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

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Abstract

Many patients undergo elective coronary angiography without pre-procedural stress testing which may be suitable if performed in patients with more angina pectoris or more frequently identified obstructive coronary artery disease (CAD). Patients in the NCDR CathPCI Registry® undergoing elective coronary angiography between July 2009 and April 2013 were assessed for differences in angina (Canadian Cardiovascular Society [CCS] class) and severity of obstructive CAD in those with and without pre-procedural stress testing, stratified by prior CAD history. Given the large sample size, differences were considered clinically meaningful if the standardized difference (SD) was >10%. Of 790,601 patients without prior CAD history, 36.9% did not undergo prior stress testing. Compared to patients with prior stress testing, patients without prior 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). Among 449,579 patients with prior CAD history, 44.2% did not undergo prior stress testing. Patients without prior 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 prior stress testing. In conclusion, approximately 40% of patients undergoing elective coronary angiography did not have pre-procedural 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.

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Keywords

Coronary angiography; stress testing; stable angina

INTRODUCTION

The importance of understanding current practice patterns of proceeding directly to coronary angiography without prior stress testing was underscored by a recent report assessing the appropriateness of elective percutaneous coronary interventions (PCIs). In that analysis of National Cardiovascular Data Registry (NCDR) CathPCI Registry® data, 11.6% of non-acute PCIs were deemed inappropriate;^{1,2} however, more than 1 in 5 patients with a non-acute PCI were excluded as they did not have a pre-procedural non-invasive 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 CAD among patients undergoing elective coronary angiography with and without pre-procedural stress testing. We also examined the likelihood of any obstructive CAD in patients without pre-procedural stress testing, as 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 prior 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 more than 1000 U.S. hospitals. Detailed information about patient demographics, clinical features, hospital information, pre-procedural stress test results, angiography 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 between July 2009 and 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 pre-procedural stress testing in non-acute presentations, where pre-procedural 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 non-invasive stress testing, defined as either exercise stress test, stress echocardiogram, stress testing with SPECT MPI, stress testing with CMR, cardiac CTA or coronary calcium scoring. To ensure that the study population did not have another clinical reason to proceed

directly to coronary angiography without prior stress testing, we excluded patients undergoing transplant evaluation (9,682 procedures), those undergoing angiography for a pre-operative evaluation for non-cardiac surgery (131,606 procedures), a diagnosis of cardiomyopathy (138,521 procedures), heart failure exacerbation within the past 2 weeks (247,640 procedures), 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 prior history of CAD and 449,579 had known CAD, which was defined as a history of prior myocardial infarction (MI), coronary artery bypass graft (CABG) 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 prior stress testing. Symptom burden was assessed using the Canadian Cardiovascular Society (CCS) functional class for angina.⁸ Angina free patients are categorized by the CathPCI 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 ≥ 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 pre-test probability for obstructive CAD is known to be higher for patients with a prior history of CAD, we conducted all analyses separately for patients without and with a prior history of known CAD. Baseline demographics and clinical characteristics were compared between patients undergoing elective coronary angiography with and without prior 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 prior 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 pre-procedural stress testing. Finally, we compared the likelihood of any obstructive CAD between patients without pre-procedural stress testing and those with a high-risk, intermediate-risk, and low-risk stress test. The severity of non-invasive imaging 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 pre-procedural stress test whose ischemia severity was not documented (172,446 patients without prior CAD history and 86,770 patients with prior CAD history).

To ensure the robustness of our findings, we conducted a sensitivity analyses by repeating the above analyses using a more restrictive definition of obstructive CAD (a >50% stenosis in the left main or >70% stenosis in a major epicardial coronary artery >2mm), as this is the usual angiographic threshold for consideration of PCI. Missing data rate was less than 1%. All statistical analyses were performed with SAS 9.2 (SAS Institute, Inc, Cary, NC) or R version 2.10.0 (R Foundation for Statistical Computing, Vienna, Austria). This research was supported by the American College of Cardiology Foundation's National Cardiovascular Data Registry (NCDR). The views expressed in this manuscript represent those of the authors, and do not necessarily represent the official views of the NCDR or its associated professional societies identified at www.ncdr.com.

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 SPECT MPI was the most common form of testing (78.0%), followed by stress echocardiogram (11.1%), exercise stress testing (9.3%) and stress CMR (0.7%). In 790,601 patients without known CAD, coronary angiography was performed in 499,015 (63.1%) patients with prior 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 two groups with regards to age, sex, race, insurance status or history of DM (Table 1). In 449,579 patients with a history of CAD, coronary angiography was performed in 250,687 (55.8%) patients with prior stress testing and 198,892 (44.2%) without. The mean age of this study cohort was 66.3 ± 11.1 years, nearly two-thirds were men and had private health insurance, and 89.7% were Caucasian. Again, there were no differences between the two groups in demographics and other clinical variables.

