Acta Cardiol Sin 2019;35:111−117
Original Article
doi: 10.6515/ACS.201903_35(2).20181004A

Coronary Artery Disease

The Utilization of Stress Tests Prior to Percutaneous Coronary Intervention for Stable Coronary Artery Disease in Taiwan

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Background: Ischemia shown in non-invasive tests is considered to be a fundamental requirement for treating patients with stable coronary artery disease (CAD) with a percutaneous coronary intervention (PCI). In a nationwide cohort, we investigated the utilization of stress tests, including myocardial perfusion imaging (MPI), treadmill exercise test (TET) and stress echocardiography (SE) prior to elective PCI.

Methods: This retrospective study used the Longitudinal Health Insurance Database 2000 (LHID2000) of the National Health Insurance program in Taiwan. The LHID2000 is comprised of one million randomly sampled beneficiaries. We enrolled patients receiving elective PCI for stable CAD from 2000 to 2013. Stress tests performed within 90 days prior to PCI and patient characteristics correlated with the utilization of stress tests were investigated.

Results: During the investigation period, 3,163 patients received elective PCI for stable CAD and 1,847 (58.4%) patients had at least one stress test within 90 days prior to PCI. Among them, 1,461 (79.1%) had MPI, 1,228 had TET (66.4%) and only 1 had SE (0.05%). Age < 80 years, regional hospital and hyperlipidemia were independently associated with an increased likelihood of receiving stress tests. On the other hand, Charlson-comorbidity index score ≥ 1, prior catheterization and heart failure were independently associated with a decreased likelihood of receiving stress tests.

Conclusions: In the setting of stable CAD, almost 60% of our patients received stress tests within 90 days prior to elective PCI, and MPI was the most commonly used test.

Key Words: Coronary artery disease • Percutaneous coronary intervention • Stress tests

INTRODUCTION

One of the major challenges for the management of stable coronary artery disease (CAD) is selecting appropriate patients for adding percutaneous coronary intervention (PCI) to optimal medical therapy.[1-4] Previous studies had shown that the utilization of stress testing prior to cardiac catheterization and angioplasty were associated with lower overall costs and better outcomes.[5-7] Practice guidelines have suggested that PCI should be performed in patients with stable CAD only for those showing moderate to severe ischemia on non-invasive testing.[8] However, prior work in the United States has shown that most patients with stable CAD did not un-

Received: May 14, 2018 Accepted: October 4, 2018
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dergo stress testing prior to elective PCI.[9]

Myocardial perfusion imaging (MPI), treadmill exercise test (TET) and stress echocardiography (SE) have been the main stress techniques used to assess myocardial ischemia in Taiwanese patients with suspected CAD.[10,11] To understand the appropriateness of PCI performed in patients with stable CAD, we conducted this nationwide cohort study to investigate the utilization of these three stress tests within 90 days prior to elective PCI.

MATERIALS AND METHODS

Data source

This retrospective cohort study used the Longitudinal Health Insurance Database 2000 (LHID2000) of the National Health Insurance (NHI) program in Taiwan. The enrollment rates in the NHI program were 96% of the entire population in 1996 and 99% in 2014 (http://nhird.nhri.org.tw/en/index.html). The LHID2000 is comprised of one million randomly sampled beneficiaries enrolled in the NHI program, which includes all records of these individuals from 1996 to 2013. Disease diagnoses were identified and coded using the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM). This study was approved by the Research Ethics Committee of China Medical University and Hospital in Taiwan (CMUH-104-REC2-115-CR2).

