Symptoms and Angiographic Findings of Patients Undergoing Elective Coronary Angiography Without Prior Stress Testing

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Many patients undergo elective coronary angiography without preprocedural stress testing that may be suitable if performed in patients with more angina pectoris or more frequently identified obstructive coronary artery disease (CAD). Patients in the National Cardiovascular Data Registry CathPCI Registry undergoing elective coronary angiography from July 2009 to April 2013 were assessed for differences in angina (Canadian Cardiovascular Society [CCS] class) and severity of obstructive CAD in those with and without preprocedural stress testing, stratified by CAD history. Given the large sample size, differences were considered clinically meaningful if the standardized difference (SD) was >10%. Of 790,601 patients without CAD history, 36.9% did not undergo preprocedural stress testing. Compared with patients with preprocedural stress testing, patients without preprocedural stress testing were more frequently angina free (CCS class 0; 28.2% with stress test vs 38.5% without, SD = 14.8%) and had similar rates of obstructive CAD (40.1% with stress test vs 35.7% without, SD = 9.0). Of 449,579 patients with CAD history, 44.2% did not undergo preprocedural stress testing. Patients without preprocedural stress testing reported more angina (CCS class III/IV angina: 17.8% vs 13.4%; SD = 11.3%) but were not more likely to have obstructive CAD (78.7% vs 81.1%; SD = 5.8%) than patients with preprocedural stress testing. In conclusion, approximately 40% of patients undergoing elective coronary angiography did not have preprocedural risk stratification with stress testing. For these patients, the clinical decision to proceed directly to invasive evaluation was not driven primarily by severe angina and did not result in higher detection rates for obstructive CAD. © 2014 Elsevier Inc. All rights reserved. (Am J Cardiol 2014;114:348−354)

The importance of understanding current practice patterns of proceeding directly to coronary angiography without preprocedural stress testing was underscored by a recent report assessing the appropriateness of elective percutaneous coronary interventions (PCIs). In that analysis of the National Cardiovascular Data Registry (NCDR) CathPCI Registry data, 11.6% of nonacute PCIs were deemed inappropriate[1,2]; however, >1 in 5 patients with a nonacute PCI were excluded as they did not have a preprocedural noninvasive stress test. Inclusion of these patients in those analyses may have significantly altered estimates of PCI appropriateness. Although a few studies have described this population, these studies were unable to provide detailed information on patients' symptoms or anatomic findings.[3,4] To address this gap in knowledge, we compared clinical characteristics, symptom severity, and the extent of obstructive coronary artery disease (CAD) between patients undergoing elective coronary angiography with and without preprocedural stress testing. We also examined the likelihood of any obstructive CAD in patients without preprocedural stress testing, compared with patients having a high-, intermediate-, and low-risk stress test result. Because the probability of significant CAD is known to be much higher in those with previous myocardial infarctions or revascularization procedures, we stratified the population into those without and with known CAD.

Methods

CathPCI Registry is an initiative of the American College of Cardiology Foundation and the Society for Cardiovascular Angiography and Interventions.[5,6] The registry consists of consecutive diagnostic coronary angiography and PCI procedures from >1,000 hospitals of the United States. Detailed information about patient demographics, clinical
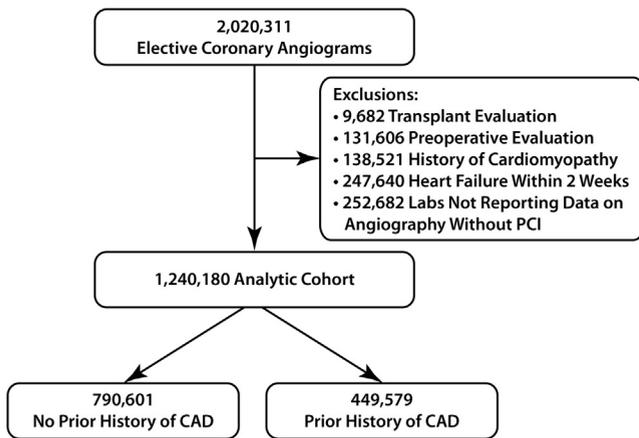
Figure 1. Study cohort.

