Usefulness of Predischarge Cardiac Testing in Low Risk Women and Men for Safe, Rapid Discharge from a Chest Pain Unit

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Predischarge cardiac testing (PDT) in low-risk patients evaluated for acute coronary syndrome in a chest pain unit (CPU) remains a challenge. It is unclear whether PDT varies by gender. We analyzed consecutive low-risk women and men evaluated in our CPU over a 2-year period and compared the utilization of PDT (exercise treadmill test, myocardial stress perfusion scintigraphy, exercise stress echocardiography, invasive coronary angiography, or no test), and incidence of major adverse cardiac events (MACE) at 30 days and 6 months. The study group comprised 619 patients (54% women). A large proportion of both genders did not undergo PDT, although this finding was more frequent in women (50% women vs 40% men, p = 0.01). At 30 days, there were no MACE in either gender. After 6 months of follow-up, MACE remained very low in both women and men (2 [1%] vs 2 [1%]), and in patients who did and did not receive PDT (2 [1%] vs 2 [1%]). Mean length of stay in the CPU was 5.4 hours in patients without PDT and 9.8 hours in those with PDT (p <0.0001) without altering postdischarge MACE. When referred for PDT, women more often underwent myocardial stress perfusion scintigraphy than men (22% vs 14%, p = 0.005) and less often received exercise treadmill test (20% vs 39%, p <0.0001). Yield of abnormal PDT was low in both women and men although it was lower in women (1% vs 5%, p = 0.02). In conclusion, many low-risk women and men evaluated in a CPU for acute coronary syndrome can be safely and rapidly discharged without PDT and with low risk for MACE at 30 days and at 6 months. Exclusion of PDT was associated with significantly reduced length of stay while maintaining safety in terms of postdischarge MACE. **(Am J Cardiol 2019;123:1772−1775)**

Chest pain is the second most frequent cause of emergency department (ED) visits in the United States, accounting for more than 6 million presentations annually.[1] The goal of evaluation is rapid identification of patients with acute coronary syndrome (ACS) or other life-threatening condition requiring urgent therapy and those with less serious entities who can be managed more deliberately and may be candidates for early discharge. Chest pain units (CPUs) serve as a safe, efficacious means of excluding ACS and its complications in low-risk patients.[2] Evaluation in the CPU typically involves clinical assessment, serial electrocardiograms, cardiac injury markers, and predischarge cardiac testing (PDT) if indicated. The optimal strategy for PDT in low-risk patients evaluated for ACS varies from application to all CPU patients to a more recent approach of PDT only in selected patients.[3−6] Additionally, whether management and clinical outcomes of patients vary by gender in the CPU is unclear, given the limited studies on this question. We hypothesized that not all low-risk women and men require PDT for safe, rapid discharge from a CPU.

Methods

We analyzed a prospectively collected database of all consecutive low-risk women and men without a history of coronary artery disease (CAD) admitted to the CPU of the University of California, Davis, Medical Center, an urban academic tertiary care institution, from January 1, 2012 to January 1, 2014 and compared the utilization of PDT and incidence of major adverse cardiac events (MACE) at 30 days and 6 months in women and men. MACE was defined as cardiac death, myocardial infarction, and revascularization. During this interval, the annual number of adult patient visits to our ED averaged approximately 55,000. Criteria for low risk of ACS were: hemodynamic stability, no arrhythmias, normal or near-normal resting electrocardiogram (ST depression no >0.5 mm, normal T waves, no arrhythmia beyond rare premature atrial or ventricular complexes, no pacing, no conduction abnormalities, or no ventricular hypertrophy), and an initial contemporary troponin I (Siemens, Malvern, PA) <99th percentile of 0.04 ng/mL.[2]

The primary outcomes were utilization of PDT and incidence of postdischarge MACE including cardiac death, myocardial infarction, and revascularization at 30-day and 6-month follow-up. Secondary outcomes were length of

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stay (LOS), type of PDT (exercise treadmill test [ETT], myocardial stress perfusion scintigraphy [MPS], exercise stress echocardiography, or invasive coronary angiography), and results of PDT. The CPU-attending physician selected patients for PDT and type of PDT. Our CPU-attending physicians are internists who also undergo additional, specialized training in management of patients presenting with chest pain and are dedicated to, and full-time, at that position. The follow-up period began when patients were discharged home from the CPU or, if they were admitted to hospital, when the patient was discharged from the index admission.