Sampled participants

We identified 8,927 patients in the LHID2000 aged ≥ 20 years undergoing PCI (NHI codes: 33076B, 33077B, 33078B) between January 1, 2000 and December 31, 2013. The date of PCI was assigned as the index date. Patients with a diagnosis of acute myocardial infarction (AMI, ICD-9-CM code 410), unstable angina (ICD-9-CM codes 411.1, 411.81, 411.89) (n = 4,798), those with the history of PCI, coronary artery bypass graft (CABG), valve surgery, acute myocardial infarction (MI) or unstable angina within 1 year prior to the index date (n = 963), and those admitted from the emergency department (n = 3) were excluded. The remaining 3,163 patients were enrolled for investigations of the three main stress tests reimbursed by the NHI program, including MPI (26025B), TET (18015B) and SE (18044B), which were performed within 90 days prior to PCI (Figure 1).

Variables of interest

Information extracted from the claims data included gender, age (< 60, 60-69, 70-79 and ≥ 80 years), geographic region (northern, central, southern, and eastern), and Charlson-comorbidity index (CCI). The CCI is a widely used tool for measuring the severity of comorbidities, and increasing CCI scores have been shown to be associated with an increasing risk of mortality for CAD patients.[12] The components of the CCI include 16 advanced medical conditions (score), including MI (1), congestive heart failure (1), peripheral vascular disease (1), cerebrovascular disease (1), dementia (1), hemiplegia (2), chronic obstructive pulmonary disease (1), connective tissue disease (1), peptic ulcer disease (1), diabetes (1 for uncomplicated, 2 for end organ damage), advanced renal disease (2), leukemia (2), malignant lymphoma (2), solid tumor (2, 6 for metastatic), liver disease (1 for mild, 3 for moderate to severe) and AIDS (6). We categorized CCI scores into 4 levels: 0, 1, 2 and 3 or more. A few comorbidities before the index date were examined for their possible association with having a stress test prior to elective PCI. These included prior coronary angiography (CAG, NHI code: 18020B, 18021B), prior MI (ICD-9-CM code 410), hypertension (ICD-9-CM codes 401-405), diabetes mellitus (ICD-9-CM code 250), heart failure (ICD-9-CM code 428), hyperlipidemia (ICD-9-CM code 272), obesity (ICD-9-CM code 278), severe

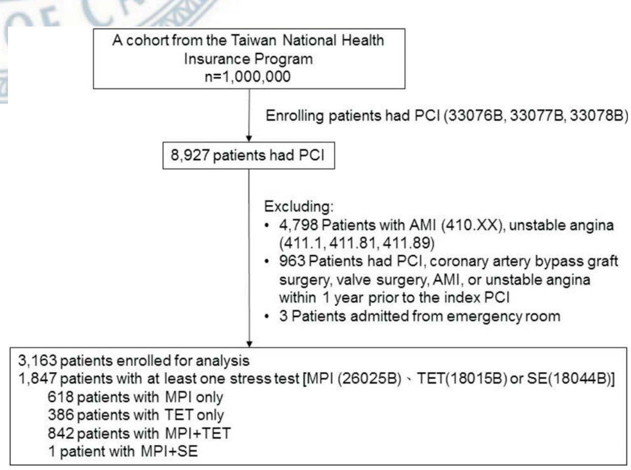

Figure 1. *Flow chart of enrolling patients into the study. AMI, acute myocardial infarction; MPI, myocardial perfusion imaging; PCI, percutaneous coronary intervention; SE, stress echocardiography; TET, treadmill exercise test.*

liver disease (ICD-9-CM code 571), cerebrovascular disease (ICD-9-CM codes 430-438), peripheral vascular disease (ICD-9-CM code 443.9), renal disease (ICD-9-CM codes 580-589) and cancer (ICD-9-CM codes 140-208).

Statistical analysis

The distributions of demographic characteristics, CCI scores and comorbidities were compared between the "prior stress test" and "no stress test" groups. The distributions were examined using the chi-square test. The mean age was measured and tested using the *t* test. Univariate and multivariate logistic regression analyses were used to calculate the odds ratios (ORs) of having a stress test and the corresponding 95% confidence intervals (95% CIs). SAS software (version 9.4; SAS Institute Inc, Cary, NC) was used to analyze data, and the statistical significance level was set at $p < 0.05$.