features, hospital information, preprocedural stress test results, angiographic findings, and in-hospital complications are abstracted by trained staff at each hospital using standardized data elements (available at *http://www.ncdr.com/WebNCDR/elements.aspx*). The CathPCI Registry conducts routine audits of their data, and a recent publication of their audit revealed an overall accuracy rate of 93.1%.[7]

We identified 2,020,311 elective coronary angiograms performed from July 2009 to April 2013 from hospitals that reported coronary angiography data (Figure 1). We included only elective coronary angiograms, as our focus was to examine the use of preprocedural stress testing in nonacute presentations, where preprocedural risk stratification is more relevant. We examined patients enrolled after July 2009 to coincide with the implementation of version 4 of the CathPCI Registry's data collection form, which contained information on noninvasive stress testing, defined as either exercise treadmill stress test, stress echocardiogram, stress testing with single-photon emission computed tomography myocardial perfusion imaging, stress testing with cardiac magnetic resonance imaging, cardiac computed tomography coronary angiography, or coronary artery calcium score. To ensure that the study population did not have another clinical reason to proceed directly to coronary angiography without preprocedural stress testing, we excluded patients undergoing transplant evaluation (9,682 procedures), those undergoing angiography for a preoperative evaluation for noncardiac surgery (131,606 procedures), patients with a diagnosis of cardiomyopathy (138,521 procedures), patients with heart failure exacerbation within the past 2 weeks (247,640 procedures), and those admitted to hospitals that do not routinely report coronary angiography results for patients not undergoing PCI (252,682 procedures). Our final study cohort included 1,240,180 patients from 940 hospitals, of which 790,601 had no history of CAD and 449,579 had known CAD, which was defined as a history of myocardial infarction, coronary artery bypass graft surgery, or PCI.

Our primary objective was to determine whether the symptom burden, rate of obstructive CAD, and severity of obstructive CAD differed between patients who underwent elective coronary angiography with and without preprocedural stress testing. Symptom burden was assessed using the Canadian Cardiovascular Society (CCS) functional class for

angina.[8] Angina-free patients are categorized by the Cath-PCI Registry as CCS class 0. Consistent with recent studies for diagnostic coronary angiography, obstructive CAD was defined as a $\geq 50\%$ stenosis of the left main or a major epicardial coronary artery of ≥ 2.0 mm in diameter.[1,4] The likelihood of obstructive CAD was then defined as the proportion of patients undergoing coronary angiography with evidence of obstructive CAD. Finally, to examine differences in the extent and severity of obstructive CAD between the 2 stress test groups, we compared the distribution of 1-, 2-, and 3-vessel obstructive CAD, as well as the frequency of proximal left anterior descending (LAD) and left main CAD.

As the pretest probability for obstructive CAD is known to be higher for patients with a history of CAD, we conducted all analyses separately for patients without and with a history of known CAD. Baseline demographics and clinical characteristics were compared between patients undergoing elective coronary angiography with and without preprocedural stress testing. Because of the large sample size, which could result in statistically significant p values without clinically relevant differences in proportions, differences between groups were evaluated by computing standardized differences (differences in group means divided by the common standard deviation) for each covariate. Based on previous work, a standardized difference of >10% was used to define a clinically meaningful difference between groups.[9]

We then examined clinically important differences in the severity of angina, the frequency of obstructive CAD, and the presence of high-risk (3-vessel, proximal LAD, or left main) CAD between patients undergoing coronary angiography with and without preprocedural stress testing. Finally, we compared the likelihood of any obstructive CAD between patients without preprocedural stress testing and those with a high-risk, intermediate-risk, and low-risk stress test result. The severity of noninvasive imaging result was defined as low, intermediate, and high risk using standardized NCDR data definitions (see Supplementary Appendix 1). For this last analysis, we excluded patients with preprocedural stress test whose ischemia severity was not documented (172,446 patients without CAD history and 86,770 patients with CAD history).

