Randomized Trial of a Noninvasive Strategy to Reduce Hospital Stay for Patients With Low-Risk Myocardial Infarction

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OBJECTIVES
This study evaluated the feasibility, pertinence and psychosocial repercussions of a noninvasive reduced hospital stay strategy (three days) for low-risk patients with acute myocardial infarction using simple clinical criteria and predischARGE 24-h ambulatory ST-segment ischemic monitoring.

BACKGROUND
Previous studies evaluating shorter stays for uncomplicated myocardial infarction have been limited by retrospective or nonrandomized design and overdependence on invasive cardiac procedures.

METHODS
One-hundred twenty consecutive patients admitted with an acute myocardial infarction fulfilling low-risk criteria were randomized 2:1 to a short hospital stay (80 patients) or standard stay (40 patients). Short-stay patients with no ischemia on ST-monitoring were discharged on day 3, returning for exercise testing a week later. All analyses were on an intention-to-treat basis.

RESULTS
Forty-one percent of all screened patients with acute myocardial infarction would have been medically eligible for the short-stay strategy. Seventeen patients (21%) were not discharged early because of ischemia on ST-monitoring or angina. Median initial hospital stay was halved from 6.9 days in the standard stay to 3.5 days in the short-stay group. At six months, median total days hospitalized were 7.5 in the standard stay and 3.6 in the short-stay group (p < 0.0001). Adverse events and readmissions were low and not significantly different, and there were 25% fewer invasive cardiac procedures in the short-stay group. Psychosocial outcomes, risk factor changes and exercise test results were similar in the two groups.

CONCLUSIONS
This reduced hospital stay strategy for low-risk patients with acute myocardial infarction is feasible and worthwhile, resulting in a substantial and sustained reduction in days hospitalized. It is without unfavorable psychosocial consequences, appears safe and does not increase the number of invasive cardiac procedures. (J Am Coll Cardiol 2001;37:1289–96) © 2001 by the American College of Cardiology

The average hospital stay for patients with an acute myocardial infarction (MI) has decreased from four to six weeks 30 years ago to two to three weeks 20 years ago, and is currently six to 10 days (1–7). Such patients are now generally observed over four to seven days, and in the absence of cardiac failure, severe arrhythmias or myocardial ischemia they are progressively mobilized while intravenous medications such as nitroglycerin and heparin are ceased. Usually, asymptomatic patients then undergo noninvasive evaluation with a simple exercise test or myocardial imaging with exercise, pharmacologic vasodilation or stress echocardiography and are generally discharged if results are favorable. If noninvasive testing suggests important residual ischemia or if there is refractory or spontaneous postinfarction angina, patients usually undergo coronary arteriography and, if feasible, either percutaneous or surgical revascularization (8).

Clinical experience suggests that whereas some patients with acute MI require longer hospital stays and more extensive investigations, others could be safely discharged earlier without invasive procedures. The only contemporary randomized study of which we are aware, made a decade ago, evaluated a three-day hospital stay for patients with acute MI. However, all patients had undergone early coronary arteriography and two-thirds had angioplasty (9). Presumably because of the requirement for invasive stratification, this study has not modified clinical practice in the majority of patients with acute MI.

We undertook a randomized feasibility trial in patients with acute MI, identified as being at low risk according to simple and prospectively defined clinical criteria, comparing a noninvasive three-day hospital stay strategy employing 24-h ambulatory electrocardiographic (ECG) ischemic monitoring to usual clinical management. The psychosocial impact, risk factor implications and follow-up outcomes of this strategy were also assessed.

METHODS
Inclusion criteria. Between May 15, 1997, and December 1, 1998, all patients admitted to the Quebec Heart
Institute/Laval Hospital, a tertiary care center, with a diagnosis of acute MI were monitored by research nurses using a checklist of eligibility criteria. The diagnosis of MI required characteristic prolonged (at least 30 min) chest pain or discomfort (or equivalent) with a creatine kinase (CK) MB fraction $\geq 5\%$ of total CK. Patients had to be ambulatory by the 36th hour of presentation, not live alone in the seven days following an eventual early discharge, be reachable directly by telephone at home and not live more than 30 min driving time from a hospital center where thrombolysis could be performed.

