Prognosis of Low-Risk Young Women Presenting to the Emergency Department With Chest Pain

Stacey M. Stauber, BS, Aleksander Teleten, PA, Zhongmin Li, PhD, Sandhya Venugopal, MD, and Ezra A. Amsterdam, MD*

Identification of patients at low risk presenting to the emergency department with chest pain is a continuing challenge. We examined a cohort of low-risk women with negative cardiac injury markers, electrocardiogram with normal results, and clinical stability. We hypothesized that these patients can be safely and accurately managed in a chest pain unit (CPU), may not require predischarge cardiac testing, and have an excellent short-term prognosis. The primary end point was major cardiovascular events during index admission or follow-up. Mean age of the 403 women was 42 ± 4.3 years (30 to 50 years). No patient had a cardiovascular event in the CPU, and none of the 321 patients followed for 6 months had a late cardiovascular event. Most (211, 52%) did not receive predischarge cardiac testing. The remaining 192 patients (48%) had predischarge exercise treadmill test, stress imaging, or cardiac catheterization. Of those patients who underwent treadmill testing, almost 90% had no exercise-induced chest pain and approximately 50% had functional capacity 8 to 14 METs. In addition, 166 patients (41%) were discharged from the CPU after <2 hours and 21% (n = 86) within 2 to 8 hours. In conclusion, this group of low-risk women was safely and accurately managed in the CPU and discharged promptly. There were no cardiac events on index admission or 6-month follow-up, and in most patients, predischarge cardiac testing was unnecessary. **(Am J Cardiol 2016;117:36−39)**

Chest pain causes >8 million visits annually to emergency departments (EDs) in this country, making it the second most frequent cause of these encounters in adults.[1,2] Half of these patients are women, most of whom do not have an acute coronary syndrome (ACS) or other life-threatening conditions and are therefore considered low risk.[1,3] However, women often present a diagnostic challenge because atypical symptoms of myocardial ischemia are frequent in this group,[1,4−6] inadvertent discharge of women with ACS is not rare,[7] and adverse outcomes have been reported in young women with ACS.[8] Furthermore, cardiovascular events have been described in women with nonobstructive coronary artery disease and symptoms of chest pain.[9,10] In the management of patients at low risk presenting to the ED with chest pain, the utility of chest pain units (CPUs) has been established.[1,11−13] However, to our knowledge, there are no data specifically addressing the problem posed by low-risk young women presenting to the ED with chest pain. We hypothesized that these patients can be safely and accurately managed in a CPU, may not require predischarge cardiac testing, and have an excellent short-term prognosis.

Methods

Patients were identified by review of the University of California (Davis) Medical Center CPU database. The study group comprised consecutive low-risk women aged 30 to 50 years admitted to the CPU from February 1995 to November 2006 with symptoms suggestive of ACS. Patients were excluded if the had (1) history of cardiovascular disease (ACS, stroke, ischemic noninvasive stress test, obstructive coronary artery disease on angiography, and heart failure), (2) serious co-morbidity, (3) diabetes mellitus, (4) history of smoking, or (5) cocaine or amphetamine use within 6 months. Low risk for ACS was based on clinical stability (no arrhythmias or hemodynamic dysfunction), normal results (<0.5 mm ST depression and no T-wave inversion) on electrocardiogram (ECG), and negative cardiac injury markers (troponin-I or creatine kinase-MB). The latter marker was used early in the study in only a small number of patients. Patients fulfilling low-risk criteria were transferred from the ED to the CPU for further evaluation, which could include exercise treadmill test, stress echocardiography, myocardial stress scintigraphy (MSS), or no predischarge test. Length of stay (LOS) from admission to the CPU to time of hospital discharge was determined in all patients. This study received approval from our institutional review board.

After initial negative evaluation in the CPU, patients were discharged either with or without a predischarge cardiac test at the discretion of the attending physician. No patients were scheduled for early (24 to 72 hours) cardiac testing after discharge. Treadmill testing was performed according to the Bruce or modified Bruce protocols. Exercise end points included symptoms (e.g., chest pain, undue dyspnea, and dizziness), ECG evidence of myocardial ischemia (1.0-mm horizontal ST shift 80 ms after the J point), 10 mm Hg decrease in systolic blood pressure, ≥3 consecutive ventricular extrasystoles, or a sustained

Division of Cardiovascular Medicine, Department of Internal Medicine, University of California (Davis) Medical Center, Sacramento, California. Manuscript received April 24, 2015; revised manuscript received and accepted September 26, 2015.

See page 38 for disclosure information.