To ensure the robustness of our findings, we conducted a sensitivity analysis by repeating the aforementioned analyses using a more restrictive definition of obstructive CAD (a $\geq 50\%$ stenosis in the left main or $\geq 70\%$ stenosis in a major epicardial coronary artery of >2 mm), as this is the usual angiographic threshold for consideration of PCI. Missing data rate was <1%. All statistical analyses were performed with SAS 9.2 (SAS Institute, Inc., Cary, North Carolina) or R version 2.10.0 (R Foundation for Statistical Computing, Vienna, Austria).

Results

A total of 1,240,180 elective coronary angiograms were identified, of which 749,702 were preceded by a stress test. Stress testing with single-photon emission computed tomography myocardial perfusion imaging was the most common form of testing (78.0%), followed by stress echocardiogram (11.1%), exercise stress testing (9.3%), and

Table 1

Baseline characteristics, stratified by prior history of CAD and preprocedural stress testing

Characteristic	Patients Without CAD History		Patients With Prior CAD History	
	Stress Test Prior to Coronary Angiogram (n = 499,015)	No Stress Test Prior to Coronary Angiogram (n = 291,586)	Stress Test Prior to Coronary Angiogram (n = 250,687)	No Stress Test Prior to Coronary Angiogram (n = 198,892)
Age (years)	61.5 ± 11.9	62.6 ± 13.3	66.4 ± 10.7	66.3 ± 11.6
Men	258,889 (51.9%)	144,915 (49.7%)	170,876 (68.2%)	127,888 (64.3%)
White	425,555 (85.3%)	251,182 (86.1%)	223,549 (89.2%)	179,673 (90.3%)
Private health insurance	350,049 (72.5%)	190,115 (68.8%)	167,690 (68.3%)	125,852 (65.6%)
No health insurance	16,269 (3.3%)	15,420 (5.3%)	5,098 (2.0%)	7,044 (3.5%)
Diabetes mellitus	142,405 (28.5%)	76,378 (26.2%)	98,076 (39.1%)	74,511 (37.5%)
On dialysis	4,955 (1.0%)	5,219 (1.8%)	3,422 (1.4%)	3,983 (2.0%)
Family history of premature CAD	136,922 (27.4%)	70,328 (24.1%)	69,772 (27.8%)	58,127 (29.2%)
Anti-anginal medications	242,533 (48.7%)	133,520 (45.9%)	184,188 (73.5%)	143,595 (72.3%)

There were no clinically meaningful differences between the group with and the group without preceding stress test within each cohort.

CAD = coronary artery disease.

Table 2

Angina severity and clinical presentation, stratified by prior history of CAD and preprocedural stress testing

Characteristic	Patients Without Prior CAD History		Patients With Prior CAD History	
	Stress Test Prior to Coronary Angiogram (n = 499,015)	No Stress Test Prior to Coronary Angiogram (n = 291,586)	Stress Test Prior to Coronary Angiogram (n = 250,687)	No Stress Test Prior to Coronary Angiogram (n = 198,892)
Anginal classification within 2 weeks (CCS)				
0 (Asymptomatic)	140,193 (28.2%)	111,782 (38.5%)*	72,668 (29.1%)	51,647 (26.1%)*
I	104,835 (21.1%)	54,910 (18.9%)*	42,331 (16.9%)	32,953 (16.6%)*
II	191,401 (38.5%)	85,977 (29.6%)*	101,415 (40.6%)	78,371 (39.5%)*
III	48,240 (9.7%)	27,232 (9.4%)*	28,386 (11.4%)	27,670 (14.0%)*
IV	12,507 (2.5%)	10,522 (3.6%)*	5,095 (2.0%)	7,554 (3.8%)*
CAD presentation				
Asymptomatic	101,493 (20.4%)	80,883 (27.8%)*	61,186 (24.4%)	40,427 (20.4%)
Symptoms unlikely myocardial ischemia	155,203 (31.1%)	103,625 (35.6%)*	43,988 (17.6%)	39,856 (20.1%)
Stable angina pectoris	242,031 (48.5%)	106,682 (36.6%)*	145,386 (58.0%)	118,348 (59.6%)

CAD = coronary artery disease; CCS = Canadian Cardiovascular Society; LAD = left anterior descending.