Among 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 pre-procedural 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 testing 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, 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 among patients without pre-procedural stress testing than among patients with (7.6% for those without vs. 9.8% for those with prior 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 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 prior CAD, patients without pre-procedural 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 (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 pre-procedural stress test was 35.7%. In contrast, the rate of obstructive CAD was 63.7% (25,124/39,450) for patients with a high-risk stress test, 44.6% (54,178/121,488) for those with an intermediate-risk stress test, and 29.8% (49,438/165,631) for those with a low-risk stress test (Figure 2). Notably, the rate of obstructive CAD for patients with an abnormal (intermediate or high risk) stress test was 49.3% (79,302/160,938) and was significantly higher ($P<0.001$) than the rate for those without pre-procedural stress testing.

Among patients with a history of CAD, the likelihood of obstructive CAD in patients without pre-procedural stress testing was 78.7%, whereas the rate of obstructive CAD was higher at 90.2% (25,094/27,824) for patients with high-risk stress tests, and was 83.6% (59,679/71,415) and 73.5% (47,521/64,678) for patients with intermediate-risk and low-risk stress tests, respectively (see Figure 2). Among patients with known CAD, the rate of obstructive CAD for patients with an abnormal stress test (85.4% [84,773/99,239]) was again significantly higher than the rate for those without pre-procedural 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 (compared with no prior stress testing) was similar when the level of stenosis to define obstructive CAD was >70% for both patients with and without a prior 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 prior stress testing. Among patients without a history of CAD, there was no evidence to suggest that clinical judgment led to a higher 'diagnostic yield' from angiography, as patients without pre-procedural stress testing did not have higher rates of obstructive CAD, or higher-risk coronary anatomic findings than those with prior stress testing. Among patients with a history of CAD, patients without prior 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 pre-procedural stress testing than those with high-risk or intermediate-risk stress tests. 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 prior studies that have described rates of pre-procedural stress testing prior to coronary angiography. Lin et al. found that nearly half of all elective PCIs were performed without pre-procedural stress testing.³ However, that study was performed in an administrative Medicare claims database and the authors 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. reported that 84% of patients had some form of noninvasive assessment prior to diagnostic coronary angiography.⁴ However, that study was unable to assess the severity of angina or ischemia, as it used a prior 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 prior studies by assessing pre-procedural angina, frequency of obstructive CAD and the severity of stress testing results.

Current guidelines recommend risk stratification in elective patients prior to angiography and PCI¹⁰—a strategy shown to be cost effective¹¹⁻¹³ and associated with improved outcomes.¹⁴ Although other considerations may influence the clinical decision to forego a pre-procedural stress test, our findings suggest that the decision to proceed directly to diagnostic coronary angiography in patients with a low pre-test 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 U.S.^{1,15,16} In these studies, there was some concern that the exclusion of patients without pre-procedural stress tests may have led to an overestimation of the inappropriate PCI rate in non-acute 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 pre-procedural 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 prior history of CAD. This suggests that a patient's pre-test probability for obstructive CAD may limit the predictive value of stress testing in patients without a prior 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 U.S. hospitals and, as such, provide the first large-scale, detailed study examining the characteristics of patients who undergo elective coronary

angiography without pre-procedural stress testing. Second, the validity of our results relies on the validity of the NCDR data. In a recent report, Messenger et al found that many fields in the NCDR accurately represent the data from the medical chart.⁷ 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 prior stress testing. Third, our study did not exclude patients who underwent coronary angiography according to pre-specified protocols (airline pilots) since 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 pre-procedural 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 prior to 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 non-invasive 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.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Study 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.

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% left main coronary artery.

Table 1
Baseline Characteristics, Stratified by Prior History of CAD and Pre-Procedural Stress Testing

<i>Characteristic</i>	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%)

Abbreviations: CAD, coronary artery disease.

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

Table 2
Angina Severity and clinical presentation, Stratified By Prior History of CAD and Pre-Procedural 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)
<i>Anginal Classification with in 2 Weeks (CCS)</i>				
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%)*
<i>CAD Presentation</i>				
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%)*

Abbreviations: CAD, coronary artery disease; CCS, Canadian Cardiovascular Society; LAD, left anterior descending

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

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

<i>Angiography</i>	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%)		

Abbreviations: 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

<i>Angiography</i>	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%)	77,508 (26.6%)*	180,310 (71.9%)	137,370 (69.1%)
No. of narrowed coronary arteries				
0	342,865 (68.7%)	214,078 (73.4%)*	70,377 (28.1%)	61,522 (30.9%)
1	81,119 (16.3%)	42,175 (14.5%)*	66,316 (26.5%)	55,938 (28.1%)
2	43,816 (8.8%)	21,685 (7.4%)*	53,769 (21.4%)	41,052 (20.6%)
3	31,215 (6.3%)	13,648 (4.7%)*	60,225 (24.0%)	40,380 (20.3%)
Proximal LAD Narrowing	45,500 (9.1%)	20,398 (7.0%)	65,444 (26.1%)	47,220 (23.7%)
Left Main Narrowing	15,807 (3.2%)	8,070 (2.8%)	27,444 (10.9%)	19,629 (9.9%)

Abbreviations: CCS, Canadian Cardiovascular Society; LAD, left anterior descending

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