In-hospital management of elderly patients undergoing myocardial perfusion scintigraphy

M. Štalc[1] MD, PhD,
N. Jerman[2],
M. Trampuš[2] MD,
M. Dolenc Novak[1] MD, Msc,
B. Gužič Salobir[1] MD, PhD

1. Department for Nuclear Medicine, University Medical Centre, Ljubljana, Slovenia
2. Faculty of Medicine, University of Ljubljana, Slovenia

Keywords: Coronary angiography
- Elderly patients
- Hospitalization
- Ischemic heart disease
- Myocardial perfusion imaging

Corresponding author:
Monika Štalc MD, PhD
Department for Nuclear Medicine,
University Medical Centre,
Ljubljana, Zaloška 7, SI-1000
Ljubljana, Slovenia
Tel.: +386-1-522-8259
monika.stalc@gmail.com

Received:
1 December 2019
Accepted revised:
6 February 2020

Abstract

Objective: To investigate the impact of myocardial perfusion scintigraphy results on the decision for invasive coronary angiography in elderly patients (≥75 years) with suspected coronary artery disease hospitalized in a single tertiary medical center. **Subjects and Methods:** In the retrospective study, data of 276 (136 elderly) consecutive hospitalized patients referred to myocardial perfusion imaging were analyzed. The clinical characteristics, myocardial perfusion scintigraphy results, invasive coronary angiography and revascularization rates and in-hospital adverse events were identified by manually reviewing the patients' records. **Results:** Ischemia was found in 40.2% of patients. There was no significant difference in the proportion of ischemia between elderly and younger patients (38.2% vs. 42.1%, P=0.508). Invasive coronary angiography was performed in 64.0% of patients with ischemia and in 6.8% of patients with normal myocardial perfusion imaging (P<0.001). The referral rate for invasive coronary angiography was not different between elderly and younger patients with ischemia (63.5% vs. 64.4%, P=0.848). Ischemia on myocardial perfusion imaging was the most predictive variable for a referral to invasive coronary angiography (odds ratio 31.8, 95 % confidence interval 14.6–69.5, P<0.001). There was no significant difference between the younger and elderly patients in revascularization rate and adverse events until discharge (39% vs. 40%, P=0.99 and 7.1% vs. 8.8%, P=0.6, respectively). **Conclusion:** Ischemia on myocardial perfusion scintigraphy is a powerful predictor for in-hospital invasive coronary angiography independent of the patient's age. Elderly patients with ischemia received invasive coronary angiography equally as their younger counterparts and have similar rates of adverse events until discharge.

Hell J Nucl Med 2020; 23(1): 6-11 *Epub ahead of print: 31 March 2020* *Published online: 30 April 2020*

Introduction

The clinical diagnosis of coronary artery disease (CAD) is more difficult in the elderly due to atypical symptoms, higher prevalence of co-morbidities and limited exercise capacity and is linked to a greater need for hospital admission [1, 2]. Testing for the presence of ischemia in patients with advanced age requires careful consideration of diagnostic utility as well as patient preferences and treatment goals.

Myocardial perfusion imaging (MPI) is an established non-invasive modality in the elderly for the detection of CAD and determining prognosis [3-5]. Myocardial perfusion imaging also plays an important role in selecting patients for invasive coronary angiography (ICA) and revascularization [6, 7]. Several studies have demonstrated that outpatients with normal MPI studies have an excellent prognosis and do not need further invasive testing [6, 8, 9]. Similar results were found for patients with chest pain referred to emergency departments or chest pain clinics [10, 11].

Patients with abnormal stress MPI are at higher risk for future cardiac events and therefore benefit more from ICA and potential revascularization [12, 13]. The benefit is even greater in older compared to younger patients [13]. Despite this fact, ICA following abnormal MPI has been shown to occur less often for elderly patients in ambulatory settings [3, 14, 15]. To date data is scarce from trials about referral rates to ICA following abnormal MPI among hospitalized elderly patients. Currently, most clinicians attempt to extrapolate findings from younger patients, applying them with some modifications to elderly patients. Since the hospitalized elderly population differs from the younger population, it is useful to study the role of a non-invasive method such as MPI in the everyday clinical practice. This study aimed to evaluate how the MPI results influence referral rates for in-hospital ICA in hospitalized elderly patients.

