

How to cite this article:

Ahmadi Esmaeilabadi E, Hashem A, Namiranian N, Jelodari MA, Razavi-Ratki SK. Pulmonary lymphangitic carcinomatosis as a rare occurrence in prostate cancer: Myocardial perfusion SPECT findings in patients with metabolic syndrome and cardiac autonomic neuropathy. Iran J Nucl Med. doi: 10.22034/irjnm.2026.130633.1782

Myocardial perfusion SPECT findings in patients with metabolic syndrome and cardiac autonomic neuropathy

Elaheh Ahmadi Esmaeilabadi¹, Aref Hashem², Nasim Namiranian³, Mohammad Ali Jelodari¹, Seid Kazem Razavi-Ratki¹

¹PET-CT Department, Shahid Sadoughi Hospital, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

²Department of Anesthesiology, Faculty of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

³Diabetes Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

Corresponding Author:

Dr. Seyed Kazem Razavi-Ratki

Address: PET-CT Department, Shahid Sadoughi Hospital, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

Email: razavi822@gmail.com

Running title: MPI in metabolic syndrome and cardiac autonomic neuropathy

Article History:

Received: 29 June 2026

Revised: 04 September 2026

Accepted: 05 September 2026

Published Online: 04 October 2026

ABSTRACT

Introduction: Cardiac autonomic neuropathy (CAN) is a common complication of diabetes and metabolic syndrome (MetS) resulting from damage to the autonomic nerves that regulate heart rate and vascular tone. In the literature, CAN has been associated with an increased risk of silent myocardial ischemia and myocardial infarction. MetS is itself an established cardiovascular risk factor. Because all patient in this study had both MetS and confirmed CAN, the study describes myocardial perfusion imaging (MPI) findings within this specific population rather than comparing patients with and without CAN. This study aimed to describe the prevalence of myocardial ischemia and its association with transient ischemic dilation (TID), increased right ventricular (RV) uptake, and increased lung uptake on single-photon emission computed tomography (SPECT) MPI in patients with MetS and CAN.

Methods: This cross-sectional, descriptive-analytical study included patients with MetS and confirmed cardiac autonomic neuropathy (borderline or definite CAN) who underwent MPI at the

How to cite this article:

Ahmadi Esmailabadi E, Hashem A, Namiranian N, Jelodari MA, Razavi-Ratki SK. Pulmonary lymphangitic carcinomatosis as a rare occurrence in prostate cancer: Myocardial perfusion SPECT findings in patients with metabolic syndrome and cardiac autonomic neuropathy. Iran J Nucl Med. doi: 10.22034/irjnm.2026.130633.1782

Nuclear Medicine Center of Shahid Sadoughi Hospital, Yazd, Iran, during 2019. Patients whose records were inaccessible or incomplete were excluded. MPI was performed using a 2-day rest/stress protocol with a low-energy high-resolution (LEHR) collimator (140 keV, 20% window); stress was induced by exercise or dipyridamole according to the patient's clinical condition, and [^{99m}Tc]Tc-MIBI (22-25 mCi) was administered for each study, with images acquired on a 64×64 matrix and ECG-gated SPECT acquisition. MetS was defined as three or more of: blood pressure $\geq 130/85$ mmHg, fasting glucose ≥ 100 mg/dL, triglycerides ≥ 150 mg/dL, HDL-cholesterol < 50 mg/dL (women) or < 40 mg/dL (men), or waist circumference > 88 cm (women) or > 102 cm (men). CAN was assessed with three tests - resting heart rate, the 30:15 heart-rate ratio on standing, and the orthostatic blood-pressure change - each scored 0 or 1 (total score 0-3), classifying patients as no neuropathy (0), borderline CAN (1), or definite CAN (2-3); only patients with borderline or definite CAN were eligible. Demographic data and MPI findings (ischemia, TID, RV uptake, lung uptake) were extracted from clinical records using a standardized checklist and analyzed in SPSS (v.21) with descriptive statistics and chi-square tests; $p < 0.05$ was considered significant.

