ORIGINAL ARTICLE

Warranty period of normal stress myocardial perfusion imaging in diabetic patients: A propensity score analysis

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Background. **We evaluated the relationship between diabetes and temporal characteristics of cardiac risk at long-term follow-up in a propensity score-matched cohort of diabetic and non-diabetic patients with normal stress myocardial perfusion single-photon emission computed tomography (MPS).**

Methods and Results. **We studied 828 consecutive patients with suspected or known coronary artery disease and normal perfusion at stress MPS. To account for differences in baseline characteristics between diabetics and non-diabetics, we created a propensity score-matched cohort considering clinical variables and stress type. After matching, clinical characteristics were comparable in 260 diabetic and 260 non-diabetic patients. All patients were followed for at least 1 year (median 53 months). End-point events were cardiac death or nonfatal myocardial infarction. At Cox analysis, diabetes (hazard ratio 3.9, $P < .01$) and post-stress left ventricular ejection fraction (LVEF) ≤45% (hazard ratio 4.1, $P < .01$) were independent predictors of events. At parametric analysis, non-diabetic patients with post-stress LVEF >45% remained at low risk for the entire length of follow-up, while the highest probability of events and the major risk acceleration was observed in patients with diabetes and post-stress LVEF ≤45%.**

Conclusions. **After a normal stress MPS, diabetic patients are at higher risk for cardiac events than non-diabetic subjects also after balancing clinical characteristics and stress type by propensity score analysis. The warranty period of a normal stress MPS varies according to diabetic status and post-stress LVEF. (J Nucl Cardiol 2014;21:50–6.)**

Key Words: Myocardial perfusion imaging • diabetes mellitus • prognosis

INTRODUCTION

Stress myocardial perfusion single-photon emission computed tomography (MPS) has taken a central role in risk stratify patients with suspected or known coronary artery disease (CAD). It has been shown that risk stratification incorporated in a testing strategy reduces the overall cost and enhances the effectiveness of testing.[1,2] Risk stratification by normal stress MPS may identify patients with and without CAD who do not require further intervention. Although the presence of a normal scan should reassure that patients prognosis is excellent, in diabetic patients a normal MPS seems to be less encouraging than in non-diabetic subjects.[3,4] In particular, Giri et al[3] demonstrated that despite the survival during the first 2 years of follow-up was identical in patients with symptoms suggestive of CAD and normal MPS irrespective to diabetic status, the event rates increased after 2 years in diabetics but not in non-diabetics. The duration of the low-risk status after a normal stress MPS depends on several factors, such as clinical characteristics, that may influence the natural progression of CAD.[5] Outcome-based multivariable risk adjustment models can to some extent account for confounding covariates. However, concerns for residual bias may limit interpretation of results.[6] Thus, we sought to evaluate the relationship between diabetes

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Received for publication Jul 5, 2013; final revision accepted Sep 13, 2013.

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1071-3581/$34.00

doi:10.1007/s12350-013-9788-x

and the temporal characteristics of cardiac risk at long-term follow-up in a propensity score-matched cohort of diabetic and non-diabetic patients with normal stress MPS.

MATERIALS AND METHODS

Patients

Between March 2006 and May 2007, 1,792 consecutive patients with suspected or known CAD underwent stress MPS for the assessment of myocardial ischemia at our institution. Patients (n = 284) have been excluded from study enrollment for: (1) recent acute coronary syndrome, stroke, or transient ischemic attack (in the last 3 months); (2) uncompensated congestive heart failure (New York Heart Association class III or IV); (3) recent myocardial revascularization procedures (in the last 3 months); and (4) a concomitant noncardiac illness that would limit follow-up for at least 1 year. Of the 1,508 patients considered for the purpose of the present investigation, 636 patients were excluded because of abnormal stress MPS. Among the 872 patients with normal stress MPS, 44 (5%) were lost at follow-up, leaving 828 patients for the analysis (Figure 1). Of these patients, 402 (48%) had a history of type-2 diabetes (diabetes duration 144 ± 98 months) and 426 did not. To account for differences in baseline characteristics between diabetic and non-diabetic patients, we created a propensity-matched cohort considering the baseline clinical variables. The review committee of our institution approved the study and all patients gave informed consent.