RESULTS

As shown in Figure 1, 3,163 patients were considered to be eligible after screening for the study criteria and were enrolled for final analysis. Of them, 1,847 (58.4%) received at least one of the three stress tests within 90 days preceding elective PCI. Of the patients with stress testing, 1,461 (79.1%) had MPI (MPI only: 618; MPI+TET: 842; MPI+SE: 1), 1,228 (66.4%) had TET (TET only: 386; MPI+TET: 842), and only one (0.05%) had SE (MPI+SE: 1). None of the remaining 1,316 (41.6%) patients had any stress test prior to PCI.

Of the 3,163 study participants (Table 1), signifi-

Table 1. Characteristics of enrolled patients with and without stress testing prior to elective percutaneous coronary intervention

Characteristics	Prior stress test (n = 1847)	No stress test (n = 1316)	p value
Gender			0.001
Female	514 (27.8)	438 (33.3)	
Male	1333 (72.2)	878 (66.7)	
Age (years), mean (standard deviation)#	65.1 (11.1)	68.8 (11.4)	< 0.001
Age (years), groups			< 0.001
< 60	631 (34.2)	318 (24.2)	
60-69	557 (30.2)	337 (25.6)	
70-79	495 (26.8)	430 (32.8)	
≥ 80	164 (8.88)	231 (17.6)	
CCI score			< 0.001
0	1088 (58.9)	555 (42.2)	
1	365 (19.8)	325 (24.7)	
2	168 (9.10)	158 (12.0)	
3+	226 (12.2)	278 (21.1)	
Geographic region			< 0.001
Northern	959 (51.9)	598 (45.4)	
Central	334 (18.1)	315 (23.9)	
Southern	471 (25.5)	342 (26.0)	
Eastern	83 (4.49)	61 (4.64)	
Health care type			0.14
Tertiary hospital	664 (36.0)	507 (38.5)	
Regional hospital	1183 (64.1)	809 (61.5)	
Prior CAG	144 (7.80)	174 (13.2)	< 0.001
Prior myocardial infarction	283 (15.3)	263 (20.0)	< 0.001
Hypertension	1595 (86.4)	1171 (89.0)	0.03
Diabetes mellitus	608 (32.9)	494 (37.5)	0.01
Heart failure	282 (15.3)	337 (25.6)	< 0.001
Hyperlipidemia	1287 (69.7)	857 (65.1)	0.01
Obesity	64 (3.47)	35 (2.66)	0.20
Severe liver disease	643 (34.8)	413 (31.4)	0.04
Cerebrovascular disease	235 (12.7)	265 (20.1)	< 0.001
Peripheral vascular disease	53 (2.87)	49 (3.72)	0.18
Renal disease	429 (23.2)	392 (29.8)	< 0.001
Cancer	81 (4.39)	66 (5.02)	0.41

Data are presented as the number of subjects in each group, with percentages given in parentheses, or mean with standard deviation given in parentheses. CAG, coronary angiography; CCI, Charlson-comorbidity index.
* Chi-square test and # *t*-test comparing subjects with and without stress test.

cantly more were male (2,211, 69.9%; p = 0.001). The mean age of the patients without stress testing was 3.7 years older than that of the patients with stress testing (68.8 ± 11.4 vs. 65.1 ± 11.1 years, respectively, p < 0.001). Significantly more patients (49.2%) lived in the northern area of Taiwan than central, southern or eastern areas (p < 0.001). In addition, 664 of 1,171 patients (56.7%) from tertiary hospitals had prior stress tests, and 1,183 of 1,992 patients (59.4%) from regional hospitals had stress tests (p = 0.14). More patients with no stress testing prior to PCI had positive CCI scores (p < 0.001), and they were more likely to have prior CAG, prior MI, hypertension, diabetes mellitus, heart failure, cerebrovascular disease and renal disease (all p < 0.05). However, patients with stress testing had a higher frequency of hyperlipidemia and severe liver disease (p < 0.05).