**Exclusion criteria.** Patients were not considered candidates for this short-stay strategy if they had any of the following:

1. Cardiac catheterization during hospitalization or any revascularization in the preceding six months.
2. Clinical evidence of cardiac failure or of moderate/severe left ventricular dysfunction, defined as any of the following: dyspnea, significant pulmonary rales, an abnormal chest roentgenogram or a left ventricular ejection fraction $< 40\%$ (all patients had an echocardiogram within 48 h).
3. Hemodynamic instability, defined as sustained hypotension (systolic pressure $< 85$ mm Hg at three intervals separated by a minimum of 15 min) with the exception of the very acute phase (first 6 to 12 h) of an inferior MI; rapid and inappropriate resting heart rate ($> 90$ beats/min) more than 24 h after presentation, documented over two consecutive hours; systolic blood pressure $\geq 160$ mm Hg and/or diastolic blood pressure $\geq 90$ mm Hg at three intervals separated by a minimum of 15 min.
4. Cardiac ischemic symptoms $> 24$ h following presentation or ST-segment depression or elevation $\geq 1$ mm (80 ms after the J-point) relative to baseline lasting $\geq 1$ min on the cardiac monitor or ECG.
5. Significant arrhythmia $> 24$ h after presentation, defined as ventricular fibrillation; sustained ventricular tachycardia ($\geq 30$ s); nonsustained repetitive ventricular tachycardia; abnormally frequent, repetitive ectopic ventricular beats ($> 60$ h); sustained bradyarrhythmia ($< 40$ beats/min) except during sleep; ventricular pause $\geq 3$ s; and in general, any symptomatic arrhythmia.
6. Significant ECG abnormality, defined as complete left bundle branch block (at any time, even transitory); new or presumed new persistent complete right bundle branch block; ventricular pacemaker-dependent rhythm; any marked repolarization abnormality, reversible or persistent $> 24$ h after presentation, suggesting to the clinician an important reversible ischemic substrate; any persistent marked ST-segment depression ($> 1$ mm) rendering ST-segment analysis difficult; in case of an anterior infarction any, even transitory, second- or third-degree atrioventricular block; in case of an inferior infarction, any daytime Mobitz type I block or second- or third-degree block $> 24$ h after admission.
7. Previous angina greater than Canadian Cardiovascular Society class II.
8. Any condition that might prolong the patient’s hospitalization or render problematic an early discharge, such as insufficient autonomy or comprehension, uncontrolled diabetes, unstable or severe chronic obstructive pulmonary disease, severe anemia, alcoholism or a psychiatric disorder.

The study was approved by the hospital ethics committee and all participating patients gave written informed consent.

**Study procedure.** With the accord of the attending physician, who accepted that patients randomized to short stay would be discharged 24 h later in the absence of ischemia, the study was proposed to patients who fulfilled the above conditions at 48 h. After consent, patients were randomized in a ratio of 2:1 to the short-stay strategy or the standard stay using sealed envelopes and random numbers prepared by the biostatistician. Standard-stay patients were managed in the usual manner by the attending physician. Patients randomized to the short-stay strategy had intravenous medications such as nitrates and heparin stopped and underwent three-channel 24-h ambulatory (Holter) ST-monitoring (Series 8500 Marquette Holter Recorder, Milwaukee, Wisconsin). This equipment adheres to current American College of Cardiology/American Heart Association ST-monitoring guidelines (10). The monitor was applied during daytime by experienced personnel trained in ECG techniques. Control recordings were taken in reclining, sitting and standing positions and after hyperventilation. Patients were encouraged to walk about the ward. They descended and ascended two flights of stairs with a nurse or physician while on the Holter monitor. If during this 48 to 72 h phase, patients manifested ischemic symptoms or other exclusion criteria, the projected short stay was cancelled and these patients reverted to usual care. During this time, patients received counseling about MI and risk factors.