* Denotes clinically meaningful difference with standardized difference >10% within the cohort.

stress cardiac magnetic resonance imaging (0.7%). In 790,601 patients without known CAD, coronary angiography was performed in 499,015 patients (63.1%) with preprocedural stress testing and 291,586 (36.9%) without. The mean age of this cohort was 61.9 ± 12.5 years, 51.1% of patients were men, 85.6% were of white race, and 71.2% had private health insurance. There were no differences between the 2 groups with regard to age, gender, race, insurance status, or history of diabetes mellitus (Table 1). In 449,579 patients with a history of CAD, coronary angiography was performed in 250,687 (55.8%) patients with preprocedural stress testing and 198,892 (44.2%) without. The mean age of this study cohort was 66.3 ± 11.1 years, nearly 2/3 were men and had private health insurance, and 89.7% were Caucasian. Again, there were no differences between the 2 groups in demographics and other clinical variables.

Of patients without a history of CAD undergoing elective coronary angiography, 32.0% reported no angina (CCS class 0) and only 12.5% reported severe angina (CCS class III or IV). Compared with patients having preprocedural

stress testing, those without stress testing were more frequently angina free (38.5% for no stress test group vs 28.2% for stress test group; standardized difference of 14.8% across the CCS classes; Table 2). In contrast, among patients with a history of CAD undergoing elective coronary angiography, those without preceding stress tests were less likely to be angina free and more likely to have severe angina (CCS class 0: 26.1% for no stress test group vs 29.1% for stress test group and CCS class III or IV: 17.8% for no stress test group vs 13.4% for stress test group; standardized difference of 11.3% across the CCS classes). When we examined the clinical presentation of angina or angina equivalent (typical, atypical, and none), we found a similar pattern (see Table 2).

Among patients without a history of CAD undergoing elective coronary angiography, rates of 3-vessel disease were lower in patients without than in patients with preprocedural stress testing (7.6% for those without vs 9.8% for those with preprocedural stress testing; standardized difference of 10.2%; Table 3). However, there were no differences in rates of proximal LAD (10.9% for no stress test

Table 3
Rates of obstructive coronary artery disease, defined as ≥50% stenosis in an epicardial or left main coronary artery, stratified by history of coronary artery disease

Angiography	Patients Without Prior CAD History		Patients With Prior CAD History	
	Stress Test Prior to Coronary Angiogram (n = 499,015)	No Stress Test Prior to Coronary Angiogram (n = 291,586)	Stress Test Prior to Coronary Angiogram (n = 250,687)	No Stress Test Prior to Coronary Angiogram (n = 198,892)
Any obstructive disease	200,211 (40.1%)	104,238 (35.7%)	203,216 (81.1%)	156,578 (78.7%)
No. of narrowed coronary arteries				
0	298,804 (59.9%)	187,348 (64.3%)*	47,471 (18.9%)	42,314 (21.3%)*
1	93,986 (18.8%)	52,131 (17.9%)*	61,817 (24.7%)	54,016 (27.2%)*
2	57,152 (11.5%)	29,853 (10.2%)*	61,323 (24.5%)	48,308 (24.3%)*
3	49,073 (9.8%)	22,254 (7.6%)*	80,076 (31.9%)	54,254 (27.3%)*
Proximal LAD narrowing	66,786 (13.4%)	31,687 (10.9%)	82,551 (32.9%)	59,885 (30.1%)
Left main narrowing	15,807 (3.2%)	8,070 (2.8%)	27,444 (10.9%)	19,629 (9.9%)

CCS = Canadian Cardiovascular Society; LAD = left anterior descending.
* Denotes clinically meaningful difference with standardized difference >10% within the cohort.