Subjects and Methods

Patient population

This was a retrospective study with a population taken from a single tertiary medical center. Data was analyzed from consecutive hospitalized patients presenting with chest pain and/or heart failure in the emergency department and who were admitted to MPI during the same hospitalization between June 2014 and June 2017. Patients were categorized into "elderly" (≥75 years) and "younger" (<75 years) groups. The clinical characteristics at admission to the hospital (patients' demographics, medical history, cardiovascular risk factors, clinical examination and electrocardiogram results (ECG), MPI results, ICA rates, data about revascularization procedures and in-hospital adverse events were identified by manually reviewing the patients' records.

Hypertension was defined as blood pressure of 140/90 mmHg or higher and/or by use of antihypertensive medications. Dyslipidemia was defined as total cholesterol >5mmol/L or low-density lipoprotein >3mmol/L and/or by use of hypolipemic drugs. Diabetes mellitus was defined with the need for insulin or oral hypoglycemic agents. A participant who smoked or stopped smoking in the past 12 months was considered as a smoker. History of myocardial infarction, percutaneous coronary intervention or coronary artery bypass grafting was considered as known CAD. The type of chest pain was classified according to the European society of cardiology guidelines [16]. Chronic kidney disease was defined as creatinine level ≥100μmol/L. The number of concomitant diseases was recorded from discharge documentation. The presence of leg edema with lung crackles or diagnosis of pulmonary edema at admission to the hospital were defined as heart failure. Twelve-lead ECG was classified as normal or abnormal depending on the assessment of rhythm, conduction and the absence or presence of ST segment and T wave changes or q waves.

This study was approved by the Slovenian ethics committee.

Myocardial perfusion scintigraphy

All patients were assigned to a 2-day stress/rest protocol. They underwent either bicycle exercise stress (Schiller ER-G911 S plus) or vasodilator stress (regadenoson 400ug or dipyridamole 0.56mg/kg). An hour following intravenous injection of technetium-99m tetrofosmin 600MBq (Myoview, GE Healthcare) we imaged the patients on GE Millennium MG (GE medical systems) or on Cardius X-ACT (Digirad). We did stress protocols, image acquisition, and reconstruction according to the European Association of Nuclear Medicine guidelines [17].

We performed ECG-gated single photon emission tomography (SPET) using eight frames per cardiac cycle and analyzed the images for the same functional variables with quantification packages recommended by its vendor for each camera: Emory Cardiac Tool Box (ECTB; Emory University Hospital. Atlanta, Georgia, USA) for GE Millennium MG and Quantitative Gated SPECT algorithm (QGS; Cedars-Sinai Medical Center. Los Angeles, California, USA) for Cardius X-ACT.

Two experienced nuclear cardiologists from our team interpreted SPET images during daily clinical reading sessions. They interpreted the scan by visual analysis of slices and polar maps. They reviewed stress and rest tomographic views side by side. Stress-induced reduction in myocardial tracer uptake that partially or completely resolved at rest in two or more contiguous segments or slices was defined as ischemia. When it was not possible to define the reversible changes due to the artifacts, we stated that the investigation was not diagnostic.

Myocardial perfusion imaging report was sent to the hospital database and it was available to the treating physician on the same day. The report did not include any suggestions about a referral to ICA.

Coronary angiography, revascularization and in-hospital adverse events

The selection of patients for ICA was the decision of the treating physicians. All procedures were performed after MPI during the same hospitalization. All patients underwent conventional coronary angiography in the catheter laboratory of the department of cardiology, using standard equipment with either femoral or radial access.

We collected the information on results of ICA and revascularization rates. We also identified clinically relevant adverse events until discharge from the hospital (major bleeding, acute renal failure, allergic reactions, stroke, acute coronary syndrome, arrhythmia, coronary artery complications, and death) manually reviewing the patients' records.

Statistical analysis

The Kolmogorov-Smirnov test was used to assess normal distribution. Normally distributed continuous variables are described as mean values (SD) and compared with t-test. Non-normally distributed continuous variables are described as medians and interquartile range and compared with Mann-Whitney U test. Categorical variables are presented as absolute numbers (percentage). Categorical variables (proportions) were compared with the χ^2 test. Univariable logistic regression was applied to determine the correlation between some variables and the decision for referral to ICA. Variables that were significantly related to the referral to ICA were then included in the model of multivariate logistic regression.