*Corresponding author: Tel: (916) 734-5491; fax: (916) 734-8394.
E-mail address: eaamsterdam@ucdavis.edu (E.A. Amsterdam).

0002-9149/15/$ - see front matter
http://dx.doi.org/10.1016/j.amjcard.2015.09.045

supraventricular tachyarrhythmia. The criterion for a test to be positive for ischemia was the previously noted exercise-induced ST alteration; a nondiagnostic test was defined by absence of ECG ischemia at a heart rate <85% of age-predicted maximum.

In patients who could not exercise or who had baseline ECG changes precluding interpretation of the exercise ECG, stress echocardiography or MSS was used. MSS was performed by single-photon emission computed tomography. Positive MSS comprised a new stress-induced myocardial perfusion defect. For patients undergoing stress echocardiography (exercise or dobutamine), the criterion for a test to be positive was a new stress-induced left ventricular wall motion abnormality. Coronary angiography was performed in multiple projections according to standard techniques. Significant coronary artery disease was defined as >50% stenosis in ≥1 major coronary arteries. We reviewed all patients' medical records to determine clinical status after discharge. Follow-up also included telephone interviews of patients or family members. Clinical end points were all-cause mortality and cardiovascular events (myocardial infarction, stroke, and revascularization).

Statistical analysis: Data are presented as mean ± SD and range. Continuous variables were analyzed by Student's *t* test, and categorical variables were analyzed by chi-square test.

Results

The study group included 403 patients (Table 1). Two thirds were aged 40 to 49 years, the largest ethnic group was white, and >80% had 0 to 1 cardiac risk factors. Cardiac testing was performed in 48% (n = 192) of patients: treadmill (Table 2) 84% (n = 162); stress imaging 14% (n = 26); coronary angiography 2% (n = 4). Predischarge testing was not performed in 52% (n = 211) of patients. There was no difference in age or ethnicity between patients who underwent predischarge testing and those who did not (42.2 vs 42.0 years). However, those who were tested had statistically significantly greater number of risk factors (1.0 vs 0.6, p <0.0001), number of serial cardiac injury markers measured (2.1 vs 1.9, p <0.04), number of 12-lead ECGs (1.9 vs 1.7, p <0.04), and LOS (10 vs 6 hours, p <0.0001).

Treadmill test results were negative in a large majority of patients, <20% were positive, and the remainder was nondiagnostic (Table 2). All but 2 patients with negative treadmill tests were discharged directly from the CPU. These 2 patients were discharged after further evaluation by negative cardiac stress imaging. Of the patients with positive treadmill tests (n = 28, 17%), 11 had further evaluation (stress imaging 10, coronary angiography 2 [1 patient had both imaging and angiography]), which was negative in all, and they were discharged directly from the CPU. In the remaining 17 patients, the treadmill test results were considered false positive and/or low risk, and these patients were also directly discharged. Of the 19 nondiagnostic treadmill tests, 18 were considered low risk, and these patients were directly discharged from the CPU without further testing. The nineteenth patient in this group was discharged after negative MSS. Approximately half of the patients who underwent treadmill testing had a functional capacity of 8 to 14 METs and almost 90% had no exercise-induced chest pain.

Table 1
Patient characteristics (n = 403)

Variable	
Age (years)	
Mean (±SD)	42 ± 4
Range	30-50
30-39	110 (27%)
40-49	278 (69%)
50	15 (4%)
Ethnicity	
White	160 (40%)
Hispanic	56 (14%)
Black	69 (17%)
Asian American*	34 (8%)
Other	20 (5%)
Unknown	64 (16%)
Cardiac risk factors	
0-1	328 (81%)
≥2	75 (19%)

* Includes Filipino, Indian, Fijian, and other Pacific Islander.

Table 2
Exercise treadmill test results (n = 162)

Test Result	
Positive*	28 (17%)
Negative	115 (71%)
Nondiagnostic	19 (12%)
METS	
≤3	13 (8%)
4-7	66 (41%)
8-10	63 (39%)
11-14	17 (10%)
>14	3 (2%)
Exercise-Induced Chest Pain	
+	20 (12%)
0	142 (88%)

* Exercise-induced ischemic ST segment depression.

Stress imaging as the initial cardiac test was performed by stress echocardiography (n = 19) or MSS (n = 7). All except 2 of these tests were negative, resulting in discharge. Two tests were positive for reversible perfusion defects, 1 of which was a false positive based on normal coronary angiography and 1 was considered low risk because the perfusion defect was small. Coronary angiography result was normal in 7 patients, and they were directly discharged. In 4 patients, this was the only test performed based on attending physician discretion. It was applied in an additional 3 patients for further evaluation of positive noninvasive tests (2 positive treadmill tests, 1 positive MSS).