Table 4
Rates of obstructive coronary artery disease, defined as ≥70% stenosis in an epicardial coronary artery or ≥50% stenosis in the left main coronary artery, stratified by history of coronary artery disease

Angiography	Patients Without Prior CAD History		Patients With Prior CAD History	
	Stress Test Prior to Coronary Angiogram (n = 499,015)	No Stress Test Prior to Coronary Angiogram (n = 291,586)	Stress Test Prior to Coronary Angiogram (n = 250,687)	No Stress Test Prior to Coronary Angiogram (n = 198,892)
Any obstructive disease	156,150 (31.3%)	77508 (26.6%)*	180,310 (71.9%)	137,370 (69.1%)
No. of narrowed coronary arteries				
0	342,865 (68.7%)	214078 (73.4%)*	70,377 (28.1%)	61,522 (30.9%)
1	81,119 (16.3%)	42175 (14.5%)*	66,316 (26.5%)	55,938 (28.1%)
2	43,816 (8.8%)	21685 (7.4%)*	53,769 (21.4%)	41,052 (20.6%)
3	31,215 (6.3%)	13648 (4.7%)*	60,225 (24.0%)	40,380 (20.3%)
Proximal LAD narrowing	45,500 (9.1%)	20398 (7.0%)	65,444 (26.1%)	47,220 (23.7%)
Left main narrowing	15,807 (3.2%)	8070 (2.8%)	27,444 (10.9%)	19,629 (9.9%)

CCS = Canadian Cardiovascular Society; LAD = left anterior descending.
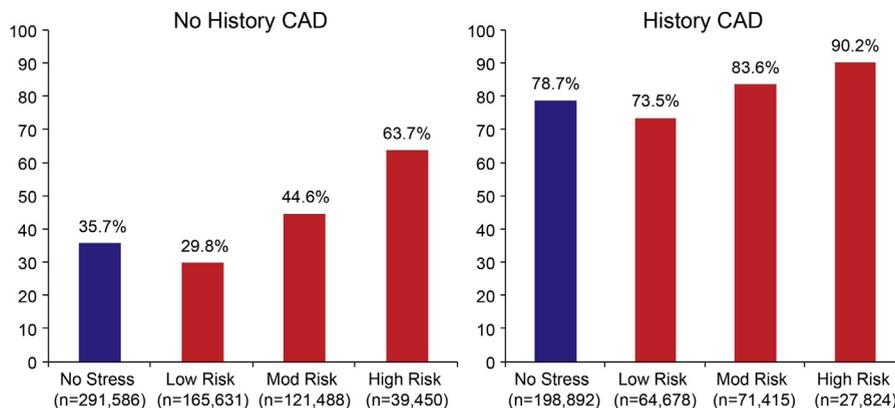* Denotes clinically meaningful difference with standardized difference >10% within the cohort.

Figure 2. Likelihood of obstructive CAD (≥50% stenosis), stratified by severity of ischemia on stress testing. Obstructive CAD was defined as a ≥50% stenosis in an epicardial or left main coronary artery. Mod = moderate.

group vs 13.4% for stress test group; standardized difference of 7.7%) and left main CAD (2.8% for no stress test group vs 3.2% for stress test group; standardized difference of 2.4%) between the 2 groups. In patients with previous CAD,