Levels of $P<0.05$ were considered statistically significant.

Results

Study population and myocardial perfusion scintigraphy

We studied 276 hospitalized patients (136 elderly) undergoing MPI. We present clinical characteristics of patients at the admission to the hospital in Table 1. The majority of patients (88%) underwent pharmacological stress testing that was more prevalent in the elderly (Table 2). There were no sig-

Table 1. *Clinical characteristics of patients at admission to the hospital.*

	All n=276	Younger n=140	Elderly n=136	P value†
Age (years) ‡	72.7±11.9	63.9±10.2	81.8±4.5	NA
Female gender, n (%)	137 (49.6%)	57 (40.7%)	80 (58.8%)	0.003
Cardiac risk factors				
Arterial hypertension, n (%)	233 (84.4%)	111 (79.2%)	122 (89.7%)	0.017
Diabetes mellitus, n (%)	91 (32.9%)	51 (36.4%)	40 (29.4%)	0.215
Hyperlipidemia, n (%)	203 (73.6%)	109 (77.8%)	94 (69.1%)	0.100
Smoking, n (%)	34 (12.3%)	28 (20.0%)	6 (4.5%)	<0.001
Known CAD, n (%)	91 (33.0%)	50 (35.7%)	41 (30.1%)	0.325
Myocardial infarction, n (%)	66 (23.9%)	37 (26.4%)	29 (21.3%)	0.320
Revascularization, n (%)	68 (24.6%)	39 (27.8%)	29 (21.3%)	0.208
Chronic kidney disease, n (%)	92 (33.3%)	41 (29.3%)	51(37.5%)	0.148
Chest pain				
Typical, n (%)	81 (29.3%)	40 (28.6%)	41 (30.1%)	0.774
Atypical, n (%)	115 (41.7%)	59 (42.1%)	56 (41.2%)	0.569
Without, n (%)	80 (29.0%)	41 (29.3%)	39 (28.7%)	0.911
Heart failure, n (%)	152 (55.1%)	64 (45.7%)	88 (64.7%)	0.001
Normal resting ECG, n (%)	55 (20.9%)	23 (16.4%)	32 (23.5%)	0.477
Concomitant diseases (n) ‡	1.7±1.6	1.5±1.5	2.0±1.5	< 0.001

† *The χ^2-test, t-test.* ‡ *Mean ± SD. CAD, coronary artery disease; ECG, electrocardiogram.*

Table 2. *The stress myocardial perfusion imaging data.*

	All n=276	Younger n=140	Elderly n=136	P value†
Pharmacological stress test, n (%)	244 (88.4%)	115 (82.1%)	129 (94.9%)	<0.001
Regadenoson, n	221	105	116	0.712
Dipyridamole, n	23	10	13	0.712
Ischemia, n (%)	111 (40.2%)	59 (42.1%)	52 (38.2%)	0.508

† *The χ^2-test.*

nificant complications reported during either pharmacological or exercise stress testing. Ischemia was found in 111 patients (40.2%). There was no significant difference in the proportion of ischemia between elderly and younger patients (Table 2). Only 4 (1.5 %) scintigrams were non-diagnostic.

The ejection fraction of the left ventricle was obtained in 238 (86.2%) patients. The mean value was 55%±15%. There were no significant differences between the elderly and younger in the ejection fraction of the left ventricle (elderly 54%±26%, younger 54%±20%, P=0.906). Resting ejection fraction of the left ventricle 40% or less was present in 46 (23 elderly and 23 younger) patients.

Referral for coronary angiography after myocardial perfusion scintigraphy

The result of MPI had a significant influence on the decision for ICA. ICA was performed in 71 (64.0%) patients with ischemia and 11 (6.8%) patients with normal MPI (P<0.001). Figure 1 shows the referral rate for ICA in younger and elderly patients with and without ischemia on MPI. There were no statistically significant differences in the proportion of elderly and younger with ischemia who underwent ICA (P=0.848).