Table 2 shows the crude and adjusted ORs of the demographic characteristics, CCI scores and comorbidities associated with having stress testing prior to elective

Table 2. Odds ratio and 95% confidence interval of characteristics associated with having stress testing prior to elective percutaneous coronary intervention

Variable	Crude		Adjusted[‡]	
	OR	(95% CI)	OR	(95% CI)
Gender (Male)	1.29	(1.11, 1.51)[†]	1.14	(0.97, 1.35)
Age group				
< 60	2.80	(2.20, 3.56)[†]	2.15	(1.66, 2.78)[†]
60-69	2.33	(1.83, 2.96)[†]	1.95	(1.51, 2.51)[†]
70-79	1.62	(1.28, 2.06)[†]	1.48	(1.16, 1.90)[†]
≥ 80	1.00	(Reference)	1.00	(Reference)
CCI score				
0	1.00	(Reference)	1.00	(Reference)
1	0.57	(0.48, 0.69)[†]	0.74	(0.60, 0.92)[†]
2	0.54	(0.43, 0.69)[†]	0.79	(0.60, 1.06)
3+	0.42	(0.34, 0.51)[†]	0.63	(0.47, 0.85)[†]
Geographic region				
Northern	1.18	(0.83, 1.67)	1.13	(0.79, 1.62)
Central	0.78	(0.54, 1.12)	0.83	(0.57, 1.21)
Southern	1.01	(0.71, 1.45)	1.00	(0.69, 1.45)
Eastern	1.00	(Reference)	1.00	(Reference)
Health care type				
Tertiary hospital	1.00	(Reference)	1.00	(Reference)
Regional hospital	1.12	(0.97, 1.29)	1.19	(1.02, 1.39)*
Prior CAG (18020B, 18021B)	0.56	(0.44, 0.70)[†]	0.61	(0.48, 0.77)[†]
Prior myocardial infarction	0.72	(0.60, 0.87)[†]	0.90	(0.74, 1.10)
Hypertension	0.78	(0.63, 0.97)[†]	1.08	(0.85, 1.36)
Diabetes mellitus	0.82	(0.70, 0.95)[#]	0.91	(0.77, 1.07)
Heart failure	0.52	(0.44, 0.63)[†]	0.80	(0.64, 1.00)
Hyperlipidemia	1.23	(1.06, 1.43)[#]	1.20	(1.02, 1.41)*
Obesity	1.31	(0.87, 2.00)	1.07	(0.69, 1.65)
Severe liver disease	1.17	(1.00, 1.36)*	1.14	(0.97, 1.34)
Cerebrovascular disease	0.58	(0.48, 0.70)[†]	0.86	(0.68, 1.09)
Peripheral vascular disease	0.76	(0.52, 1.13)	1.00	(0.66, 1.51)
Renal disease	0.71	(0.61, 0.84)[†]	0.93	(0.77, 1.11)
Cancer	0.87	(0.62, 1.21)	1.03	(0.73, 1.46)

[‡] Adjusted for gender, age, CCI score, Region, prior CAG, prior myocardial infarction, hypertension, DM, heart failure, hyperlipidemia, obesity, severe liver disease, cerebrovascular disease, peripheral vascular disease, renal disease, and cancer.
CAG, coronary angiography; CCI, Charlson-comorbidity index; CI, confidence intervals; DM, diabetes mellitus; OR, odds ratios.
* p < 0.05; [#] p < 0.01; [†] p < 0.001.

PCI. Figure 2 shows the factors predictive of having a stress test. Age < 80 years, regional hospitals and hyperlipidemia were independent predictors of having a stress test after adjusting for confounding factors. On the other hand, patients without prior stress testing were significantly associated with a CCI score ≥ 1, prior CAG and heart failure.