At the completion of recording, the Holter data were fed into the Marquette Tape Acquisition Unit and transferred to the MARS Unity Workstation (Software Version 3.1, 1997) (Marquette Co., Milwaukee, Wisconsin). The tape was analyzed during daytime by one of the study cardiologists. The three-channel recording was first examined in trend mode and then scrutinized entirely beat-by-beat in accelerated time. The display screen is highly interactive and can be flexibly configured for amount and manner of tracing display, magnification, printing and turnover speed. Optimal reading can be performed with 1 min of three-channel
tracing displayed every second. An entire reading thus takes approximately 20 to 25 min. The usual criteria of ischemic positivity were applied, that is, ≥1 min of ≥1 mm sustained ST-segment depression or elevation 80 ms after the J point compared with baseline. No more than 1 mm baseline ST-segment depression was permitted for eligibility to this study because of the difficulty in interpreting a truly ischemic change in the presence of marked baseline ST-segment depression. If there was baseline 1 mm ST-depression, the criteria for ischemia required 1.5 mm ST-depression from this baseline. A single ischemic episode disqualified patients from early discharge and they then reverted to usual care. Early discharge was also cancelled in the event of a significant arrhythmia, as previously defined. If the Holter reading was negative, patients were promptly discharged.

Patients discharged early had 24-h access by telephone to study personnel and were all contacted by telephone the day after discharge. Patients were instructed not to engage in more than light activity until the following week, when they returned for a symptom-limited modified Bruce protocol ECG treadmill exercise test and visits with the treating cardiologist and a dietician. If exercise testing was not feasible, dipyridamole-thallium myocardial imaging was substituted.

Patients were contacted at one and six months. Coronary events (any death, myocardial reinfarction, unstable angina), counting the most serious event per patient, were noted, as was the cardiac-related rehospitalization rate. Unstable angina was defined as prolonged (>5 min) ischemic symptoms occurring at rest or minimal exertion and requiring rehospitalization. Rates of coronary arteriography, angioplasty and bypass surgery and the total number of these invasive cardic procedures in the two groups were noted. If coronary arteriography and angioplasty were performed at the same time, they were considered a single invasive procedure. Follow-up exercise test results, lipid and diabetic status, smoking habits and medications were also evaluated.

Psychosocial assessment. The psychosocial impact of the short-stay strategy was assessed in the last 85 randomized patients. In addition, we evaluated 30 consecutive nonrandomized low-risk patients from another hospital to control for institutional and study selection bias. This was a non-tertiary center and the same selection criteria were used, but these patients were unaware they were being identified as a low-risk group and they had standard care. Psychosocial outcomes were measured using: 1) the Beck Inventory, assessing depression at discharge and at six months (11); 2) Spielberger’s State-Trait Anxiety Inventory, a current state-of-anxiety evaluation at hospital discharge (12); 3) the Maeland and Havik Expectations Questionnaire, assessing patients’ perception of loss of autonomy, physical capacity, emotional control and work adequacy at discharge and one month later (13); 4) the Maeland and Havik Cardiac Knowledge Questionnaire, assessing comprehension of coronary artery disease, at one month (13); and 5) Godin’s Leisure Time Physical Activity Index, at one month (14).

Statistical analysis. In a preliminary pilot observation, we found that the median hospital stay for 50 consecutive patients with acute MI fulfilling these low-risk criteria was 6.3 days. Therefore, a sample size of 120 patients, with randomization to a short-stay strategy or standard stay in a 2:1 ratio, would be necessary to show a 50% reduction in total days hospitalized at six months with a power of 90% and an alpha of 0.01. Because this was a low-risk group, it was expected that the risk of death, reinfarction and recurrent ischemia on six-month follow-up would be quite low, so that an unrealistically large sample size would be necessary to establish equivalence in terms of adverse clinical events. Therefore, these were not end points, although they were considered in the evaluation of the two approaches. All analyses were on an intention-to-treat basis.