We applied univariable logistic regression to selected variables (age above 75 years, gender, known CAD, chronic kidney disease, presence of chest pain, abnormal ECG at the admission and ischemia on MPI) to determine which were significantly associated with proceeding to ICA. The following were revealed as independent predictors for the referral to ICA: gender, ischemia on MPI, known CAD and abnormal ECG at the admission, which were then tested in multivariate analysis. In the multivariate analysis, ischemia on MPI, gender and abnormal ECG remained the significant predictive factors (Table 3).

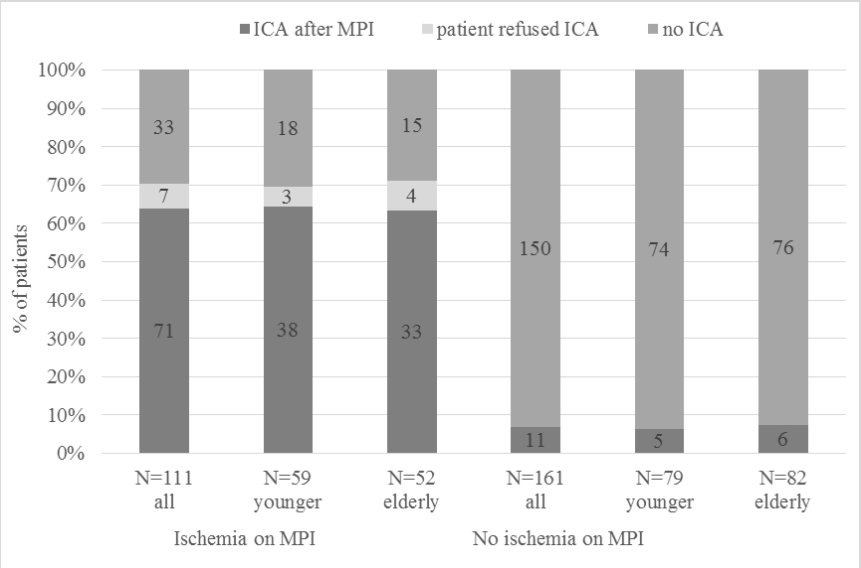

Figure 1. The referral rate for ICA in "all", "younger" and "elderly" patients with and without ischemia on MPI. There were no statistically significant differences in the proportion of elderly and younger with ischemia who underwent ICA (P=0.848).

Table 3. *Univariable and multivariable predictors of referral to invasive coronary angiography.*

	Univariate analysis OR (95% CI)	Multivariate analysis OR (95% CI)
Age >75 years	0.94 (0.57-1.56), P=0.83	/
Male gender	2.63 (1.55-4.45), P=0.0003	2.03 (1.01-4.09), P=0.046
Known CAD	1.9 (1.11-3.19), P= 0.019	0.6 (0.3-1.3), P=0.189
Chronic kidney disease	1.18 (0.70-2.02), P=0.52	/
Presence of chest pain	1.07 (0.61-1.87), P=0.82	/
Abnormal ECG	3.75 (1.6-8.7), P=0.002	2.9 (1.0-8.1), P=0.043
Ischemia on MPI	28.1 (13.8-57.4), P<0.001	31.8 (14.6-69.5), P<0.001

CAD, coronary artery disease; CI, confidence interval; ECG, electrocardiography; MPI, myocardial perfusion imaging; OR, odds ratio.

Coronary angiography results, revascularization and in-hospital adverse events

Nine (12.7%) patients with ischemia and 10 patients (90.9%) without ischemia on MPI had normal ICA.

Twenty nine (40.8%) patients were revascularized during the index hospitalization. There was no significant difference between the younger and elderly patients in whom MPI showed ischemia in revascularization rate (39% vs. 40%, P=0.99).

In-hospital adverse events were detected in 22 (8.0%) patients. There were no differences in the proportions of elderly and younger with adverse events (7.1% vs. 8.8%, P=0.6). Among patients referred to ICA, adverse events occurred in six elderly and five younger patients (18% vs. 13%, P=0.50): three major bleedings, two acute coronary syndromes, two arrhythmias, one allergic reaction, one stroke, one dissection and one perforation of the coronary artery.