MPS

All patients underwent stress technetium-99m sestamibi gated MPS by physical exercise or dipyridamole stress test, according to the recommendations of the European Association of Nuclear Medicine and European Society of Cardiology.[7] In all patients, beta-blocking medications and calcium antagonists were withheld for 48 hours and long-acting nitrates for 12 hours before testing. For patient undergoing exercise test, symptom-limited treadmill standardized protocols were performed, with monitoring of heart rate and rhythm, blood pressure, and electrocardiography (ECG). Test endpoints were achievement of 85% maximal predicted heart rate, horizontal or downsloping ST-segment depression >2 mm, ST-segment elevation >1 mm, moderate to severe angina, systolic blood pressure decrease >20 mm Hg, blood pressure >230/120 mm Hg, dizziness, or clinically important cardiac arrhythmia. For dipyridamole stress test, patients were instructed not to consume products containing caffeine for 24 hours before the test. Dipyridamole was infused at dose of 0.142 $mg \cdot kg^{-1} \cdot minute^{-1}$ intravenous over 4 minutes. A dose of 100 mg of aminophylline was administered intravenously in the event of chest pain or other symptoms, or after significant ST depression.

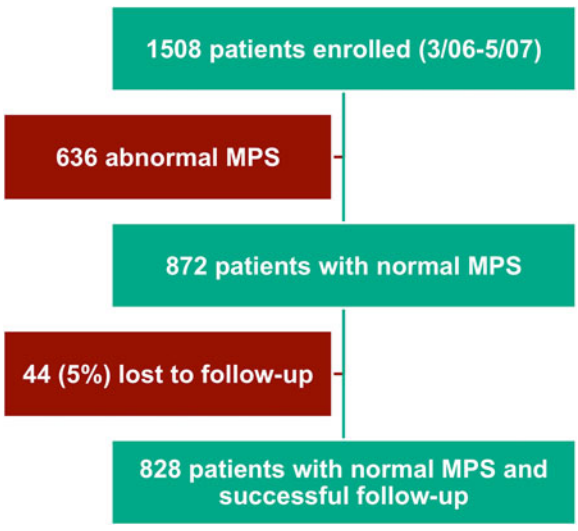

Figure 1. Outline of patient selection. *MPS*, stress myocardial perfusion single-photon emission computed tomography.

At peak exercise, or 4 minutes after completion of dipyridamole infusion, a bolus of 370 MBq of Tc-99m sestamibi was intravenously injected. Patients continued the exercise for additional 60 seconds after tracer injection. For both types of stress, heart rate, blood pressure, and 12-lead ECG data were recorded at rest, at the end of each stress stage, at peak stress and in the delay phases at rest. Maximal degree of ST-segment change at 80 ms after the J-point of the ECG was measured and assessed as horizontal, downsloping or upsloping. For both types of stress, imaging was started 30 minutes after tracer injection using a dual-head rotating gamma camera (E.CAM, Siemens Medical Systems, Hoffman Estates, IL, USA) equipped with a low-energy, high-resolution collimator and connected with a dedicated computer system.[8] No attenuation or scatter correction was used. For gating, a cardiac cycle was divided into eight frames. The R-R interval and heart rate histogram were recorded to monitor arrhythmia. An average R-R interval of ±15% was accepted for gating. Perfusion imaging was reconstructed by summing the gated data at each projection into an ''ungated'' raw data file before low phase prefiltering and ramp filtered back projection. An automated software program (e-soft, 2.5, QGS/QPS, Cedars-Sinai Medical Center, Los Angeles, CA) was used to calculate left ventricular (LV) volumes and ejection fraction (EF) and the scores incorporating both the extent and severity of perfusion defects, using standardized segmentation of 17 myocardial regions.[9] Briefly, this commercial package determines reconstruction limits for the projection dataset, reconstruct the projection images into transaxial images using standard filtered backprojection, and then reorient the transaxial images into short-axis images. LV contours were checked visually and manually adjusted if the computer-generated automatic contours were found to be incorrect. Quantitative defect extent and severity were defined from sex-specific normal limits, and summed stress score was obtained by adding the scores of the 17 segments (0 = normal to 4 = absent perfusion) of the stress images. A post-stress LVEF >45% and a summed stress score <3 were considered normal.[10] The cut-off of 45% was chosen for reduced post-stress LVEF,

according to previous data demonstrating that it was the optimal threshold for the prediction of hard cardiac events.[11]