Results: A total of 268 patients with MetS and CAN were evaluated (mean age 58.11 ± 11.68 years, range 27-84); 83 (31%) were male and 185 (69%) were female. Myocardial ischemia was present in 97 patients (36.2%), TID in 21 (7.8%), increased RV uptake in 20 (7.5%), and increased lung uptake in 11 (4.1%). TID and increased RV uptake were both significantly more frequent among patients with ischemia than among those without (TID: 15/97, 15.5% vs. 6/171, 3.5%, $p = 0.001$; RV uptake: 15/97, 15.5% vs. 5/171, 2.9%, $p = 0.001$), while increased lung uptake did not differ significantly (7/97, 7.2% vs. 4/171, 2.3%; $p = 0.053$). Ischemia prevalence did not differ by sex ($p = 0.173$).

Conclusion: In this selected cohort of patients already diagnosed with both MetS and CAN, myocardial perfusion abnormalities - most notably ischemia, TID, and increased RV uptake - were frequent and tended to co-occur. Because the study lacked a comparison group without CAN, these findings describe the pattern of MPI abnormalities in this population rather than establish that CAN increases ischemic risk. Prospective, controlled studies with confounder adjustment and outcome data are needed before MPI screening can be recommended for this population.

Keywords: Cardiac autonomic neuropathy; Metabolic syndrome; Myocardial perfusion imaging; Myocardial ischemia

INTRODUCTION

Ischemic heart disease is the leading cause of morbidity and mortality worldwide. Myocardial ischemia occurs when the oxygen supply to the heart is insufficient to meet its metabolic demands, resulting in cardiac dysfunction, arrhythmias, myocardial infarction, and even sudden cardiac death. Its clinical manifestations vary and primarily arise from impaired coronary blood flow due to atherosclerotic plaque formation, thrombosis, or excessive vasoconstriction and vasospasm in both epicardial and microvascular coronary arteries. Gender-related differences also contribute to the development and presentation of ischemic heart disease, partly influenced by variations in estrogen levels [1].

The cluster of metabolic abnormalities now known as MetS was first described in the 1920s by Kylin, who characterized it as the simultaneous presence of hypertension, hyperglycemia, and gout. Over time this concept has evolved, and "metabolic syndrome" is now the most widely

How to cite this article:

Ahmadi Esmailabadi E, Hashem A, Namiranian N, Jelodari MA, Razavi-Ratki SK. Pulmonary lymphangitic carcinomatosis as a rare occurrence in prostate cancer: Myocardial perfusion SPECT findings in patients with metabolic syndrome and cardiac autonomic neuropathy. Iran J Nucl Med. doi: 10.22034/irjnm.2026.130633.1782

accepted descriptor for this constellation of interrelated metabolic risk factors, which are strongly associated with cardiovascular disease and are powerful predictors of future diabetes [2].

CAN is a serious, often underdiagnosed complication of diabetes, with prevalence estimates ranging from about 2.5% in low-risk populations to nearly 90% among individuals with long-standing type 1 diabetes. CAN arises from damage to the autonomic nerve fibers innervating the heart and blood vessels, impairing regulation of heart rate and vascular tone. Its clinical spectrum ranges from orthostatic hypotension to myocardial infarction, reflecting involvement of multiple organ systems [3-6].

Several studies have reported that MetS is independently associated with silent coronary artery disease in patients with diabetes, and that CAN is associated with an increased risk of silent myocardial ischemia or infarction [7]. However, most of this evidence comes from studies comparing patients with and without CAN; less is known about the pattern of MPI findings in patients who already carry both diagnoses.

SPECT is a widely used nuclear imaging modality that produces a three-dimensional representation of the distribution of a radioactive tracer taken up by specific tissues, allowing assessment of tissue perfusion and functional activity rather than structural anatomy alone [8].

SPECT-based MPI is widely used to assess patients with known or suspected coronary artery disease. Since its introduction in the 1970s, SPECT camera technology has advanced considerably, including solid-state detectors and collimator designs optimized for cardiac imaging [9].

Although the individual associations of CAN and MetS with myocardial ischemia have each been studied, there are few reports describing MPI findings specifically within patients who already have both conditions. The objective of this study was therefore to describe MPI findings - the prevalence of myocardial ischemia and its association with TID, RV uptake, and lung uptake - in patients with MetS and confirmed CAN referred to the Nuclear Medicine Center of Shahid Sadoughi Hospital, Yazd. As all included patients had both MetS and CAN and no comparison group without CAN was available, the study is descriptive of MPI patterns in this population; it was not designed to test whether CAN increases ischemic risk, and the results should be interpreted accordingly.

