was postdischarge revascularization. An acute myocardial infarction was defined as a new episode of chest pain with increased troponin I levels. Acute myocardial infarction was also diagnosed if creatine kinase MB mass increased to 3 times or more the upper limit of normal after coronary angioplasty or to 5 times or more the upper limit of normal after coronary bypass surgery.

STATISTICAL ANALYSES

Differences in baseline characteristics and outcomes were compared among the 3 study groups using the χ^2 test. A specific analysis was undertaken to assess the protective effects of revascularization at the index episode on outcomes in group 3. Because of the differences in the baseline characteristics between patients with and without revascularization, a propensity score method was applied. Baseline variables associated with revascularization ($P < .25$) were identified by univariate analysis. These variables were used

FIGURE 1. Flowchart describing the study groups. ED = emergency department.

in a logistic regression model to calculate the probability that each patient would require revascularization. This probability constituted the propensity score. Patient outcomes were distributed among quartiles of the propensity score.

Variables that may predict outcomes were investigated in group 3. The association between revascularization at the index episode and patient outcome was analyzed by univariate analysis using the χ^2 test. In addition, crude estimates were calculated as hazard ratios (HRs) with their respective 95% confidence intervals (CIs) using a univariate Cox regression analysis. A multivariate Cox regression analysis was performed, which included the baseline clinical predictive variables ($P < .20$) in the univariate analysis as well as revascularization and the propensity score. The proportional hazards assumption was also evaluated. This test provided evidence that the variable in-hospital revascularization did not fulfill the proportionality assumption, thereby accounting for the accumulation of periprocedural myocardial infarctions at the index episode in revascularized patients. Therefore, in addition to the multivariate Cox model, a

parametric proportional hazards model with Gompertz distribution was used in the analysis.

Parametric survival analysis with accelerated failure time parameterization is an alternative to the Cox model for the analysis of time-to-event data while permitting relaxation of the proportionality assumption. Differences between groups are expressed as a direct effect of time. This is in contrast to the Cox proportional hazards model, which models group differences in terms of the risk of the event of interest at any given time. Under the accelerated failure time parameterization, the effect of the exposure and covariables is assumed to act additively on the log time scale. In this case, the coefficient of the exposure variable represents the (adjusted) difference in the median survival times on the log scale between the 2 levels of the variable; the exponentiated value is the ratio of the medians on the time scale itself. We found that the Gompertz distribution fits the trajectory of the instantaneous hazard across time for our data. Because the Gompertz distribution does not have an accelerated failure time parameterization, the results are presented as HRs.

TABLE 1. Characteristics of the Patient Population^a

	Group 1 (n=424)	Group 2 (n=208)	Group 3 (n=456)	P value
Clinical presentation				
Typical chest pain ^b	184 (43)	117 (56)	334 (73)	.001
≥2 episodes of pain in past 24 h	102 (24)	66 (32)	233 (51)	.001
Killip class >1	0 (0)	1 (0.5)	26 (6)	.001
Coronary risk factors				
Age (y), mean ± SD	61±11	64±11	67±11	.001
Men	274 (65)	115 (55)	330 (72)	.001
Current smokers	105 (25)	46 (22)	91 (20)	.20
Hypertension	227 (54)	126 (61)	300 (66)	.001
Hypercholesterolemia	221 (52)	114 (55)	243 (53)	.80
Diabetes mellitus	94 (22)	50 (24)	151 (33)	.001
Family history	47 (11)	23 (11)	56 (12)	.80
Prior myocardial infarction	61 (14)	30 (14)	164 (36)	.001
Prior coronary artery stenosis ≥50%	55 (13)	26 (13)	163 (36)	.001
Use of aspirin	98 (23)	71 (34)	270 (59)	.001
History of heart failure	7 (2)	4 (2)	19 (4)	.05
Prior coronary angioplasty	28 (7)	19 (9)	69 (15)	.001
Prior coronary bypass surgery	23 (5)	4 (2)	48 (11)	.001
Peripheral arterial disease	4 (1)	7 (3)	37 (8)	.001
Prior stroke	13 (3)	15 (7)	49 (11)	.001
Creatinine ≥1.4 mg/dL ^c	22 (5)	21 (10)	55 (12)	.001
Electrocardiographic findings				
Left bundle branch block	0 (0)	17 (8)	18 (4)	.001
T-wave inversion (≥1 mm)	31 (7)	22 (11)	66 (15)	.01
Treatment at discharge				
Aspirin	124 (29)	89 (43)	411 (90)	.001
Clopidogrel	11 (3)	9 (4)	155 (34)	.001
Statins	219 (52)	122 (59)	296 (65)	.001
β-Blockers	44 (10)	42 (20)	301 (66)	.001

^a Data are given as number (percentage) of patients, unless otherwise indicated.