LOS varied from <2 to >24 hours. Mean LOS in patients without cardiac stress testing was significantly shorter than in those with testing (6 vs 10 hours, p <0.0001). In patients who underwent cardiac testing, LOS was <2 hours in 32% and ≤12 hours in 66%. In patients who did not undergo cardiac stress testing, LOS was <2 hours in 50% and ≤12 hours in 84%.

Follow-up status was obtained in 87% of patients (n = 349) at 30 days after discharge and in 80% of patients (n = 321) at

6 months. There were no major adverse outcomes in any of the patients. Thirteen percentage of patients (n = 54) were lost to follow-up, and in 20%, follow-up was <6 months. Although age was greater in the followed group ($p < 0.05$), this difference was not clinically important (followed 42.3 vs no followed 41.3 years). Average number of cardiac risk factors in the followed and no followed groups was <1 in each.

Discussion

To our knowledge, this is the first study that exclusively evaluates young women presenting to the ED with apparently low-risk chest pain. In this selected group of patients, no one had ACS on index admission or follow-up. Our results support our hypothesis that low-risk women can be accurately and safely managed in a CPU and promptly discharged. In addition, not all such patients require predischarge cardiac testing. Our criteria for low risk were verified by patients' benign outcomes. Low risk was further supported by the absence of exercise-induced chest pain in almost 90% of our study cohort and good-to-excellent functional capacity in approximately 50%.

Although whites comprised the largest ethnic group in our study, other ethnicities were represented. The cardiac profiles of these patients indicated low risk for ACS based on age, number of risk factor, and no history of coronary disease. This group accounts for a significant proportion of women presenting to the ED with chest pain.[1,12] Furthermore, young women with ACS have a high morbidity and mortality and are a group in which ACS diagnosis is most frequently missed in the ED.[7,8] It is therefore essential that these patients receive thorough evaluation when presenting to the ED with chest pain.[1,7,13]

Recent data indicate that predischarge cardiac testing may not be necessary in evaluation of patients at very low risk and emphasize the utility of physician discretion in the evaluation of this group.[14–17] These findings support a changing paradigm in the management of patients at low risk presenting to the ED. A key factor in cost-effectiveness of patient management is LOS, and rapid evaluation in CPUs has contributed to this goal.[1] Utilization of computed tomography coronary angiography also reduces LOS compared with usual care of low-risk chest pain. In one report, this method decreased LOS to 23 hours compared with 31 hours with usual care.[18] In contrast, our study demonstrated that LOS was only 10 hours in patients receiving cardiac testing and 6 hours in the nontested patients. Even shorter LOS has been reported with a 2-hour accelerated diagnostic protocol using high-sensitivity cardiac troponin and no cardiac testing.[19] Thus, recognition that all patients at low risk do not require predischarge testing can significantly decrease LOS and improve cost-effectiveness.

Our study has several limitations, which include the inherent obstacles of a retrospective investigation. However, it is the only study of which we are aware devoted exclusively to low-risk young women presenting to the ED with chest pain. Although 6-month follow-up is incomplete (80%), this is relatively high for a retrospective study, and there were no clinically important differences in those lost to follow-up and those with 6-month follow-up. In addition, duration of follow-up (6 months) is longer than the conventional 30-day period in many post-CPU studies. Details of patients' chest pain did not serve as selection criteria for predischarge cardiac testing, physician discretion determined the application of this approach. However, there were no significant differences between tested and nontested patients in age and ethnicity, and the average number of risk factors in both groups was very low.

Disclosures

There was no funding support for this study.