Discussion

The role of MPI in hospitalized patients has not been extensively studied yet, and literature data is scarce on hospitalized elderly patients undergoing MPI. With the aging of the population, the proportion of hospitalized elderly patients who need diagnostic procedures for ischemic heart disease is increasing [18]. In our study, almost half of the subjects were over 75 years of age. In previously published studies involving predominantly outpatients, the proportion of elderly people was lower (from 3.9% to 41%) [3, 19]. Like in other studies, we also showed that the elderly and the younger participants differed significantly in some clinical characteristics [20]. Among the elderly, there were more women, more non-smokers, more patients with arterial hypertension, and more patients with heart failure. Since the mean value of ejection fraction was in the normal range in both groups, the reason for the higher prevalence of heart failure in elderly could be heart failure with a preserved ejection fraction that is more prevalent in elderly [21].

Similar to the other studies [22-24], elderly patients in our study were less capable of physical exercise and underwent pharmacological stress testing more often than younger (95% vs. 82%). More comorbidities in our elderly patients could contribute to this finding. Compared with studies that

include elderly outpatients, the proportion of pharmacological stress testing in our hospitalized elderly patients was higher [7, 25]. This might be because the hospitalized patients more often presented with decompensated heart failure, changes in ECG and elevated troponin levels, which are all contraindications for the physical exercise test.

We found ischemia in 40% of the patients, with no significant difference among the younger and elderly patients. This is similar to the results of Miller et al (2007), who found ischemia in 47% of their patients [6]. Some other studies report lower percentages of ischemia, from 7% to 32%, which might be due to the populations consisting of low-risk outpatients, younger patients, or patients without previously known CAD [3, 19, 26].

A number of studies have shown that MPI plays an important role in selecting patients for ICA and subsequent revascularization [6, 27]. Also, in our study ischemia on MPI turned out in multivariate analysis as the most important predicting factor for a referral to ICA. Some clinical variables like patient's age, known CAD, presence of chest pain and chronic kidney disease did not significantly influence the decision for ICA. Of all the patients with ischemia, 70% were scheduled for ICA by their treating physicians. Finally, 64% of patients with ischemia underwent the procedure. Seven patients refused the procedure, with no difference among the younger and elderly patients. As far as we found, only one study included exclusively hospitalized patients (mean age of 57). The rate of referral to ICA in that study was similar to our study, around 60% [26]. In studies that included predominantly outpatients, the decision to proceed with ICA was lower (12%-36%) [27]. Even with ischemia on MPI, the elderly were less likely to be referred to the ICA [14, 19]. Contrary to the literature, we found no significant difference in the percentage of referrals to ICA between the groups of the elderly and the younger with diagnosed ischemia on MPI [14, 28, 29]. There may be several reasons for these differences. In elderly hospitalized patients, who are at a higher risk than their ambulatory counterparts, the physicians are more likely to decide for ICA to confirm the diagnosis of CAD, offer the best treatment, and to discharge the patient as soon as possible. Almost 40% of our patients referred to ICA underwent a revascularization procedure without differences in the proportion of revascularization between elderly and younger groups. Technological improvements in ICA and revascularization techniques with consequently less serious complications among elderly encourage the current doctors to refer elderly patients to ICA. This is also confirmed by our study since the proportion of complications until discharge did not differ between younger and elderly groups.

The choice for ICA and revascularization could also be influenced by the number of comorbidities and/or renal function. Our younger and elderly patients did not differ in the proportion of chronic kidney disease. Although elderly patients had statistically significantly more concomitant diseases than younger patients, the number of comorbidities was still low. It is possible that hospitalized fragile elderly patients were not even referred for MPI because their physicians classified them as too risky for MPI and/or ICA. Such a decision-making process seems reasonable, as the diagnostic procedure with no influence on further treatment strategy is neither cost effective nor professionally justified. Finally, greater differences between older and younger patients may be found similar to Zeltser et al. (2017) if the age limit for the elder's age was raised to 80 or more years [19].

In our study, only 6.8% of patients with normal scans were referred to ICA. No differences were found between younger and elderly patients. Han et al. (2011) reported that 15% of hospitalized patients with normal MPI were referred to the ICA [26]. As 92% of patients had normal scans in that hospital, the direct comparison with our study is not objective. The referral rates for ICA in patients with normal MPI from other studies are low (1%-6%) [6, 30]. In our study only one patient with normal MPI had the revascularization procedure, and no one with normal MPI died during the index hospitalization. In order to determine the prognostic significance of MPI in elderly hospitalized patients, longer follow-up periods would be required. Although this was not the goal of our research, it would be worthwhile to define it in further research.