Follow-Up

Patient follow-up was obtained by use of a questionnaire that was assessed by a phone call to all patients and/or general practitioners or cardiologists and by review of hospital or physicians' records by individuals blinded to the patient's test results. The primary end-point was the occurrence of cardiac death or nonfatal myocardial infarction, whichever occurred first. Cardiac death, defined as due to acute myocardial infarction, ventricular arrhythmias, refractory heart failure, or cardiogenic shock, was confirmed by review of death certificate, hospital chart, or physician's records. Nonfatal myocardial infarction was defined based on the criteria of typical chest pain, elevated cardiac enzyme levels, and typical ECG alterations. The date of the last examination or consultation was used to determine the length of follow-up.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation and categorical data as percentages. Differences between groups were analyzed by t test and χ^2 analysis, as appropriate. A P value $<.05$ was considered statistically significant. To create a matched cohort of diabetic and non-diabetic patients, a propensity score (logit model) was calculated for each individual based on the baseline clinical variables (age, sex, dyslipidemia, smoking, hypertension, family history of CAD, chest pain symptoms, history of myocardial infarction, or revascularization procedures), and stress type. A 1-to-1 matched analysis without replacement was performed on the basis of the estimated propensity score of each patient.[12] To perform the matching and to select the final data set for analysis, the nearest available Mahalanobis metric matching method with caliper size specification ($0.25 \times$ standard deviation of propensity score) was used. After propensity score matching, baseline characteristics were compared. In addition, we assessed the success of propensity score matching using standardized differences.[13] Propensity score analyses were conducted using the Stata module PSMATCH2.[14]

Univariable associations with cardiac events were determined by Cox proportional hazards regression, and event-free survival stratified by diabetes was estimated with Kaplan-Meier survival methods. A multivariable risk model for cardiac events was constructed using a stepwise Cox regression strategy ($P < .05$ for model entry and $P < .10$ for model retention). To form this risk model, patients' baseline clinical variables, diabetes, stress type, and post-stress LVEF ≤45% were considered in the model selection process. The proportional hazard assumption of the Cox model was checked separately for each covariate by graphical and analytical methods before performing the regression analysis. The proportional hazard assumption was not rejected for any covariate included in the Cox model.

A parametric survival model was used to identify how the variables influenced time to event and to estimate risk-adjusted event rates during the follow-up (JMP by SAS Institute Inc., Cary, NC). For these purposes, the estimated probability of event, defined as: 1—estimated event-free survival probability, was calculated. Based on the distribution of survival times in our cohort, a Weibull distribution was selected for parametric survival. In this distribution if the shape parameter >1 the hazard rate increases with time, if <1 the hazard rate decreases with time and if = 1 the hazard rate is constant.

RESULTS

Patient Characteristics Before and After Matching

Baseline patient characteristics compared by diabetic status before and after propensity score matching are shown in Table 1. Before matching, diabetic patients were older and had a higher prevalence of smoking, hypertension, family history of CAD, and previous myocardial infarction. A higher number of diabetic patients were referred for a pharmacologic stress test. After propensity score matching, all characteristics were comparable in 260 diabetic and 260 non-diabetic subjects.