METHODS

This cross-sectional, descriptive-analytical study was conducted at the Nuclear Medicine Center of Shahid Sadoughi Hospital, Yazd, Iran, during 2019. Patients with MetS according to the criteria below, who also had confirmed CAN (borderline or definite) and had undergone MPI at the same center, were identified from clinical records for inclusion. Patients whose records were inaccessible or incomplete were excluded, yielding 268 patients for the final analysis. An earlier draft of this manuscript referred to approximately 550 patients screened prior to inclusion; this figure was a drafting error. There was no larger separate screening pool: the study cohort comprised the 268 patients with confirmed MetS and CAN identified from clinical records, and this cohort should be regarded as a selected, single-arm sample from routine referrals rather than a consecutive series drawn from an unselected screening population.

MPI acquisition protocol

Myocardial perfusion imaging was performed using a 2-day protocol, with separate imaging sessions for the rest and stress studies. All images were acquired using a gamma camera with a low-energy high-resolution (LEHR) collimator. The energy window was centered at 140 keV for

How to cite this article:

Ahmadi Esmailabadi E, Hashem A, Namiranian N, Jelodari MA, Razavi-Ratki SK. Pulmonary lymphangitic carcinomatosis as a rare occurrence in prostate cancer: Myocardial perfusion SPECT findings in patients with metabolic syndrome and cardiac autonomic neuropathy. Iran J Nucl Med. doi: 10.22034/irjnm.2026.130633.1782

[^{99m}Tc]Tc-MIBI, with a 20% energy window. For the stress study, pharmacological stress with dipyridamole or physical stress with exercise testing was selected according to the patient's clinical condition and exercise capacity; all participants underwent both rest and stress myocardial perfusion imaging. Approximately 22-25 mCi (814-925 MBq) of [^{99m}Tc]Tc-MIBI was administered for each study, and images were acquired using a 64 × 64 matrix. Attenuation correction was performed using the gamma-camera system's built-in processing algorithm, and ECG-gated SPECT acquisition was performed for each study.

MetS was defined as the presence of at least three of the following criteria, based on the harmonized definition of the metabolic syndrome [2]: systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg; fasting blood glucose ≥100 mg/dL; triglyceride level ≥150 mg/dL; HDL-cholesterol <50 mg/dL in women or <40 mg/dL in men; or waist circumference >88 cm in women or >102 cm in men.

CAN was evaluated after instructing participants to avoid strenuous activity and rest supine for at least 10 minutes, during which electrocardiography and blood pressure were recorded from standard bipolar limb leads. Three standard tests were used: resting heart rate (mean over 5 minutes; >100 beats/min considered abnormal), the heart-rate response to standing (30:15 ratio - the ratio of the R-R interval at the 30th beat to that at the 15th beat after standing), and orthostatic blood-pressure change (a fall of >20 mmHg systolic or >10 mmHg diastolic within 2 minutes of standing considered abnormal). Each test was scored 0 (normal) or 1 (abnormal); with three binary tests, the total score ranges from 0 to 3. Patients were classified as having no neuropathy (score 0), borderline CAN (score 1), or definite CAN (score 2-3). Only patients classified as borderline or definite CAN met the eligibility criteria for this study; a breakdown of the number of included patients in each of these two categories was not available in the source data and is noted as a limitation.

Myocardial ischemia, TID, increased RV uptake, and increased lung uptake were each recorded as present or absent, as documented in the original clinical MPI report for each patient; a standardized quantitative scoring method (e.g., summed stress/rest/difference scores) and explicit numeric thresholds for TID, lung uptake, and RV uptake were not available in the source dataset. All SPECT images were reviewed by a single experienced nuclear medicine physician with expertise in myocardial perfusion imaging, blinded to participants' clinical and laboratory data, including metabolic syndrome status, to minimize assessment bias; interpretation followed standard myocardial perfusion criteria. As images were evaluated by a single reader, interobserver agreement was not applicable.

Demographic characteristics and MPI findings were collected using a standardized checklist. Data were analyzed using SPSS software (version 21). Descriptive statistics and chi-square tests were applied, with $p < 0.05$ considered statistically significant; effect sizes (e.g., odds ratios) and confidence intervals were not computed, and multivariable analysis adjusting for cardiovascular confounders was not performed, as individual-level confounder data (diabetes status and duration, HbA1c, hypertension, dyslipidemia, smoking, obesity, known coronary artery disease, prior infarction, medication use including beta-blockers, and renal function) were not available in the source dataset. These are addressed further in the Limitations section.