The present study had several limitations. The study was retrospective and taken from one center. Decisions for referrals to MPI were made individually by the treating physicians. We did not collect the selection criteria data for MPI. Because of the small number of patients, we did not separately analyze the subgroups of the elderly patients (e.g., 75-85 years and >85 years). This would have contributed to a clearer interpretation of the role of MPI in the very elderly patients and highlights the need for further research in this field. Biological age (or fragility) is even more crucial for the ICA referral decision than chronological age. Since fragile patients represent a big portion of the elderly group, clarification of the role of MPI in them would be very important for future clinical work. We also planned to collect data about the presence of dementia, cancer, immobility or living in a nursing home. Unfortunately, these data points were not available in the documentation for most patients.

Based on the results of our study, we can conclude that MPI significantly impacts the decision to perform ICA in hospitalized patients irrespective of the age. We found that some other important clinical characteristics such as renal function, known CAD, and presence of chest pain were not associated significantly with proceeding to ICA. Contrary to the literature, we found that the elderly patients and younger patients referred for the MPI are managed equally. As the population of hospitalized elderly is very heterogeneous, further research is still warranted in the subgroups of hospitalized elderly patients.

Bibliography

1. Makaryus AN, Diamond JA. Nuclear stress testing in elderly patients: a review of its use in the assessment of cardiac risk, particularly in patients undergoing a preoperative risk assessment. *Drugs Aging* 2007; 24: 467-79.
2. Dai X, Busby-Whitehead J, Forman DE, Alexander KP. Stable ischemic heart disease in older adults. *J Geriatr Cardiol* 2016; 13: 109-14.
3. Hachamovitch R, Kang X, Amanullah AM et al. Prognostic Implications of Myocardial Perfusion Single-Photon Emission Computed Tomography in the Elderly. *Circulation* 2009; 120: 2197-206.
4. Katsikis A, Theodorakos A, Manira V et al. Long-term prognostic implications of myocardial perfusion imaging in octogenarians: an all-comer, cohort study. *Eur J Nucl Med Mol Imaging* 2017; 44: 1547-58.