Values are expressed as means ± standard deviations or medians as appropriate. Data were analyzed using analysis of variance. The Beck Depression Inventory and the Maeland and Havik Expectations Questionnaire were analyzed with repeated measures using a two-way analysis of variance. The normality assumption was verified with the Shapiro-Wilk test and Bartlett’s statistic was used to verify homogeneity of variances. When normality and homogeneity of variances assumptions were not fulfilled, Wilcoxon’s rank sum test was used. The Fisher exact test was used to compare categorical variables. A p value <0.05 was considered statistically significant. The statistical package program SAS was used (SAS Institute Inc., Cary, North Carolina).

RESULTS

During the study period, 525 patients admitted with an acute MI were screened, and 120 patients (23%) were randomized, 80 patients to the short-stay strategy and 40 patients to the standard stay. Numbers of patients excluded and the reasons are shown in Figure 1. An analysis of these exclusions showed that 94 patients (18% of all those screened) had no a priori cardiac or other medical reason for exclusion and would have been potentially eligible candidates for the short-stay strategy. These were cases of patient refusal, clinician’s reluctance, direct angioplasty or early angiography without definite overriding indications for these procedures and patients living alone or too far away. If these patients are added to those randomized, 214 patients or 41% of all screened patients with MI would have been potential candidates for the short-stay strategy.

Mean age of the patients in this study was 56 ± 9 years and 85% were men. Clinical profiles and MI characteristics of the short- and standard-stay arms were well balanced (Table 1). In the study group as a whole, a Q-wave MI occurred in 48 patients (40%); 56 patients (47%) underwent thrombolysis. The presenting ECG showed ST-elevation in 67 patients (56%), ST-depression (and no ST elevation) in 10 patients (8%), and T-wave inversion only in 14 patients
Myocardial infarction was anterior in 20 patients (17%). Peak CK value was 1,234 ± 1,181 U/L.

Of the 80 patients randomized to the short-stay strategy, 17 (21%) were not discharged at three days because of ischemia on 48 to 72 h Holter monitoring in 11 patients (symptomatic in one of these patients) and because of angina with negative Holter findings in the other six patients.

The median (and mean ± standard deviations) duration of initial hospitalization was halved from 6.9 (8.3 ± 5.0) days in the standard-stay group to 3.5 (4.9 ± 3.8) days in the short-stay group (p < 0.0001, Wilcoxon test). This proportion was sustained when cumulative hospitalization at six months was examined (7.5 [9.3 ± 5.4] days compared with 3.6 [6.0 ± 4.9] days, respectively, p < 0.0001) (Fig. 2).

Before hospital discharge, one death occurred in the standard-stay group within 24 h of coronary bypass surgery in a patient with diabetes. This patient had painless ischemia on an exercise test of 7 metabolic equivalents and coronary angiography showed three-vessel disease. One small in-hospital reinfarction (peak CK <300 U/L) occurred in a short-stay patient before 72 h. Findings on six-month follow-up are shown in Table 2. Adverse coronary events after hospital discharge occurred in eight (10%) short-stay and three (7.5%) standard-stay patients (p = NS). All of these were unstable angina episodes except for one MI (peak CK <200 U/L) occurring 11 days after discharge in a short-stay patient. Median time to occurrence of these events was more than one week after discharge in both groups. There was a similar incidence of rehospitalization in the two groups. All patients who underwent angioplasty had diagnostic coronary angiography at the same time, thus counting as a single invasive procedure. There were 25% fewer invasive cardiac procedures performed in the short-stay arm (30 procedures in 80 patients) than in the standard-stay arm (25 procedures in 40 pa-
tients). Intracoronary stents were used in 86% of the short-stay and 90% of the standard-stay patients who had angioplasty. Exercise test results and the proportion of tests positive for ischemia were very similar in the two groups (Table 2). Low density lipoprotein cholesterol levels on follow-up were $2.9 \pm 0.8 \text{ mmol/L}$ in the short-stay arm and $3.0 \pm 1.0 \text{ mmol/L}$ in the standard-stay arm ($p = 0.6$).