DISCUSSION

In this study, more than a half of the patients with stable CAD received at least one stress test within 90 days prior to elective PCI. Compared to similar investigations in the United States, the utilization rate in the current study was higher than the 29% in the study by Topol et al. in 1995[13] and the 44.5% reported by Lin et al. in 2008.[9] The most likely reason for the higher utilization rate in Taiwan may be related to the insurance reimbursement policy. The NHI administration, Ministry of Health and Welfare, Taiwan announced a new policy for elective PCI in 2008, in that the hospital had to provide evidence of ischemia shown on non-invasive tests to the case review committee to evaluate the appropriateness of PCI. If the case review concluded that the PCI was inappropriate, the reimbursement would be taken back and a penalty might be given. About 40% of the stable CAD patients still received elective PCI without receiving prior stress tests. We assume that many of them underwent invasive CAG and PCI based on the findings of coronary CT angiography.[14] According to the policy of the Taiwan NHI program, PCI is appropriate for stenosis of more than 70% shown on invasive CAG.[15]

An interesting finding of this study was that the utilization rate of MPI was higher than that of TET (79.1% vs. 66.4%). This finding was not consistent with our general impression that TET should be the most commonly used stress test in the assessment of ischemia for patients suspected of having CAD.[16] It should be noted that more than a half of the patients who received PCI during the investigation period were not enrolled in our study based on our exclusion criteria (AMI/unstable angina, PCI/CABG/valve surgery within 1 year of the index PCI, and those admitted from the emergency department). We believe that many stable CAD patients undergoing TET as the stress test prior to elective PCI were excluded based on these exclusion criteria.[17] Another important finding of this study was that SE was rarely used prior to elective PCI for stable CAD.[18] Although a possible explanation might also be related to the strict criteria for enrolling patients, it was obvious that the priority of SE is low for most cardiologists in Taiwan when selecting a stress test to evaluate patients with suspected CAD. Potential reasons might include the complexity of the technique, high operator dependence[19] and the very low insurance reimbursement from the Taiwan NHI program (about 90 US dollars).

MPI has been found to be very useful for identifying CAD patients for appropriate revascularization. A landmark study by Hachamovitch et al. showed that revascularization had an increasing survival benefit over medical therapy when moderate to severe ischemia was present on MPI. In contrast, medical therapy has shown survival advantages over revascularization in the setting of no or mild ischemia.[20] Our recent study further showed that a selective strategy guided by MPI was associated with lower rates of revascularization and MI and better survival in comparison with routine invasive CAG in patients with suspected stable CAD.[21] We believe that these results will further enhance the utilization of MPI in Taiwan as the leading modality of choice prior to elective PCI for stable CAD.

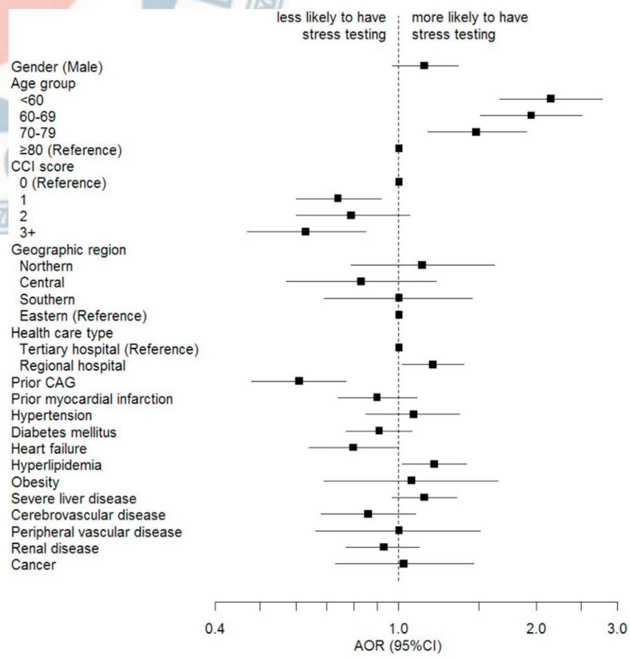

Figure 2. *Factors predictive of having stress testing prior to elective percutaneous coronary intervention.*