patients without preprocedural stress testing had lower rates of 3-vessel disease (27.3% for no stress test group vs 31.9% for stress test group; standardized difference of 10.7%) but similar rates of proximal LAD and left main CAD disease
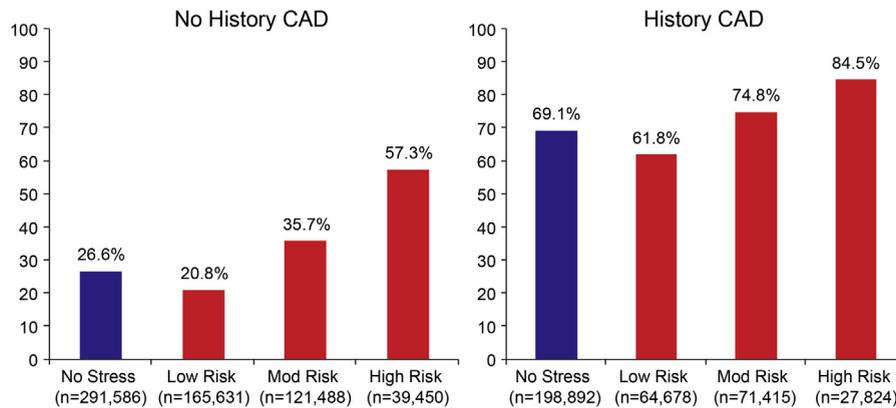
Figure 3. Likelihood of obstructive CAD (≥70% stenosis), stratified by severity of ischemia on stress testing. Obstructive CAD was defined as a ≥70% stenosis in an epicardial or ≥50% stenosis in a left main coronary artery. Mod = moderate.

(see Table 3). These angiographic findings remained similar when we used a more restrictive definition of ≥70% stenosis for an epicardial branch coronary artery (Table 4).

Among patients without a history of CAD, the likelihood of obstructive CAD on coronary angiography in patients without a preprocedural stress test was 35.7%. In contrast, the rate of obstructive CAD was 63.7% (25,124 of 39,450) for patients with a high-risk stress test result, 44.6% (54,178 of 121,488) for those with an intermediate-risk stress test result, and 29.8% (49,438 of 165,631) for those with a low-risk stress test result (Figure 2). Notably, the rate of obstructive CAD for patients with an abnormal (intermediate or high risk) stress test result was 49.3% (79,302 of 160,938) and was significantly higher (p <0.001) than the rate for those without preprocedural stress testing.

Among patients with a history of CAD, the likelihood of obstructive CAD in patients without preprocedural stress testing was 78.7%, whereas the rate of obstructive CAD was higher at 90.2% (25,094 of 27,824) for patients with high-risk stress test results and was 83.6% (59,679 of 71,415) and 73.5% (47,521 of 64,678) for patients with intermediate-risk and low-risk stress test results, respectively (see Figure 2). Among patients with known CAD, the rate of obstructive CAD for patients with an abnormal stress test result (85.4% [84,773 of 99,239]) was again significantly higher than the rate for those without preprocedural stress testing (p <0.001).

Finally, this pattern of a higher likelihood of obstructive CAD when coronary angiography is performed in patients with a high- or intermediate-risk stress test result (compared with no preprocedural stress testing) was similar when the level of stenosis to define obstructive CAD was ≥70% for patients with and without a history of CAD (Figure 3).

Discussion

In this large, contemporary, national sample of patients undergoing elective coronary angiography, we found that a substantial proportion (∼40%) of patients proceeded directly to invasive management without preprocedural stress testing. In patients without a history of CAD, there was no evidence to suggest that clinical judgment led to a greater "diagnostic yield" from angiography, as patients without preprocedural stress testing did not have higher rates of obstructive CAD or higher risk coronary anatomic findings than those with preprocedural stress testing. Among patients with a history of CAD, patients without preprocedural stress testing were more likely to have severe angina pectoris, but rates of class III or IV angina were low, at 17.7%, and the rates of obstructive CAD and high-risk CAD were comparable between the 2 groups. Moreover, the likelihood of obstructive CAD was lower among patients without preprocedural stress testing than those with high-risk or intermediate-risk stress test results. Collectively, our findings suggest that the clinical decision to proceed directly to elective coronary angiography in routine practice may not always be influenced by severe angina symptoms or result in higher detection rates for obstructive CAD.