Predictors of Cardiac Events

The Kaplan-Meier analysis showed that the overall event-free survival was lower in diabetic than in non-diabetic patients both before ($\chi^2 = 9.2$; $P < .005$) and after ($\chi^2 = 8.2$; $P < .005$) matching (Figure 2). In the propensity score-matched cohort, during follow-up (median 53 months, inter-quartile range 44-63) 18 events (11 cardiac death and 7 nonfatal myocardial infarction) occurred in diabetic and 6 events (2 cardiac death and 4 nonfatal myocardial infarction) in non-diabetic subjects. Univariable associations of patients' baseline clinical variables, diabetes, stress type, and post-stress LVEF ≤45% with cardiac events were measured (Table 2). As shown, diabetes and post-stress LVEF ≤45% were predictors of events. The annual event rate was 1.7% in diabetic and 0.5% in non-diabetic patients ($P < .005$). At multivariable analysis, independent predictors of cardiac events were diabetes and post-stress LVEF ≤45%.

Change in Risk with Time

Parametric survival analysis including in the model diabetes and post-stress LVEF ≤45% (global $\chi^2 = 12.8$, $P < .001$) showed that the hazard rate increases with time with a shape parameter of 1.2. The highest

Table 1. Baseline patient characteristics by diabetic status before and after propensity score matching

	Before propensity score match			After propensity score match		
	Diabetes (n = 402)	No diabetes (n = 426)	*P* value	Diabetes (n = 260)	No diabetes (n = 260)	*P* value
Age (years)	62 ± 9	59 ± 10	<.001	61 ± 9	61 ± 10	.30
Male gender	214 (53%)	256 (60%)	.05	143 (55%)	144 (55%)	.93
Dyslipidemia	201 (50%)	189 (44%)	.11	132 (51%)	127 (49%)	.71
Smoking	122 (30%)	58 (14%)	<.001	45 (17%)	48 (18%)	.85
Hypertension	300 (75%)	234 (55%)	<.001	175 (67%)	176 (68%)	.88
Family history of CAD	98 (24%)	77 (18%)	<.05	55 (21%)	50 (19%)	.64
Chest pain symptoms	149 (37%)	165 (39%)	.90	95 (36%)	96 (37%)	.60
History of myocardial infarction	63 (16%)	97 (23%)	<.05	52 (20%)	46 (18%)	.64
Prior revascularization	122 (30%)	117 (27%)	.35	78 (30%)	76 (29%)	.88
Dipyridamole stress test	199 (49%)	140 (33%)	<.001	117 (45%)	111 (43%)	.71

Values are expressed as mean value ± standard deviation or as number (percentage) of subjects.
CAD, coronary artery disease.

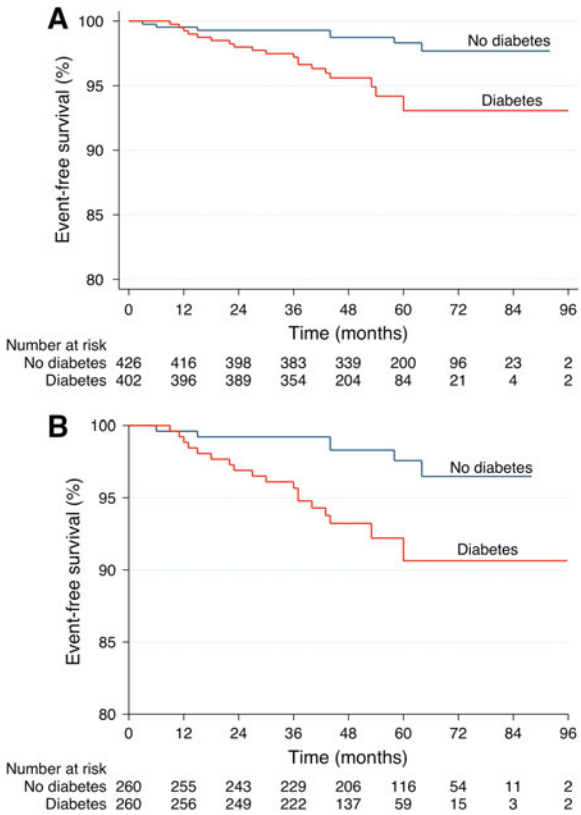

Figure 2. Kaplan-Meier event-free survival curves in patients with and without diabetes before (**A**) and after (**B**) propensity score matching.