^b Total score of ≥10 points on the questionnaire developed by Geleijnse et al.¹⁴

^c To convert creatinine values to μmol/L, multiply by 88.4.

Calculations were performed using the SPSS software version 9.0 (SPSS, Chicago, IL) and the STATA software version 8.2 (STATA Statistical Software, College Station, TX).

RESULTS

Baseline characteristics of patients from groups 1, 2, and 3 are presented in Table 1. As expected, group 3 showed the highest-risk profile. A complete follow-up examination was obtained in 1055 (97%) of the patients; 33 patients (3%) were not followed up for a full year but did not die. These patients were considered at risk until the date of final contact,

at which point they were censored. During follow-up, patients from group 3 presented the highest rate of myocardial infarction or death (62 [13.6%] for group 3 vs 7 [1.7%] for group 1 and 1 [0.5%] for group 2; $P=.001$) and the highest rate of postdischarge revascularization (32 [7%] for group 3 vs 8 [1.9%] for group 1 and 2 [1%] for group 2; $P=.001$).

REVASCULARIZATION AT THE INDEX EPISODE

Unstable evolution occurred shortly after hospitalization but before revascularization could be carried out in 11 patients from group 3 (3 who died and 8 who experienced a nonfatal myocardial infarction). These patients were excluded from the analysis of the prognostic influence of revascularization. Of the remaining 445 patients, 146 (33%) had a positive finding on an exercise stress test, 39 (9%) had an inconclusive exercise stress test, and 137 (31%) underwent primary angiography. At the index episode, 183 patients (41%) were revascularized and 79 (43%) of these patients had positive findings on a noninvasive test, 20 (11%) had an inconclusive noninvasive test, and 84 (46%) underwent direct angiography.

Differences in baseline characteristics between patients with and without revascularization are summarized in Table 2. Nonrevascularized patients showed a poor risk profile and tended to be older men with a higher frequency of a Killip class greater than 1 at admission and women with extracardiac disease or prior myocardial infarction, coronary artery stenosis, or coronary bypass surgery. In addition, these patients underwent exercise testing (63 [24%] vs 77 [42%]; $P=.001$), cardiac magnetic resonance imaging (24 [9%] vs 25 [14%], $P=.30$), and coronary angiography (100 [38%] vs 183 [100%]; $P=.001$) less frequently than the other patients. At discharge, nonrevascularized patients received aspirin, clopidogrel, statin, or β-blocker treatment less frequently than did the other patients.

A propensity score for revascularization was constructed that included the following baseline variables in the univariate analysis: 2 or more episodes of pain in the past 24 hours, Killip class greater than 1, older age, male sex, smoking, hypertension, diabetes, prior myocardial infarction, prior coronary artery stenosis, prior coronary bypass surgery, extracardiac disease, left bundle branch block, and any complementary study performed (noninvasive stress test or coronary angiography). The c statistic (0.83) of the propensity score was adequate. No patient with a propensity score in the lowest quartile was revascularized, whereas 74% of the patients in the highest quartile were revascularized ($P=.001$).

EFFECT OF REVASCULARIZATION ON PROGNOSIS

Despite the poor baseline risk profile of nonrevascularized patients, univariate analysis showed no differences in the primary end point between patients with and those without

TABLE 2. Characteristics of Group 3 Patients With and Without Revascularization^a