**Table 1.** Clinical and MI Characteristics in the Two Patient Groups

<table>
<thead>
<tr>
<th></th>
<th>Short-Stay Strategy (n = 80)</th>
<th>Standard Stay (n = 40)</th>
</tr>
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<tbody>
<tr>
<td><strong>Baseline Characteristics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (yr)*</td>
<td>56 ± 10</td>
<td>57 ± 8</td>
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<tr>
<td>Male gender</td>
<td>68 (85%)</td>
<td>34 (85%)</td>
</tr>
<tr>
<td>Current smokers</td>
<td>39 (49%)</td>
<td>19 (48%)</td>
</tr>
<tr>
<td>Ex-smokers</td>
<td>34 (43%)</td>
<td>14 (35%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>20 (25%)</td>
<td>7 (18%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>6 (8%)</td>
<td>5 (13%)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>75 (94%)</td>
<td>37 (93%)</td>
</tr>
<tr>
<td>Previous MI</td>
<td>11 (14%)</td>
<td>6 (15%)</td>
</tr>
<tr>
<td>Previous angina</td>
<td>1 (1%)</td>
<td>2 (5%)</td>
</tr>
<tr>
<td>Previous coronary angioplasty</td>
<td>1 (1%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Previous bypass surgery</td>
<td>4 (5%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td><strong>MI Characteristics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q-wave</td>
<td>30 (38%)</td>
<td>18 (45%)</td>
</tr>
<tr>
<td>Thrombolysis</td>
<td>34 (43%)</td>
<td>22 (55%)</td>
</tr>
<tr>
<td>Anterior MI</td>
<td>15 (19%)</td>
<td>5 (13%)</td>
</tr>
<tr>
<td>ST elevation†</td>
<td>41 (51%)</td>
<td>26 (65%)</td>
</tr>
<tr>
<td>ST depression†</td>
<td>6 (8%)</td>
<td>4 (10%)</td>
</tr>
<tr>
<td>T-wave inversion†</td>
<td>9 (11%)</td>
<td>5 (13%)</td>
</tr>
<tr>
<td>Peak CK (U/L)</td>
<td>$1,228 \pm 1,225$</td>
<td>$1,245 \pm 1,102$</td>
</tr>
<tr>
<td>LV ejection fraction (%)*</td>
<td>$57.4 \pm 6.8$</td>
<td>$56.8 \pm 7.4$</td>
</tr>
</tbody>
</table>

*Plus-minus values are means ± SD. †These abnormalities required at least 1 mm in at least two contiguous leads. If more than one of these abnormalities was present, only one was retained in the order in which they are listed. There were no significant differences in any baseline or MI characteristics between the two groups.

*Invasive cardiac procedures include coronary angiography, angioplasty and bypass surgery. The total number is counted in each group. Because angioplasty was always performed at the same time as angiography, both are counted as a single procedure.

Figure 2. Initial hospital stay and total days hospitalized at six-month follow-up in the short-stay and standard-stay groups. Results are represented as scatter plots with small squares indicating medians.
Previous studies. The clinical management of acute MI has evolved considerably since Lewis advocated eight weeks bed rest in 1937 (15). Twenty years ago, a one-week hospital stay for uncomplicated MI was proposed after an evaluation of 67 patients, half of whom were discharged at one week (4). In 1986 to 1987, Topol et al. (9) randomized 80 patients to conventional (7 to 10 days) or early discharge (three days) provided they had an "uncomplicated" MI and a negative tomographic thallium exercise test. In addition, nearly all patients had reperfusion therapy, all underwent early cardiac catheterization and two-thirds had coronary angioplasty. In similar vein, other studies have advocated three- to four-day hospital stays for low-risk patients stratified using coronary angiography and treated with angioplasty (16,17). It is not surprising that such studies have not changed general clinical practice because most centers treating patients with MI do not have tertiary care facilities and most patients probably do not need to undergo invasive cardiac procedures for stratification and treatment (18). Studies proposing a shorter hospital stay have also been limited by retrospective design, absence of randomization and restrictive definitions of qualifying MI (19–24). Moreover, easily applicable criteria defining low-risk patients have been insufficiently developed, accounting for the wide range of estimate of eligible patients for earlier discharge (19–21,23,25). Unresolved questions, such as the duration of heparin therapy and the role and safety of exercise testing very early after MI, have also contributed to a resistance to earlier discharge (26). Finally, the psychosocial repercussions of a shorter hospitalization for acute MI have been little explored. It has not been established whether a shorter stay generates excessive insecurity and anxiety with unfavorable consequences and increased readmission (27). Any study proposing a shorter hospitalization should evaluate whether the reduction can be sustained on follow-up. The present study. This feasibility study addressed these issues with a prospective and randomized design, a priori consideration for study of all MI patients, an initially noninvasive approach, a comparative psychosocial analysis and use of ambulatory ST-segment ischemic monitoring instead of exercise testing to permit early discharge. This is the only recent and the largest such randomized study of which we are aware.