probability of cardiac events and the major risk acceleration was observed in diabetic patients with post-stress LVEF ≤45% (Figure 3). Conversely, non-diabetic patients with normal post-stress LVEF had the lowest probability of events. The probability of events was comparable in non-diabetic patients with post-stress LVEF ≤45% and diabetic patients with normal post-stress LVEF. The time to achieve a cumulative cardiac risk level >3% in diabetic and non-diabetic patients according to post-stress LVEF is depicted in Figure 4. Non-diabetic patients with normal post-stress LVEF remained at low risk for the length of follow-up, while in diabetic patients with post-stress LVEF ≤45% the time to achieve a risk level of events >3% was 12 months. Non-diabetic patients with post-LVEF ≤45% and diabetic patients with normal post-stress LVEF achieved a risk >3% after 40 months.

DISCUSSION

The results of this study demonstrate that after a normal stress MPS, diabetic patients are at higher risk for cardiac death and nonfatal myocardial infarction compared to non-diabetic subjects also after balancing clinical characteristics and stress type by propensity score analysis. In addition, our data indicate that the warranty period of a normal stress MPS varies according to diabetic status and post-stress LVEF.

Table 2. Univariable and multivariable Cox analyses for the occurrence of cardiac death or nonfatal myocardial infarction in the propensity score-matched patients (n = 520)

	Univariable analysis				Multivariable analysis			
	Hazard ratio	95% CI	χ^2	*P* value	Hazard ratio	95% CI	χ^2	*P* value
Age	1.0	0.9-1.1	2.8	.09				
Male gender	1.2	0.5-2.7	0.2	.60				
Dyslipidemia	0.7	0.3-1.6	0.5	.50				
Smoking	0.9	0.3-2.8	0.1	.90				
Hypertension	1.8	0.7-4.9	1.6	.20				
Family history of CAD	0.9	0.3-2.6	0.1	.80				
Chest pain symptoms	2.2	0.9-5.4	3.1	.08				
History of myocardial infarction	1.0	0.3-2.8	0.1	.90				
Prior revascularization	1.1	0.5-2.7	0.1	.80				
Diabetes	3.6	1.4-9.1	8.5	<.01	3.9	1.2-12.0	6.9	<.01
Dipyridamole stress test	1.5	0.7-3.4	1.1	.30				
Post-stress LVEF ≤45%	4.3	1.4-13	4.9	<.01	4.1	1.3-12.4	4.8	<.01

CI, confidence interval; *CAD*, coronary artery disease; *LVEF*, left ventricular ejection fraction.

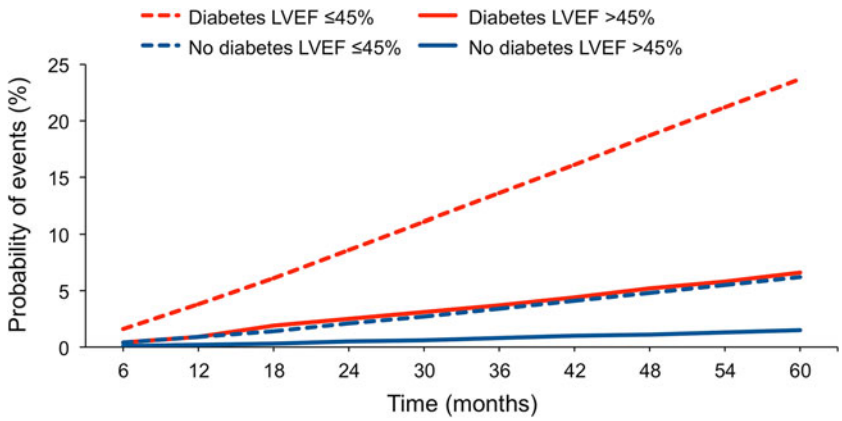

Figure 3. Estimated probability of cardiac death or nonfatal myocardial infarction in a propensity score-matched cohort of diabetic and non-diabetic patients stratified by post-stress left ventricular ejection fraction (LVEF). Diabetic patients with post-stress LVEF ≤45% vs the other three groups: $P < 0.05$. Diabetic patients with post-stress LVEF >45% vs diabetics with post-stress LVEF > 45% and non-diabetics with post-stress LVEF ≤45%: $P < 0.05$.