	Revascularization Without (n=262)	With (n=183)	P value
Clinical presentation			
Typical chest pain ^b	193 (74)	131 (72)	.70
≥2 episodes of pain in past 24 h	116 (44)	111 (61)	.001
Killip class >1	21 (8)	4 (2)	.01
Coronary risk factors			
Age (y), mean ± SD	69±11	65±10	.001
Men	177 (68)	144 (79)	.01
Current smokers	42 (16)	48 (26)	.01
Hypertension	179 (68)	113 (62)	.20
Hypercholesterolemia	135 (52)	101 (55)	.50
Diabetes mellitus	79 (30)	68 (37)	.20
Family history	27 (10)	18 (10)	>.99
Prior myocardial infarction	104 (40)	57 (31)	.07
Prior coronary artery stenosis ≥50%	107 (41)	52 (28)	.01
Use of aspirin	159 (61)	104 (57)	.40
History of heart failure	11 (4)	7 (4)	>.99
Prior coronary angioplasty	36 (14)	31 (17)	.40
Prior coronary bypass surgery	38 (15)	10 (6)	.01
Extracardiac disease ^c	78 (30)	40 (22)	.06
Electrocardiographic findings			
Left bundle branch block	14 (5)	4 (2)	.10
T-wave inversion (≥1 mm)	36 (14)	26 (14)	.90
Treatment at discharge			
Aspirin	225 (86)	178 (97)	.001
Clopidogrel	24 (9)	126 (69)	.001
Statins	157 (60)	133 (73)	.01
β-Blockers	148 (57)	146 (80)	.001

^a Data are given as number (percentage) of patients, unless otherwise indicated.

^b Total score ≥10 points on the questionnaire developed by Geleijnse et al.¹⁴

^c Peripheral arterial disease or prior stroke or a creatinine level ≥1.4 mg/dL (to convert creatinine values to μmol/L, multiply by 88.4) at admission.

revascularization (22 [12%] vs 29 [11%]; HR, 1.2; 95% CI, 0.7-2.0; *P*=.60) in the univariate analysis. Neither were there differences in the individual end points: mortality (7 [3.8%] vs 15 [5.7%]; HR, 0.7; 95% CI, 0.3-1.7; *P*=.40) and acute myocardial infarction (17 [9.3%] vs 19 [7.3%]; HR, 1.3; 95% CI, 0.7-2.6; *P*=.40). The event rate did not differ between patients with and without positive findings on a noninvasive test (12 [8%] vs 39 [13%]; HR, 0.6; 95% CI, 0.3-1.2; *P*=.20).

In the revascularized subgroup, 4 intervention-related deaths occurred (all at the index episode) vs 1 death in the nonrevascularized subgroup (at the follow-up). Procedure-related nonfatal myocardial infarctions occurred in 15 patients (8%) of the revascularized subgroup at the index episode and in 1 patient of the nonrevascularized subgroup at the follow-up. Mean ± SD creatine kinase-MB levels were 61.5±42.0 ng/mL (range, 19.5-184.0 ng/mL).

By Cox regression analysis, myocardial infarction or death at 1 year was associated with 2 or more episodes of pain in the past 24 hours (HR, 2.2; 95% CI, 1.2-3.9;

P=.01), age older than 65 years (HR, 1.8; 95% CI, 0.9-3.5; *P*=.10), diabetes (HR, 2.0; 95% CI, 1.1-3.4; *P*=.02), prior coronary bypass surgery (HR, 1.9; 95% CI, 0.9-3.9; *P*=.06), extracardiac disease (HR, 1.6; 95% CI, 0.9-6.2; *P*=.10), and left bundle branch block (HR, 2.4; 95% CI, 1.0-6.2; *P*=.06). In-hospital revascularization (HR, 1.4; 95% CI, 0.7-2.5; *P*=.40) and the propensity score (*P*=.80) were not associated with the primary end point. The parametric proportional hazard model with Gompertz distribution also showed the lack of a significant association between in-hospital revascularization and outcome (HR, 1.7; 95% CI, 0.80-3.5; *P*=.20).

As depicted in the Kaplan-Meier curves adjusted by the covariate clinical factors independently associated with the outcome, the time course of events was different in patients with and without revascularization (Figure 2). Revascularized patients showed an initial increase of the primary end point during hospitalization that depended on revascularization, with only a few events after discharge. In nonrevascularized patients, a progressive increase in the primary end point was observed throughout the follow-up period. After 1 year, there were no significant differences between revascularized and nonrevascularized patients. If periprocedural myocardial infarctions are excluded, then in-hospital revascularization reduces the primary end point (HR, 0.3; 95% CI, 0.1-0.9; *P*=.03).

Revascularization at the index episode was associated with a lesser frequency of postdischarge revascularization by univariate (6 [3.3%] vs 26 [9.9%]; *P*=.01) and multivariate (HR, 0.3; 95% CI, 0.1-0.7; *P*=.01) analysis. The propensity score was unrelated to this event (*P*=.50).