ETT was considered positive for ischemia based on exercise-induced ST segment depression of ≥1.0 mm for 60 to 80 milliseconds after the J point and negative for ischemia if there was <1.0 mm ST segment depression during exercise testing and heart rate reached ≥85% of age-predicted maximum. If there was no evidence of exercise-induced ischemia but peak exercise heart rate was <85% of predicted maximum, the ETT was defined as nondiagnostic. MPS was positive if there was a new stress-induced myocardial perfusion defect. Exercise stress echocardiogram was considered positive based on a new stress-induced left ventricular wall motion abnormality. For coronary angiography, the definition of obstructive CAD was ≥50% stenosis of the left main coronary artery and ≥70% stenosis of a coronary artery or major branch.

The CPU has a separate, prospectively collected database completed by the attending physician at the end of each patient's evaluation. Data entered include symptoms, demographic features, cardiac risk factors, history of CAD, baseline electrocardiogram, type of PDT, and its results. In order to determine the incidence of MACE, we reviewed all patients' medical records up to 6 months following their CPU evaluation; to determine all-cause mortality, we queried the electronic medical record and/or the Social Security Death Index for all patients.

Continuous data are presented as mean ± SD and range or percentage. Continuous variables were analyzed by Student's *t* test and categorical variables were analyzed by chi square and logistic regression. Differences were considered significant if $p < 0.05$. The JMP statistical package (JMP 13.0.0 for Macintosh) was used for analysis. This study was approved by the University of California, Davis, Human Subjects Review Committee.

Results

The study group comprised 619 patients with approximately half women (Table 1). A large proportion of both genders did not undergo PDT, although this applied to more women (Table 1). Use of PDT as compared with no PDT did not vary by age (58 vs 56 years, p = NS) or mean number of cardiac risk factors (1 vs 1, p = NS). Among the patients who were referred for PDT, women more often underwent MPS than men and men more often received ETT than women (Table 1). Mean LOS was shorter in patients with no PDT compared with those with PDT (5 vs 10 hours, $p < 0.0001$, respectively) and did not vary between women and men (Table 1).

At 30 days, there were no MACE in either gender. Clinical follow-up was obtained in 465 patients (75%), including 265 women (80%) and 200 men (70%). The 171 patients (24%) in whom clinical follow-up was not obtainable had similar mean number of cardiac risk factors but younger age (53 vs 58 year, $p < 0.0001$) compared with those with 30-day follow-up.

At 6 months, MACE rate was low in both women and men (Table 2) and in patients with no PDT and PDT (n = 2 [1%] vs n = 2 [1%]). The single cardiac death occurred in a 92-year-old woman who, on her initial CPU admission, did not undergo PDT. At 5-month follow-up, she sustained a fatal cardiac arrest on the day of admission for a hip fracture before surgical intervention. Six-month follow-up was obtained in 443 patients (72%) including 252 women (76%) and 191 men (67%). The patients in whom clinical follow-up was not obtainable were similar to those patients without 30-day follow-up.

Table 1
Patient clinical features

Variable	Total patients (n = 619)	Women (n = 332)	Men (n = 287)	p
Age* (years)	57 ± 12 (27-92)	59 ± 12 (30-92)	54 ± 12 (27-89)	<0.0001
Cardiac risk factors				
0-1	259 (42%)	132 (40%)	127 (44%)	NS
≥2	360 (58%)	200 (60%)	160 (56%)	NS
Hypertension	383 (62%)	225 (68%)	158 (55%)	0.0011
Hyperlipidemia	292 (47%)	166 (50%)	126 (44%)	NS
Type 2 diabetes mellitus	160 (26%)	96 (29%)	64 (22%)	NS
Tobacco use	137 (22%)	55 (17%)	82 (29%)	0.0003
Family history of heart disease	144 (23%)	78 (23%)	66 (23%)	NS
Predischarge cardiac testing				
No test	283 (46%)	167 (50%)	116 (40%)	0.01
Myocardial perfusion scintigraphy	113 (18%)	74 (22%)	39 (14%)	0.0048
Exercise treadmill test	179 (29%)	68 (20%)	111 (39%)	<0.0001
Exercise stress echocardiogram	34 (5%)	18 (5%)	16 (6%)	NS
Coronary angiogram	10 (2%)	5 (2%)	5 (2%)	NS
Length of stay (hours)	7.9	7.9	7.8	NS

* mean ± SD (range).