1. Amsterdam EA, Kirk JD, Bluemke DA, Diercks D, Farkouh ME, Garvey JL, Kontos MC, McCord J, Miller TD, Morise A, Newby LK, Ruberg FL, Scordo KA, Thompson PD. Testing of low-risk patients presenting to the emergency department with chest pain: a scientific statement from the American Heart Association. *Circulation* 2010;122:1756–1776.
2. Pitts S, Niska RW, Xu J, Burt CW. National hospital ambulatory medical care survey: 2006 emergency department summary. *Natl Health Stat Rep* 2008;7:1–38.
3. Lee TH, Goldman L. Evaluation of the patient with acute chest pain. *N Engl J Med* 2000;342:1187–1195.
4. Milner KA, Funk M, Richards S, Wilmes RM, Vaccarino V, Krumholz HM. Gender differences in symptom presentation associated with coronary heart disease. *Am J Cardiol* 1999;84:396–399.
5. Patel H, Rosengren A, Ekman I. Symptoms in acute coronary syndromes: does sex make a difference? *Am Heart J* 2004;148:27–33.
6. Bairey Merz CN, Shaw LJ, Reis SE, Bittner V, Kelsey SF, Olson M, Johnson BD, Pepine CJ, Mankad S, Sharaf BL, Rogers WJ, Pohost GM, Lerman A, Quyyumi AA, Sopko G. Insights from the NHLBI-Sponsored Women's Ischemia Syndrome Evaluation (WISE) Study: Part II: gender differences in presentation, diagnosis, and outcome with regard to gender-based pathophysiology of atherosclerosis and macrovascular and microvascular coronary disease. *J Am Coll Cardiol* 2006;47(Suppl 3):S21–S29.
7. Pope JH, Aufderheide TP, Ruthazer R, Woolard RH, Feldman JA, Beshansky JR, Griffith JL, Selker HP. Missed diagnoses of acute cardiac ischemia in the emergency department. *N Engl J Med* 2000;342:1163–1170.
8. Vaccarino V, Parsons L, Every NR, Barron HV, Krumholz HM. Sex-based differences in early mortality after myocardial infarction. National Registry of Myocardial Infarction. *N Engl J Med* 1999;341:217–225.
9. Johnson BD, Shaw LJ, Pepine CJ, Reis SE, Kelsey SF, Sopko G, Rogers WJ, Mankad S, Sharaf BL, Bittner V, Bairey Merz CN. Persistent chest pain predicts cardiovascular events in women without obstructive coronary artery disease: results from the NIH- NHLBI-sponsored Women's Ischaemia Syndrome Evaluation (WISE) study. *Eur Heart J* 2006;27:1408–1415.
10. Jespersen L, Hvelplund A, Abildstrom SZ, Pedersen F, Galatius S, Madsen JK, Jorgensen E, Kelbaek H, Prescott E. Stable angina pectoris with no obstructive coronary artery disease is associated with increased risks of major adverse cardiovascular events. *Eur Heart J* 2012;33:734–744.
11. Farkouh ME, Smars PA, Reeder GS, Zinsmeister AR, Evans RW, Meloy TD, Kopecky SL, Allen M, Allison TG, Gibbons RJ, Gabriel SE. A clinical trial of a chest-pain observation unit for patients with unstable angina. Chest Pain Evaluation in the Emergency Room (CHEER) Investigators. *N Engl J Med* 1998;339:1882–1888.
12. 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;40:251–256.
13. Diercks DB, Kirk JD, Amsterdam EA. Chest pain units: management of special populations. *Cardiol Clin* 2005;23:540–557.
14. Prasad V, Cheung M, Cifu A. Chest pain in the emergency department: the case against our current practice of routine noninvasive testing. *Arch Intern Med* 2012;172:1506–1509.
15. Safavi KC, Li SX, Dharmarajan K, Venkatesh AK, Strait KM, Lin H, Lowe TJ, Fazel R, Nallamothu BK, Krumholz HM. Hospital variation

in the use of noninvasive cardiac imaging and its association with downstream testing, interventions, and outcomes. *JAMA Intern Med* 2014;174:546−553.
16. Amsterdam EA, Aman E. The patient with chest pain: low risk, high stakes. *JAMA Intern Med* 2014;174:553−554.
17. Winchester DE, Brandt J, Schmidt C, Allen B, Payton T, Amsterdam EA. Diagnostic yield of routine noninvasive cardiovascular testing in low-risk acute chest pain patients. *Am J Cardiol* 2015;116:204−207.
18. Hoffmann U, Truong QA, Schoenfeld DA, Chou ET, Woodard PK, Nagurney JT, Pope JH, Hauser TH, White CS, Weiner SG, Kalanjian S, Mullins ME, Mikati I, Peacock WF, Zakroysky P, Hayden D, Goehler A, Lee H, Gazelle GS, Wiviott SD, Fleg JL, Udelson JE. Coronary CT angiography versus standard evaluation in acute chest pain. *N Engl J Med* 2012;367:299−308.
19. Than M, Aldous S, Lord SJ, Goodacre S, Frampton CM, Troughton R, George P, Florkowski CM, Ardagh M, Smyth D, Jarine DL, Peacock WF, Young J, Hamilton G, Deely JM, Cullen L, Richards AM. A 2-hour diagnostic protocol for possible cardiac chest pain in the emergency department: a randomized clinical trial. *JAMA Intern Med* 2014;174:51−58.