DISCUSSION

Our findings show that a chest pain unit protocol that ensures a safe patient discharge is associated with either

FIGURE 2. Adjusted Kaplan-Meier curves depicting the time course of events in patients with and without revascularization.

early patient discharge after negative findings on an exercise test or a late discharge after further in-hospital explorations to rule out unstable angina. However, the performance of noninvasive tests and coronary angiography prompted a number of revascularizations that did not improve the prognosis in terms of myocardial infarction or death, although they decreased the occurrence of postdischarge revascularization procedures.

This systematic study of patients in chest pain units revealed a number of angiographic candidates for revascularization. It is unclear if revascularization provides any benefit to the patient. The COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) trial showed that coronary angioplasty is not superior to medical treatment in stable patients.¹⁶ Although randomized trials on non-ST-segment elevation acute coronary syndromes have shown that an invasive approach improves patient prognosis,¹⁷ the subgroup of patients without ST-segment deviation or troponin elevation,^{7,8} such as those found in the chest pain unit, do not receive any benefit. However, these trials, which involved a high proportion of patients with acute myocardial infarction, are not a proper comparison for patients in a chest pain unit population. In the current study of patients in a chest pain unit, revascularization was not associated with a better outcome such as lower rates of myocardial infarction or death; however, the need for postdischarge revascularization procedures was reduced.

A number of revascularized patients experienced periprocedural myocardial infarctions. The meaning of periprocedural infarctions and the exact threshold of myonecrosis that is clinically relevant remain a matter of debate.¹⁸ Risk of myocardial necrosis related to the revascularization procedure must be considered when deciding to perform revascularization in a low-risk population such as patients in a chest pain unit. Although periprocedural infarctions might be considered a benign phenomenon, some studies indicate that any increase in necrosis markers has prognostic value.¹⁹ The threshold for creatine kinase-MB elevation used in the current study (>3 times the upper limit of normal after angioplasty and >5 times the upper limit of normal after surgery) is accepted as clinically relevant.²⁰⁻²²

Troponin markers have improved the sensitivity of the diagnosis of acute myocardial infarction.² Implementation of chest pain unit protocols leads to detailed study and medical observation in all patients and reduces the number of inappropriate discharges.^{3,12,23-30} In the current study, patients discharged early after negative findings on an exercise test and those who were found not to have unstable angina after in-hospital evaluation had an excellent prognosis. However, this screening method requires

many resources. In many instances, it is difficult to promptly implement an exercise testing program that provides access to patients 24 hours daily 7 days per week, and noninvasive imaging and coronary angiography require that patients be hospitalized. Simple clinical risk scores and biomarkers that are easy to measure (such as N-terminal pro-brain natriuretic peptide levels) have prognostic value, although they may not have been prospectively evaluated for decision making.^{11,31,32} Clinical risk scores and biomarkers better predict events such as myocardial infarction or death than revascularization, a procedure that is chosen using the results of noninvasive tests or angiography.^{31,32} According to our results, however, early revascularization did not affect the occurrence of myocardial infarction or death. Therefore, simpler and faster risk stratification using clinical data and conceivably biomarkers could be used as an initial management strategy. Further studies could be postponed in lower-risk patients. This approach would allow a complete diagnosis, and the decision to proceed with revascularization could be made in an ambulatory setting.

Because this was a retrospective cohort study and revascularization was not randomized, differences in baseline characteristics could have influenced the results. A propensity score for revascularization with a *c* statistic of 0.83 was used to minimize potential bias, and multivariate analysis for outcomes was performed, including baseline characteristics and the propensity score.

CONCLUSION

Early revascularizations associated with chest pain unit protocols may not improve 1-year outcomes (myocardial infarction or death), although they decrease the need for postdischarge revascularization procedures. Further studies are warranted to define both the subgroup of patients who require intense study and revascularization at the index episode and the subgroup of patients whose evaluation could be deferred after simple clinical risk stratification and medical treatment. Therefore, a chest pain unit protocol should be flexible and allow consideration of different approaches to treatment depending on the baseline risks of the patients analyzed.