Table 2
Major adverse cardiovascular events at 6 months according to gender

Major adverse cardiovascular events	Total patients with 6-month follow-up (n = 443)	Women (n = 252)	Men (n = 191)
Cardiac death	1 (0.2%)	1 (0.4%)	0
Myocardial infarction	2 (0.5%)	1 (0.4%)	1 (0.5%)
Revascularization	1 (0.2%)	0	1 (0.5%)
Total	4 (0.9%)	2 (0.8%)	2 (1.1%)

Table 3
Results of predischarge cardiac testing by gender

Predischarge cardiac test result	Total patients (n = 336)	Women (n = 165)	Men (n = 171)	p
Positive	10 (3%)	2 (1%)	8 (5%)	0.03
Nondiagnostic	30 (9%)	10 (6%)	20 (12%)	0.02
Negative	296 (88%)	153 (93%)	143 (84%)	0.009

Yield of abnormal PDT was low in both women and men (Table 3). Women had significantly fewer positive tests than men and significantly more negative tests (Table 3). Of 10 patients with positive PDTs, 9 patients (8 men, 1 woman) underwent subsequent coronary angiography during the index admission and 1 woman declined further evaluation. Only men were found to have obstructive CAD (0 women vs 7 [78%] men); and 6 men underwent revascularization (5 percutaneous coronary interventions and 4 coronary artery bypass graft surgeries).

Discussion

Our findings suggest that many low-risk women and men evaluated for ACS in a CPU can be safely and rapidly discharged without PDT while maintaining a low rate of MACE at short- and intermediate-term follow-up. Importantly, absence of PDT was associated with significantly reduced LOS in both women and men. The yield of positive PDT was low in both genders.

This study is one of the first to assess utilization of PDT in the CPU by gender and to highlight the safety of no PDT in both men and women in the CPU. Previous studies differ on the frequency of PDT in women and men, as reflected by a report that the likelihood of PDT in women was 1.6 times higher than in men,[7] whereas a large investigation of 6,000 patients revealed higher rates of PDT in men.[8] The variable results likely reflect differences in patient populations and physician preferences. We found that large proportions of both women and men were discharged from the CPU without PDT. Omitting PDT did not affect postdischarge MACE. This extends our previous results in 400 low-risk women who also had no MACE at 6 months[5] and adds a comparison of MACE in low-risk men and women. The comparable clinical outcomes between patients with and without PDT suggest that the decision to omit PDT was appropriate and PDT was not necessary to enhance safe discharge. This is likely in part because the yield of PDT is very low. We found that both genders had <10% positive tests which supports the rationale against routine PDT in the low-risk ED chest pain population.[3,9,10] Our findings advocate for selection of patients for PDT rather than the current approach of routine PDT,[2] given the lack of improvement in clinical outcomes and potential for harm with further testing.[3,9,11]

Not only is PDT mandatory to enhance safe discharge, but elimination of testing affords reduced LOS. A more judicious use of PDT can decrease resource utilization and costs and improve use of personnel with no compromise of patient safety. Other studies reported that PDT increased LOS for patients evaluated in a CPU[4,5,12–14] and increased hospital charges,[13] but did not improve postdischarge event rates between no-test versus tested patients.

The management of women and men in our cohort was largely similar in regard to utilization of PDT and clinical outcomes, but the modality of PDT varied between the genders (Table 1). Women more often received MPS and men more often underwent ETT. The PROMISE trial which assessed outpatients with stable chest pain similarly found that women more often received pharmacologic stress imaging than functional testing.[15] We have extended these findings to the low-risk CPU population. It is notable that more frequent stress imaging in women diverges from the recommendations of the American College of Cardiology/American Heart Association for ETT as the initial noninvasive test of choice and stress imaging as the test for patients with an abnormal baseline ECG or functional limitations precluding adequate exercise.[16] Although these guidelines are primarily intended for outpatient stress testing, our population in the CPU similar to outpatients in that they are low risk, stable, and undergo symptom limited maximal stress tests. The reason why women undergo more MPS than ETT is likely multifactorial, although in our cohort, it may have been related to older age in women and concern regarding potential inadequate exercise capacity. From 1993 to 2010, analysis of the National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey revealed that cardiac stress tests with imaging comprised a growing proportion of tests, increasing from 59% in 1993 to 1995 to 87% in 2008 to 2010, a trend that could not be explained by population demographics, risk factors, or provider characteristics.[17] Although excessive false positive ETTs in women have been a concern, we have reported that the concept of a high false positive rate of ETT in women is related to a predominance of younger women in early studies of exercise testing,[18] which utilized coronary angiography as the gold standard. The positive predictive value of ETT was significantly higher in older than younger women: up to 80% in women >65 years old.[18]

A number of limitations of our study require consideration. This is a retrospective investigation and entails the inherent limitations of that method. However, the database was prospectively collected, and the study cohort comprised consecutive patients. The study was performed at a single center, so our results may not be generalizable to other institutions or settings; however, our patients represented a "real world" population. Although our follow-up data are not complete, detailed follow-up was obtained in the substantial proportion of approximately 3/4 of patients, and the demographic, clinical risk profiles and SSDI mortality data

of the entire followed and not followed groups are comparable, except for older age in women and fewer men in the followed group at 6 months, which would tend to have balancing effects on risk in these patient subsets.