We found that certain characteristics of the patients were correlated to having stress testing prior to elective PCI. These findings are similar to previous studies,[9] such as the association of an increased likelihood of stress testing with younger age but decreased likelihood with comorbidities. The reason for a higher frequency of prior stress testing in younger patients may be related to the higher frequency of intolerance to stress testing in older patients. The study of Lin et al. only enrolled patients aged 65 years or older, and that might be one of the reasons contributing to a lower utilization rate of stress tests compared to our study. However, the frequency of prior stress testing was 50% for patients aged 70 years or older and 55% for those aged 60 years or older, both significantly higher than the 44.5% in the study of Lin et al.

In this study, hyperlipidemia was found to be an independent predictor of having a stress test, and this result is different to that in the study by Lin et al.[9] A possible explanation is due to systematic differences in coding for hyperlipidemia between the two databases. Our cohort had a nearly 8-fold higher prevalence of dyslipidemia compared to the prior study (68% vs. 8.5%). For a population undergoing PCI, a prevalence of dyslipidemia less than 10% seems unexpectedly low.[22]

We also compared the utilization of stress testing between tertiary hospitals and regional hospitals. Although there was no significant difference in the frequency of having a stress test between the tertiary and regional hospitals (56.7% vs. 59.4%, $p = 0.14$), regional hospital was found to be an independent predictor (OR, 1.19; 95% CI, 1.02-1.39) after adjusting for confounding factors. A possible reason may be due to the wide availability of nuclear medicine facilities in both tertiary and regional hospitals, but a relative lack of alternative imaging modalities (such as coronary computed tomographic angiography and stress echocardiography) in the regional hospital.

In contrast to patients with a CCI score of 0, those with a CCI score ≥ 1 were associated with a lower likelihood of prior stress testing. The reason for this was likely related to less tolerance to stress testing for patients with multiple comorbidities. In addition, prior CAG was highly related to not having a prior stress test, possibly because of a higher probability of obstructive CAD shown on invasive CAG in this group of patients.[9]

Our study also demonstrated a significant geographical variation in stress testing as seen in previous studies.[23,24] In our data, the northern region of Taiwan was the only area that showed an increased likelihood of having a stress testing prior to PCI, whereas the other three regions showed a decreased likelihood. We hypothesize that this might be related to differences in the intensity of post-procedure payment review for the appropriateness of PCI conducted by the NHI administration.

Some limitations should be considered in our study. First, disease diagnoses in the NHI database used ICD-9-CM codes. Although ICD-9-CM codes are among the most frequently used codes for disease diagnoses in claims databases, such coding does not always precisely fit the clinical condition of interest. Moreover, the NHI database did not contain detailed information such as primary presenting symptoms, family history of CAD, relevant medications and test results. Further investigations are required to confirm our findings.

CONCLUSIONS

In the setting of elective PCI for stable CAD patients in Taiwan, nearly 60% of the patients had non-invasive stress testing within the preceding 90 days. The utilization rate was relatively high and better than in the United States. Age < 80 years, regional hospitals and hyperlipidemia were associated with having stress tests, whereas a CCI score ≥ 1, prior catheterization and heart failure were associated with not having a stress test. Nuclear testing with MPI is currently the leading modality of choice for assessing the presence and degree of ischemia when making decisions regarding elective PCI in patients with suspected CAD.

ACKNOWLEDGEMENT

This study is supported in part by Taiwan Ministry of Health and Welfare Clinical Trial Center (MOHW108-TDU-B-212-113004), China Medical University Hospital, Academia Sinica Taiwan Biobank Stroke Biosignature Project (BM10701010021) and Taiwan Ministry of Science and Technology (107-2314-B-758-001-MY3). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

DECLARATION OF CONFLICT OF INTEREST

All the authors declare no conflict of interest.

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