REFERENCES

1. Lee TH, Goldman L. Evaluation of the patient with acute chest pain. *N Engl J Med*. 2000;342(16):1187-1195.
2. Jaffe AS, Babuin L, Apple FS. Biomarkers in acute cardiac disease: the present and the future. *J Am Coll Cardiol*. 2006 Jul 4;48(1):1-11. Epub 2006 Jun 12.
3. Amsterdam EA, Kirk JD, Diercks DB, Lewis WR, Turnipseed SD. Immediate exercise testing to evaluate low-risk patients presenting to the emergency department with chest pain. *J Am Coll Cardiol*. 2002;40(2):251-256.

4. Jeetley P, Burden L, Stoykova B, Senior R. Clinical and economic impact of stress echocardiography compared with exercise electrocardiography in patients with suspected acute coronary syndrome but negative troponin: a prospective randomized controlled study. *Eur Heart J*. 2007 Jan;28(2):204-211. Epub 2007 Jan 16.
5. Candell-Riera J, Oller-Martínez G, de León G, Castell-Conesa J, Aguadé-Bruix S. Yield of early rest and stress myocardial perfusion single-photon emission computed tomography and electrocardiographic exercise test in patients with atypical chest pain, nondiagnostic electrocardiogram and negative biochemical markers in the emergency department. *Am J Cardiol*. 2007 Jun;99(12):1662-1666. Epub 2007 May 4.
6. Goldstein JA, Gallagher MJ, O'Neill WW, Ross MA, O'Neil BJ, Raff GL. A randomized controlled trial of multi-slice coronary computed tomography for evaluation of acute chest pain. *J Am Coll Cardiol*. 2007 Feb 27;49(8):863-871. Epub 2007 Feb 12.
7. FRagmin and Fast Revascularisation during InStability in Coronary artery disease (FRISC II) Investigators. Invasive compared with non-invasive treatment in unstable coronary-artery disease: FRISC II prospective randomised multicentre study. *Lancet*. 1999;354(9180):708-715.
8. Cannon CP, Weintraub WS, Demopoulos LA, et al; TACTICS (Treat Angina with Aggrastat and Determine Cost of Therapy with an Invasive or Conservative Strategy)—Thrombolysis in Myocardial Infarction 18 Investigators. Comparison of early invasive and conservative strategies in patients with unstable coronary syndromes treated with the glycoprotein IIb/IIIa inhibitor tirofiban. *N Eng J Med*. 2001;344(25):1879-1887.
9. Apple FS, Wu AH, Jaffe AS. European Society of Cardiology and American College of Cardiology guidelines for redefinition of myocardial infarction: how to use existing assays clinically and for clinical trials. *Am Heart J*. 2002;144(6):981-986.
10. Sanchis J, Bodí V, Llacer A, et al. Emergency room risk stratification of patients with chest pain without ST-segment elevation [in Spanish]. *Rev Esp Cardiol*. 2003;56(10):955-962.
11. Sanchis J, Bodí V, Núñez J, et al. New risk score for patients with acute chest pain, non-ST-segment deviation, and normal troponin concentrations: a comparison with the TIMI risk score. *J Am Coll Cardiol*. 2005;46(3):443-449.
12. Sanchis J, Bodí V, Núñez J, et al. Usefulness of early exercise testing and clinical risk score for prognostic evaluation in chest pain units without preexisting evidence of myocardial ischemia. *Am J Cardiol*. 2006 Mar 1;97(5):633-635. Epub 2006 Jan 6.
13. Sanchis J, Bodí V, Núñez J, et al. A practical approach with outcome for the prognostic assessment of non-ST-Segment elevation chest pain and normal troponin. *Am J Cardiol*. 2007 Mar 15;99(6):797-801. Epub 2007 Jan 30.
14. Geleijnse ML, Elhendy A, Kasprzak JD, et al. Safety and prognostic value of early dobutamine-atropine stress echocardiography in patients with spontaneous chest pain and a non-diagnostic electrocardiogram. *Eur Heart J*. 2000;21(5):397-406.
15. Bodí V, Sanchis J, Lopez-Lereu MP, et al. Prognostic value of dipyridamole stress cardiovascular magnetic resonance imaging in patients with known or suspected coronary artery disease. *J Am Coll Cardiol*. 2007 Sep 18;50(12):1174-1179. Epub 2007 Sep 4.