Stress MPS is a well-established method in the risk stratification of patients with suspected and known CAD.[15] One of the major strengths of stress MPS is the low subsequent cardiac event rate in patients with normal findings.[16] A negative stress MPS reliably predicts an excellent outcome, as less than 1% of patients with a normal study will experience hard cardiac events such as cardiac death or nonfatal myocardial infarction. However, it has been demonstrated that 1% can be shortened or lengthened based on patients' age, sex, presence of coronary risk factors, cardiac symptoms, history of CAD, and the need of pharmacological stress.[4] Thus, it appears that the expected event rate is driven not only by MPS findings but also by the underlying risk factors and comorbidity burden as well as the extent of atherosclerosis.[17]

Diabetes is an important predictor of hard event in patients with suspected and known CAD.[18] It has been also demonstrated that the incremental prognostic value of MPS is greater in diabetic patients than in those without.[18,19] However, a normal stress MPS seems to be less reassuring in diabetic patients than in non-diabetic

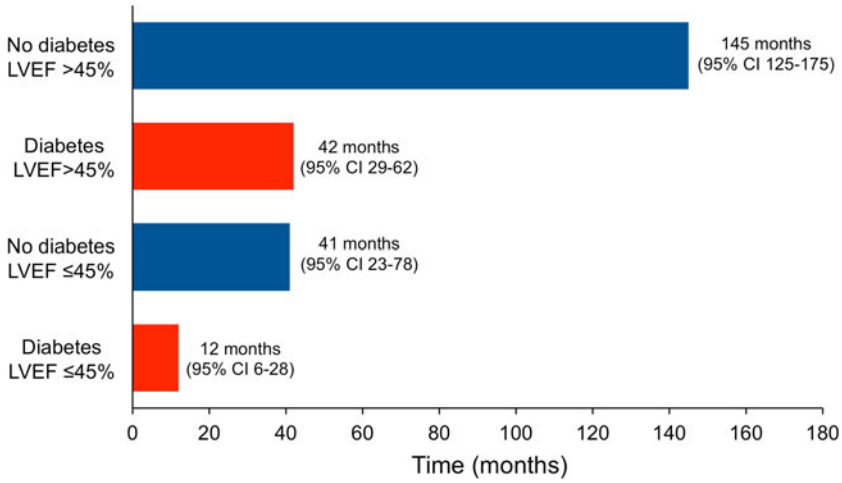

Figure 4. Estimated time (mean with 95% confidence intervals, CI) from stress myocardial perfusion single-photon emission computed tomography to reach a defined level of risk for cardiac death or nonfatal myocardial infarction in a propensity score-matched cohort of diabetic and non-diabetic patients stratified by post-stress left ventricular ejection fraction (LVEF).

subjects.[3,4] Several potential confounding, such as concomitant cardiovascular risk factors, may affect the results previously reported. To overcome this potential bias, we used a propensity score-matched analysis of a large cohort of diabetic and non-diabetic patients with normal stress MPS findings. After matching for the baseline clinical variables and stress type, we found a higher annual event rate in diabetic patients as compared to non-diabetics. These data are in agreement with those of a previous unmatched study demonstrating a difference in mortality between diabetic and non-diabetic patients with normal stress MPS, with a very low rate of events in patients without diabetes.[18]

Observable factors such as the degree of underlying LV dysfunction, has been associated to a higher annual event rate in the setting of normal stress MPS findings in patients with suspected or known CAD.[20] In particular, combining perfusion and functional data, patients with normal perfusion and LV function had a higher annualized event rate as compared to those with discordant perfusion and LV function.[20] Accordingly, from our results it emerged that a post-stress LVEF $\leq$45% in patients with normal stress MPS is an important predictor of cardiac event at long-term follow-up. The highest probability of cardiac death or nonfatal myocardial infarction and the major risk acceleration was observed in patients with diabetes and abnormal post-stress LVEF. Also in patients without diabetes, post-stress LVEF $\leq$45% was associated to a higher probability of events as compared to patients with normal post-stress LVEF. However, the probability of events was comparable in patients without diabetes and abnormal post-stress LVEF and in those with diabetes and normal post-stress LVEF. These findings further support the view of diabetes as CAD equivalent also in the setting of normal myocardial perfusion.