Ethical considerations

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was

How to cite this article:

Ahmadi Esmailabadi E, Hashem A, Namiranian N, Jelodari MA, Razavi-Ratki SK. Pulmonary lymphangitic carcinomatosis as a rare occurrence in prostate cancer: Myocardial perfusion SPECT findings in patients with metabolic syndrome and cardiac autonomic neuropathy. Iran J Nucl Med. doi: 10.22034/irjnm.2026.130633.1782

approved by the Ethics Committee of Shahid Sadoughi University of Medical Sciences (Project identification code: IR.SSU.MEDICINE.REC.1399.034). Patient confidentiality was maintained throughout, and no additional cost was imposed on participants.

RESULTS

A total of 268 patients with MetS and CAN were evaluated, with a mean age of 58.11 ± 11.68 years (range 27-84), including 83 males (31%) and 185 females (69%) (Table 1). MPI revealed myocardial ischemia in 97 patients (36.2%), TID in 21 patients (7.8%), increased RV uptake in 20 patients (7.5%), and increased lung uptake in 11 patients (4.1%) (Table 1).

Ischemia prevalence did not differ significantly by sex: among patients with ischemia, 35 were male and 62 were female, and although ischemia was numerically more frequent in women, this difference was not statistically significant ($p=0.173$).

Table 2 compares MPI secondary findings between patients with and without myocardial ischemia. TID was present in 15 of 97 patients with ischemia (15.5%) versus 6 of 171 patients without ischemia (3.5%); this association was statistically significant ($p=0.001$). Increased RV uptake was present in 15 of 97 patients with ischemia (15.5%) versus 5 of 171 patients without ischemia (2.9%); this association was also significant ($p=0.001$). Increased lung uptake was present in 7 of 97 patients with ischemia (7.2%) versus 4 of 171 patients without ischemia (2.3%); this difference did not reach statistical significance ($p=0.053$).

Among the 21 patients with TID, increased RV uptake was present in 8 (38.1%), compared with 4.9% of patients without TID - a statistically significant association ($p=0.001$). Increased lung uptake was likewise present in 8 of the 21 patients with TID (38.1%), a significant association with TID ($p=0.001$).

Because all patients in this cohort had both MetS and CAN, these associations describe how ischemia, TID, RV uptake, and lung uptake relate to one another within the same MPI examination in this population; they do not, by themselves, establish a relationship between CAN and myocardial ischemia, since no patients without CAN were available for comparison. Representative MPI examples of combined TID and ischemia are shown in Figures 1 and 2.

DISCUSSION

In this cohort of 268 patients who already had both MetS and confirmed CAN, myocardial ischemia detected by MPI in more than one-third of patients (36.2%), and both TID and increased RV uptake were significantly more common among ischemic compared to non-ischemic patients whereas, increased lung uptake showed a similar but non-significant trend. Ischemia prevalence did not differ between men and women. Because every patient in the study had CAN, these findings characterize the frequency and co-occurrence of MPI abnormalities in this specific high-risk population rather than demonstrate that CAN itself increases the risk of ischemia; that question would require a comparison group without CAN, which was not available in this study.

CAN is a recognized complication of MetS and diabetes and has been associated in prior work with increased morbidity and mortality related to silent myocardial ischemia, arrhythmias, and sudden cardiac death. Because patients with CAN are often asymptomatic, autonomic dysfunction can impair cardiovascular regulation without producing clinical warning signs. Reported CAN prevalence varies widely (roughly 16-64%) depending on diagnostic criteria, population, and the number and type of tests used. In a cohort of patients with type 1 diabetes, CAN prevalence was substantial and independently associated with markers of metabolic disturbance, consistent with

How to cite this article:

Ahmadi Esmailabadi E, Hashem A, Namiranian N, Jelodari MA, Razavi-Ratki SK. Pulmonary lymphangitic carcinomatosis as a rare occurrence in prostate cancer: Myocardial perfusion SPECT findings in patients with metabolic syndrome and cardiac autonomic neuropathy. Iran J Nucl Med. doi: 10.22034/irjnm.2026.130633.1782

the view that CAN reflects broader metabolic and vascular dysregulation rather than a purely neurological process [10].