16. Boden WE, O'Rourke RA, Teo KK, et al; COURAGE Trial Research Group. Optimal medical therapy with or without PCI for stable coronary disease. *N Eng J Med*. 2007 Apr 12;356(15):1503-1516. Epub 2007 Mar 26.
17. Bavry AA, Kumbhani DJ, Rassi AN, Bhatt DL, Askari AT. Benefit of early invasive therapy in acute coronary syndromes: a meta-analysis of contemporary randomized clinical trials. *J Am Coll Cardiol*. 2006 Oct 3;48(7):1319-1325. Epub 2006 Sep 12.
18. Akkerhuis KM, Alexander JH, Tardiff BE, et al. Minor myocardial damage and prognosis: are spontaneous and percutaneous coronary intervention-related events different? *Circulation*. 2002;105(5):554-556.
19. Ioannidis JP, Karvouni E, Katritsis DG. Mortality risk conferred by small elevations of creatine kinase-MB isoenzyme after percutaneous coronary intervention. *J Am Coll Cardiol*. 2003;42(8):1406-1411.
20. Nallamothu BK, Bates ER. Periprocedural myocardial infarction and mortality: causality versus association [editorial]. *J Am Coll Cardiol*. 2003;42(8):1412-1414.
21. Costa MA, Carere RG, Lichtenstein SV, et al. Incidence, predictors, and significance of abnormal cardiac enzymes rise in patients treated with bypass surgery in the arterial revascularization therapies study (ARTS). *Circulation*. 2001;104(22):2689-2693.
22. Thygesen K, Alpert JS, White HD; Joint ESC/ACCF/AHA/WHF Task Force for the Redefinition of Myocardial Infarction. Universal definition of myocardial infarction. *Eur Heart J*. 2007;28(20):2525-2538.
23. Kerns JR, Shaub TF, Fontanarosa PB. Emergency cardiac stress testing in the evaluation of emergency patients with atypical chest pain. *Ann Emerg Med*. 1993(5);22:794-798.
24. Lewis WR, Amsterdam EA. Utility and safety of immediate exercise testing of low-risk patients admitted to the hospital for suspected acute myocardial infarction. *Am J Cardiol*. 1994;74(10):987-990.
25. Farkouh ME, Smars PA, Reeder GS, et al; Chest Pain Evaluation in the Emergency Room (CHEER) Investigators. A clinical trial of a chest-pain observation unit for patients with unstable angina. *N Eng J Med*. 1998;339(26):1882-1888.
26. Kirk JD, Turnipseed S, Lewis WR, Amsterdam EA. Evaluation of chest pain in low-risk patients presenting to the emergency department: the role of immediate exercise testing. *Ann Emerg Med*. 1998;32(1):1-7.
27. Polanczyk CA, Johnson PA, Hartley LH, Walls RM, Shaykevich S, Lee TH. Clinical correlates and prognostic significance of early negative exercise tolerance test in patients with acute chest pain seen in the hospital emergency department. *Am J Cardiol*. 1998;81(3):288-292.
28. Lewis WR, Amsterdam EA, Turnipseed S, Kirk JD. Immediate exercise testing of low risk patients with known coronary artery disease presenting to the emergency department with chest pain. *J Am Coll Cardiol*. 1999; 33(7):1843-1847.
29. Diercks DB, Gibler WB, Liu T, Sayre MR, Storrow AB. Identification of patients at risk by graded exercise testing in an emergency department chest pain center. *Am J Cardiol*. 2000;86(3):289-292.
30. DeFilippi CR, Rosanio S, Tocchi M, et al. Randomized comparison of a strategy of predischarge coronary angiography versus exercise testing in low-risk patients in a chest pain-unit: in-hospital and long-term outcomes. *J Am Coll Cardiol*. 2001;37(8):2042-2049.
31. Sanchis J, Bosch X, Bodí V, et al. Combination of clinical risk profile, early exercise testing and circulating biomarkers for evaluation of patients with acute chest pain, without ST-segment deviation or troponin elevation. *Heart*. 2008 Mar;94(3):311-315. Epub 2007 Jul 16.
32. Sanchis J, Bodí V, Núñez J, et al. Limitations of clinical history for evaluation of patients with acute chest pain, non-diagnostic electrocardiogram and normal troponin. *Am J Cardiol*. 2008 Mar 1;101(5):613-617. Epub 2007 Dec 21.