A significant change in risk may occur over time after normal MPS as a function of the clinical and historical factors of the patients. Evidence suggests that repeat testing <2% years without clinical symptoms occur can be inappropriate in the presence of normal MPS.[4] Giri et al[3] found that the survival during the first 2 years of follow-up was identical in patients with normal MPS results, irrespective of their diabetic status. However, after 2 years the event rate increased in diabetics but not in non-diabetics, with an apparent more rapid progression of the disease in the presence of diabetes. Our propensity score analysis demonstrates the more rapid progression of disease, accelerating over time, in diabetic patients than in non-diabetics also after reducing potential bias due to differences in baseline clinical characteristics. The results of the present study also suggest that the warranty period for a normal stress MPS varies according to patient clinical characteristics and LV function. Therefore, these variables should be considered in establishing the time at which repeat testing might be appropriate. Recently, Simonsen et al[21] evaluated long-term temporal risk variations in patients with suspected or known CAD and suggested a warranty period of 5 years following a normal MPS. However, these authors did not stratify according to LVEF.[21] From our data, it emerged that the warranty period of a normal stress MPS is lower in diabetic compared to non-diabetic patients after reducing potential bias by propensity score analysis. Patients with diabetes and abnormal post-stress LVEF showed the poorest outcome and the time to

achieve the cardiac risk level >3% was less than 12 months. Conversely, patients without diabetes and with normal post-stress LVEF remained at low risk during follow-up. Interestingly, patients without diabetes and abnormal post-stress LVEF and those with diabetes and normal post-stress LVEF achieved a risk >3% after 40 months.

This study has some limitations. The relatively small number of events during the follow-up may explain the lack of prognostic significance of traditional risk factors. Moreover, grouping of patients by diabetes and post-stress LVEF ends up with small event rate in each of the groups. Another limitation of this study is the lack of hemoglobin A_{1c} levels, which was not available in all patients due to the retrospective study design.

CONCLUSION

After a normal stress MPS, diabetic patients are at higher risk for cardiac events than non-diabetic subjects also after balancing clinical characteristics and stress type by propensity score analysis. The warranty period of a normal stress MPS varies according to diabetic status and post-stress LVEF and diabetic patients with diabetes and abnormal post-stress LVEF show the poorest outcome.

Conflict of interest

The authors have indicated that they have no financial conflict of interest.