5. Nudi F, Biondi-Zoccai G, Schillaci O et al. Prognostic accuracy of myocardial perfusion imaging in octogenarians. *J Nucl Cardiol* 2018; 25: 1342-9.
6. Miller TD, Hodge DO, Milavetz JJ, Gibbons RJ. A normal stress SPECT scan is an effective gatekeeper for coronary angiography. *J Nucl Cardiol* 2007; 14: 187-93.
7. Lin GA, Dudley RA, Lucas FL et al. Frequency of Stress Testing to Document Ischemia Prior to Elective Percutaneous Coronary Intervention. *JAMA* 2008; 300: 1765-73.
8. Hachamovitch R, Rozanski A, Shaw LJ et al. Impact of ischaemia and scar on the therapeutic benefit derived from myocardial revascularization vs. medical therapy among patients undergoing stress-rest myocardial perfusion scintigraphy. *Eur Heart J* 2011; 32: 1012-24.
9. Doukky R, Frogge N, Balakrishnan G et al. The prognostic value of cardiac SPECT performed at the primary care physician's office. *J Nucl Cardiol* 2013; 20: 519-28.
10. Better N, Karthikeyan G, Vitola J et al. Performance of rest myocardial perfusion imaging in the management of acute chest pain in the emergency room in developing nations (PREMIER trial). *J Nucl Cardiol* 2012; 19: 1146-53.
11. Cremer PC, Khalaf S, Agarwal S et al. Myocardial perfusion imaging in emergency department patients with negative cardiac biomarkers: yield for detecting ischemia, short-term events, and impact of downstream revascularization on mortality. *Circ Cardiovasc Imaging* 2014; 7: 912-9.
12. Hachamovitch R, Hayes SW, Friedman JD et al. Comparison of the short-term survival benefit associated with revascularization compared with medical therapy in patients with no prior coronary artery disease undergoing stress myocardial perfusion single photon emission computed tomography. *Circulation* 2003; 107: 2900-7.
13. Shaw LJ, Berman DS, Maron DJ et al. COURAGE Investigators. Optimal medical therapy with or without percutaneous coronary intervention to reduce ischemic burden: results from the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial nuclear substudy. *Circulation* 2008; 117: 1283-91.
14. Lauer MS, Pashkow FJ, Snader CE et al. Age and referral to coronary angiography after an abnormal treadmill thallium test. *Am Heart J* 1997; 133: 139-46.
15. Nair SU, Ahlberg AW, Mathur S et al. The clinical value of single photon emission computed tomography myocardial perfusion imaging in cardiac risk stratification of very elderly patients (≥80 years) with suspected coronary artery disease. *J Nucl Cardiol* 2012; 9: 244-55.
16. Task Force Members, Montalescot G, Sechtem U et al. 2013 ESC guidelines on the management of stable coronary artery disease: the Task Foce on the management of stable coronary artery disease of the European Society of Cardiology. *Eur Heart J* 2013; 34: 2949-3003.
17. Verberne HJ, Acampa W, Anagnostopoulos C et al. EANM procedural guidelines for radionuclide myocardial perfusion imaging with SPECT and SPECT/CT: 2015 revision. *Eur J Nucl Med Mol Imaging* 2015; 42: 1929-40.
18. Madhavan MV, Gersh BJ, Alexander KP et al. Coronary Artery Disease in Patients ≥80 Years of Age. *J Am Coll Cardiol* 2018; 71: 2015-40.
19. Zeltser R, Tortez LM, Druz RS et al. Downstream resource utilization following SPECT: Impact of age and gender. *J Nucl Cardiol* 2017; 24: 1657-61.
20. Zafrir N, Mats I, Solodky A et al. Characteristics and outcome of octogenarian population referred for myocardial perfusion imaging: comparison with non-octogenarian population with reference to gender. *Clin Cardiol* 2006; 29: 117-20.
21. Bhatia RS, Tu JV, Lee DS et al. Outcome of Heart Failure with Preserved Ejection Fraction in a Population-Based Study. *N Engl J Med* 2006; 355: 260-9.
22. Schinkel AF, Elhendy A, Biagini E et al. Prognostic stratification using dobutamine stress ^{99m}Tc-tetrofosmin myocardial perfusion SPECT in elderly patients unable to perform exercise testing. *J Nucl Med* 2005; 46: 12-8.
23. Yao Z, Zhu H, Li W et al. Adenosine triphosphate stress myocardial perfusion imaging for risk stratification of patients aged 70 years and older with suspected coronary artery disease. *J Nucl Cardiol* 2017; 24: 429-33.
24. Roest S, Boiten HJ, van Domburg RT et al. Prediction of 14-year cardiovascular outcomes by dobutamine stress ^{99m}Tc-tetrofosmin myocar-dial perfusion SPECT in elderly patients unable to perform exercise testing. *J Nucl Cardiol* 2018; 25: 63-71.
25. Lima RSL, De Lorenzo A, Pantoja MR, Siqueira A. Incremental prognostic value of myocardial perfusion 99m-technetium-sestamibi SPECT in the elderly. *Int J Cardiol* 2004; 93: 137-43.
26. Han PP, Tian YQ, Fang W et al. Impact of myocardial perfusion imaging on in-hospital coronary angiography and revascularization of patients with suspected coronary artery disease. *Chin Med J (Engl)*. 2011; 124: 1603-9.
27. Nallamothu N, Pancholy SB, Lee KR et al. Impact on exercise single-photon emission computed tomographic thallium imaging on patient management and outcome. *J Nucl Cardiol* 1995; 2: 334-8.
28. Martin AC, Dumas F, Spaulding C, Manzo-Silberman S. Management and decision-making process leading to coronary angiography and revascularization in octogenarians with coronary artery disease: Insights from a large single-center registry. *Geriatr Gerontol Int* 2015; 15: 544-52.
29. Cockburn J, Hildick-Smith D, Trivedi U, de Belder A. Coronary revascularisation in the elderly. *Heart* 2017; 103: 316-24.
30. Hachamovitch R, Nutter B, Hlatky MA et al. Patient Management After Noninvasive Cardiac Imaging. *J Am Coll Cardiol* 2012; 59: 462-74.