Over the study period, 23% of all patients presenting with an acute MI were randomized. More detailed analysis showed that 41% would have been eligible for consideration of such an approach. This is consistent with other studies estimating the substantial proportion of low-risk patients and justifies the strategy employed (19,23,25). Moreover, the very low serious event rate in the study group supports the pertinence of the relatively simple noninvasive criteria used to identify such patients. The study not only shows that a substantial and sustained reduction in days hospitalized is feasible but also suggests, contrary to previous studies, that such an approach is not dependent on a greater need for invasive cardiac procedures (9,16,17).

Psychosocial considerations. Myocardial infarction is an important event in the life of an individual. It is frequently the first indication of previously unsuspected coronary artery disease and cannot but redefine a person’s prognosis, attitudes and lifestyle. The psychosocial implications of this are complex and profound and may themselves condition prognosis (28–30). Because this matter is obviously more important than a question of days hospitalized, a caveat of this study is that a short-stay approach must be associated with a comprehensive approach to patient counseling and risk factor education and the presence of an effectively supportive infrastructure. In such conditions, this study suggests that a short-stay strategy is not accompanied by adverse psychological consequences such as undue anxiety and emotional distress. In addition, patient illness perception...
and motivating lifestyle modifications do not appear unfavorably affected.

**Ambulatory ST-segment monitoring.** An originality of this study was the use of ambulatory ST-segment monitoring for ischemia on days 2–3 in lieu of predischarge exercise testing. This is attractive for several reasons. Such monitoring is relatively easy to perform because it can be applied and the data processed seven days a week by personnel already available for obtaining hospital ECGs, and tracings can be readily analyzed by clinicians trained in cardiac care. Early exercise testing following MI might raise concerns about the risks of unstable reactivation, unfavorable remodeling and cardiac rupture, especially if exercise were symptom-limited (26). As patients descended and ascended two flights of stairs while on ST-segment monitoring, they in fact performed the equivalent of a low-level exercise test. Above all, use of ST-monitoring for ischemia is more an evaluation for the presence of spontaneous myocardial ischemia than of coronary artery reserve, which is more adequately the role of the exercise test. Therefore, this technique appears more appropriate for monitoring the activity of the unstable plaque and might more confidently confirm stabilization of the acute coronary syndrome. Indeed, this technique has been shown to be a sensitive and specific indicator of risk following an acute coronary event (31–33) and was recently found superior to exercise testing in evaluating risk in patients after MI (34).

**Conclusions.** We conclude that it is possible to identify an important proportion of low-risk MI patients using noninvasive easily applicable clinical criteria and it appears feasible to discharge such patients at three days after negative ambulatory 24-h ST-segment monitoring. Although these findings must be tempered by the number of patients studied, this approach does not appear to be associated with adverse clinical consequences or unfavorable repercussions on psychosocial rehabilitation. Compared with contemporary clinical practice, this approach may result in fewer invasive cardiac procedures while permitting a substantial and sustained reduction in days hospitalized. More experience and perhaps a larger study may confirm the pertinence of this new clinical management strategy for low-risk patients with acute MI.

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