In conclusion, this study demonstrated that many low-risk women and men evaluated in a CPU for ACS can be safely and rapidly discharged without PDT and with low risk for MACE at 1 month and at 6 months. Additionally, exclusion of PDT was associated with significantly reduced LOS while maintaining patient safety in terms of postdischarge MACE.

Disclosures

The authors have no conflicts of interest to disclose.

1. Pitts J, Flack J, Goodfellow J. Improving nutrition in the cystic fibrosis patient. *J Pediatr Health Care* 2008;22:137–140.
2. 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. American Heart Association Exercise, Cardiac Rehabilitation, and Prevention Committee of the Council on Clinical Cardiology Council on Cardiovascular Nursing, and Interdisciplinary Council on Quality of Care and Outcomes Research. 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.
3. Amsterdam EA, Aman E. The patient with chest pain: low risk, high stakes. *JAMA Intern Med* 2014;174:553–554.
4. Howell SJ, Bui J, Thevakumar B, Amsterdam EA. Utility of physician selection of cardiac tests in a chest pain unit to exclude acute coronary syndrome among patients without a history of coronary artery disease. *Am J Cardiol* 2018;121:825–829.
5. Stauber SM, Teleten A, Li Z, Venugopal S, Amsterdam EA. Prognosis of low-risk young women presenting to the emergency department with chest pain. *Am J Cardiol* 2016;117:36–39.
6. 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.
7. Napoli A, Choo EK. Gender and stress test use in an ED chest pain unit. *Am J Emerg Med* 2012;30:890–895.
8. Chang AM, Mumma B, Sease KL, Robey JL, Shofer FS, Hollander JE. Gender bias in cardiovascular testing persists after adjustment for presenting characteristics and cardiac risk. *Acad Emerg Med* 2007;14:599–605.
9. 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.
10. Redberg RF. Coronary CT angiography for acute chest pain. *N Engl J Med* 2012;367:375–376.
11. 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.
12. Wang H, Watson K, Robinson RD, Domanski KH, Umejiego J, Hamblin L, Overstreet SE, Akin AM, Hoang S, Shrivastav M, Collyer M, Krech RN, Schrader CD, Zenarosa NR. Chest pain risk scores can reduce emergent cardiac imaging test needs with low major adverse cardiac events occurrence in an emergency department observation unit. *Crit Pathw Cardiol* 2016;15:145–151.
13. Frisoli TM, Nowak R, Evans KL, Harrison M, Alani M, Varghese S, Rahman M, Noll S, Flannery KR, Michaels A, Tabaku M, Jacobsen G, McCord J. Henry Ford HEART score randomized trial: rapid discharge of patients evaluated for possible myocardial infarction. *Circ Cardiovasc Qual Outcomes* 2017;10:1–7.
14. Baugh CW, Greenberg JO, Mahler SA, Kosowsky JM, Schuur JD, Parmar S, Ciociolo GR Jr., Carr CW, Ghazinouri R, Scirica BM. Implementation of a risk stratification and management pathway for acute chest pain in the emergency department. *Crit Pathw Cardiol* 2016;15:131–137.
15. Hemal K, Pagidipati NJ, Coles A, Dolor RJ, Mark DB, Pellikka PA, Hoffmann U, Litwin SE, Daubert MA, Shah SH, Ariani K, Bullock-Palmer RP, Martinez B, Lee KL, Douglas PS. Sex differences in demographics, risk factors, presentation, and noninvasive testing in stable outpatients with suspected coronary artery disease: insights from the PROMISE trial. *JACC Cardiovasc Imaging* 2016;9:337–346.
16. Mieres JH, Gulati M, Bairey Merz N, Berman DS, Gerber TC, Hayes SN, Kramer CM, Min JK, Newby LK, Nixon JV, Srichai MB, Pellikka PA, Redberg RF, Wenger NK, Shaw LJ. American Heart Association Cardiac Imaging Committee of the Council on Clinical C, Cardiovascular I, Intervention Committee of the Council on Cardiovascular R and Intervention. Role of noninvasive testing in the clinical evaluation of women with suspected ischemic heart disease: a consensus statement from the American Heart Association. *Circulation* 2014;130:350–379.
17. Ladapo JA, Blecker S, Douglas PS. Physician decision making and trends in the use of cardiac stress testing in the United States: an analysis of repeated cross-sectional data. *Ann Intern Med* 2014;161:482–490.
18. Levisman JM, Aspry K, Amsterdam EA. Improving the positive predictive value of exercise testing in women for coronary artery disease. *Am J Cardiol* 2012;110:1619–1622.