References

1. Shaw LJ, Iskandrian AE. Prognostic value of gated myocardial perfusion SPECT. J Nucl Cardiol 2004;11:171-85.
2. Shaw LJ, Hage FG, Berman DS, Hachamovitch R, Iskandrian A. Prognosis in the era of comparative effectiveness research: Where is nuclear cardiology now and where should it be? J Nucl Cardiol 2012;19:1026-43.
3. Giri S, Shaw LJ, Murthy DR, Travin MI, Miller DD, Hachamovitch R, et al. Impact of diabetes on the risk stratification using stress single-photon emission computed tomography myocardial perfusion imaging in patients with symptoms suggestive of coronary artery disease. Circulation 2002;105:32-40.
4. Hachamovitch R, Hayes S, Friedman JD, Cohen I, Shaw LJ, Germano G, et al. Determinants of risk and its temporal variation in patients with normal stress myocardial perfusion scans: What is the warranty period of a normal scan? J Am Coll Cardiol 2003;41:1329-40.
5. Schinkel AFL, Boiten HJ, van der Sijde JN, Ruitinga PR, Sijbrands EJG, Valkema R, et al. 15-Year outcome after normal exercise 99mTc-sestamibi myocardial perfusion imaging: What is the duration of low risk after a normal scan? J Nucl Cardiol 2012;19:901-6.
6. Rubin DB. Use propensity score to help design observational studies: Application to the tobacco litigation. Health Serv Outcomes Res Methodol 2001;2:169-88.
7. Hesse B, Tägil K, Cuocolo A, Anagnostopoulos C, Bardiés M, Bax J, et al. EANM/ESC procedural guidelines for myocardial perfusion imaging in nuclear cardiology. Eur J Nucl Med Mol Imaging 2005;32:855-97.
8. Acampa W, Petretta M, Evangelista L, Daniele S, Xhoxhi E, De Rimini ML, et al. Myocardial perfusion imaging and risk classification for coronary heart disease in diabetic patients. The IDIS study: A prospective, multicentre trial. Eur J Nucl Med Mol Imaging 2012;39:387-95.
9. Germano G, Kavanagh PB, Waechter P, Areeda J, Van Kriekinge S, Sharir T, et al. A new algorithm for the quantitation of myocardial perfusion SPECT. I: Technical principles and reproducibility. J Nucl Med 2000;41:712-9.
10. Acampa W, Petretta M, Daniele S, Del Prete G, Assante R, Zampella E, et al. Incremental prognostic value of stress myocardial perfusion imaging in asymptomatic diabetic patients. Atherosclerosis 2013;227:307-12.
11. Sharir T, Germano G, Kavanagh PB, Lai S, Cohen I, Lewin HC, et al. Incremental prognostic value of post-stress left ventricular ejection fraction and volume by gated myocardial perfusion single photon emission computed tomography. Circulation 1999;100:1035-42.
12. Heinze G, Jüni P. An overview of the objectives of and the approaches to propensity score analyses. Eur Heart J 2011;32:1704-8.
13. Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. Stat Med 2009;28:3083-107.
14. Leuven E, Sianesi B. PSMATCH2: Stata module to perform full Mahalanobis and propensity score matching, common support graphing, and covariate imbalance testing. Statistical Software Components S432001. Chestnut Hill: Boston College, Department of Economics; 2003 (revised 19 July 2012).
15. Carryer DJ, Askew JW, Hodge DO, Miller TD, Gibbons RJ. The timing and impact of follow-up studies after normal stress single-photon emission computed tomography sestamibi studies. Circ Cardiovasc Imaging 2010;3:520-6.
16. Ghatak A, Padala S, Katten DM, Polk DM, Heller GV. Risk stratification among diabetic patients undergoing stress myocardial perfusion imaging. J Nucl Cardiol 2013;20:529-38.
17. Shaw LJ, Bugiardini R, Merz CN. Women and ischemic heart disease: Evolving knowledge. J Am Coll Cardiol 2009;54:1561-75.
18. Berman DS, Kang X, Hayes SW, Friedman JD, Cohen I, Abidov A, et al. Adenosine myocardial perfusion single-photon emission computed tomography in women compared with men. Impact of diabetes mellitus on incremental prognostic value and effect on patient management. J Am Coll Cardiol 2003;41:1125-33.
19. Kang X, Berman DS, Lewin HC, Cohen I, Friedman JD, Germano G, et al. Incremental prognostic value of myocardial perfusion single photon emission computed tomography in patients with diabetes. Am Heart J 1999;138:1025-32.
20. Navare SM, Katten D, Johnson LL, Mather JF, Fowler MS, Ahlberg AW, et al. Risk stratification with electrocardiographic-gated dobutamine stress technetium-99m sestamibi single-photon emission tomographic imaging. Value of heart rate response and assessment of left ventricular function. J Am Coll Cardiol 2006;47:781-8.
21. Simonsen JA, Gerke O, Rask CK, Tamadoni M, Thomassen A, Hess S, et al. Prognosis in patients with suspected or known ischemic heart disease and normal myocardial perfusion: Long-term outcome and temporal risk variations. J Nucl Cardiol 2013;20:347-57.