Our study extends the observations of previous studies that have described rates of preprocedural stress testing before coronary angiography. Lin et al[3] found that nearly 1/2 of all elective PCIs were performed without preprocedural stress testing. However, that study was performed in an administrative Medicare claims database, and the investigators were unable to examine whether patients who proceeded directly to invasive treatment had more severe symptoms (e.g., CCS class III or IV angina) or higher rates of obstructive CAD. In another study of patients within the CathPCI Registry, Patel et al[4] reported that 84% of patients had some form of noninvasive assessment before diagnostic coronary angiography. However, that study was unable to assess the severity of angina or ischemia, as it used a previous version of the CathPCI data collection form that did not contain detailed information on CCS angina class and stress testing results. By leveraging the information on new variables that are now included in version 4 of the CathPCI Registry, our study was able to extend the findings from previous studies by assessing preprocedural angina, frequency of obstructive CAD, and the severity of stress testing results.

Current guidelines recommend risk stratification in elective patients before angiography and PCI[10]—a strategy shown to be cost-effective[11−13] and associated with improved outcomes.[14] Although other considerations may influence the clinical decision to forego a preprocedural stress test, our findings suggest that the decision to proceed

directly to diagnostic coronary angiography in patients with a low pretest probability of obstructive CAD (e.g., lack of severe angina) and without other corroborating evidence of functional ischemia from noninvasive testing may be premature in some patients.

Our study also provides important insights into the patients who were excluded from recent evaluations of the appropriateness of PCI in the United States[1,15,16] In these studies, there was some concern that the exclusion of patients without preprocedural stress tests may have led to an overestimation of the inappropriate PCI rate in nonacute settings, especially if patients undergoing PCI without stress tests were to have more severe angina and CAD than those with stress tests. Our findings do not support this concern and may suggest the contrary—that patients who proceed to invasive management without preprocedural stress testing do not have more severe angina or higher risk coronary anatomy and thus may have PCIs which are even less likely to be beneficial than the patients who were included in the previously published appropriateness assessments.

Finally, we found that the likelihood of finding obstructive CAD in patients with significant ischemia on stress testing was imperfect and was highly influenced by whether patients had a history of CAD. This suggests that a patient's pretest probability for obstructive CAD may limit the predictive value of stress testing in patients without a history of CAD, and future studies may be warranted to further clarify the prognostic utility of stress testing.

Our study should be interpreted in the context of the following potential limitations. First, hospital participation in the CathPCI Registry is voluntary, and our results may not be generalizable to all hospitals that do not participate in the CathPCI Registry. However, our findings were derived from data at 940 hospitals in the United States and, as such, provide the first, large-scale, detailed study examining the characteristics of patients who undergo elective coronary angiography without preprocedural stress testing. Second, the validity of our results relies on the validity of the NCDR data. In a recent report, Messenger et al[7] found that many fields in the NCDR accurately represent the data from the medical chart. However, our findings may be affected if many sites do not routinely submit all their diagnostic cardiac catheterization procedures to the CathPCI Registry or if patients with stress testing at outside hospitals were misclassified as having no previous stress testing. Third, our study did not exclude patients who underwent coronary angiography according to prespecified protocols (airline pilots), because the CathPCI Registry does not collect the data necessary to identify such patients. However, these scenarios should represent a small minority of the examined studies and are unlikely to have affected our findings. Moreover, we were unable to assess other uncommon reasons to proceed directly to coronary angiography, such as new wall motion abnormalities on echocardiography. In addition, it is possible that some patients were misclassified as not having a preprocedural stress test if this information was not available in their medical records. Nonetheless, most institutions do routinely collect information on whether stress testing (yes vs no) was performed before coronary angiography even if the stress test result was not available, so it is unlikely that such misclassification

represented a significant proportion of the patient group without stress tests. Finally, the reasons for foregoing risk stratification with noninvasive stress testing are not collected by the CathPCI Registry. Therefore, we were unable to provide insights as to which patient and physician factors influenced the decision to proceed directly to angiography in the absence of severe angina symptoms.

Disclosures

Supplementary Data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.amjcard.2014.04.047.

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