Silent myocardial ischemia has been reported to be common among patients with diabetes and often goes undetected due to the absence of typical symptoms, particularly in those with autonomic neuropathy. In a cross-sectional study by Abdul Manan et al., silent ischemia was observed in 37.6% of diabetic adults, with predictors including long-standing diabetes, poor glycemic control, hypertension, dyslipidemia, smoking, and older age [11]. The ischemia prevalence in the present study (36.2%) is numerically similar; however, because symptom status was not recorded in the present dataset, we cannot confirm whether the ischemia was clinically silent, and have refrained from describing it as such.

Large-scale evidence also supports a link between reduced heart-rate variability - an established marker of CAN - and incident silent myocardial infarction in adults with type 2 diabetes, independent of baseline atherosclerotic disease [7]. Our findings of substantial ischemia, TID, and increased RV uptake in patients with MetS and CAN are consistent with this broader literature associating autonomic dysfunction with subclinical ischemic findings. However, the present cross-sectional, single-arm design cannot establish a causal or even a comparative relationship between CAN and ischemia; it can only describe the co-occurrence of these findings within a population selected for having both MetS and CAN.

Taken together, these findings suggest that patients with both MetS and CAN represent a population with a substantial burden of MPI abnormalities. These observations provide a rationale for further, appropriately designed studies - rather than an immediate recommendation for screening - to determine whether CAN independently contributes to ischemic risk in this population, and whether early imaging changes management or outcomes.

Recommendations

Future studies should include a comparison group of patients with MetS but without CAN (and ideally a group with neither) to test whether CAN is independently associated with ischemic MPI findings. Studies should prospectively collect data on diabetes status and control, hypertension, dyslipidemia, smoking, obesity, prior cardiac disease, and medications so that multivariable analysis can be performed; use Fisher's exact test where cell counts are small; report effect sizes with confidence intervals; and, where feasible, incorporate an independent reference standard (e.g., coronary angiography, CT coronary angiography, or clinical follow-up) to assess the prognostic significance of MPI findings. Larger, multicenter, prospective studies with standardized imaging protocols and blinded, multi-reader interpretation would also help clarify the role of MPI in this population before any recommendation for routine screening can be made.

Limitations

This study has several limitations: First, because all patients had both MetS and CAN without a non-CAN comparison group, causality cannot be established. Second, CAN-severity subgroups, key cardiovascular confounders, and a reference standard for ischemia were not available in the source data. Third, MPI was interpreted by a single reader, precluding interobserver agreement assessment. Finally, some subgroup comparisons involved small cell counts; and the single-center, cross-sectional design without outcome or cost-effectiveness data precludes recommendations for routine screening.

How to cite this article:

Ahmadi Esmailabadi E, Hashem A, Namiranian N, Jelodari MA, Razavi-Ratki SK. Pulmonary lymphangitic carcinomatosis as a rare occurrence in prostate cancer: Myocardial perfusion SPECT findings in patients with metabolic syndrome and cardiac autonomic neuropathy. Iran J Nucl Med. doi: 10.22034/irjnm.2026.130633.1782

CONCLUSION

Among patients with both MetS and CAN, over one-third had myocardial ischemia on MPI which was significantly associated with TID and increased RV uptake but not increased lung uptake. While these findings demonstrate a substantial burden of MPI abnormalities in this selected population, given the absence of a comparison group and other limitations noted above, this cross-sectional study cannot establish a causal link between CAN and ischemic risk. Therefore, these findings should be viewed as hypothesis-generating rather than a basis for routine screening recommendations.

REFERENCES

1. Shimokawa H, Yasuda S. Myocardial ischemia: current concepts and future perspectives. *J Cardiol*. 2008;52(2):67-78.
2. Alberti KG, Zimmet P, Shaw J. The metabolic syndrome--a new worldwide definition. *Lancet*. 2005;366(9491):1059-62.
3. Agashe S, Petak S. Cardiac autonomic neuropathy in diabetes mellitus. *Methodist Debaquey Cardiovasc J*. 2018;14(4):251-6.
4. Dimitropoulos G, Tahrani AA, Stevens MJ. Cardiac autonomic neuropathy in patients with diabetes mellitus. *World J Diabetes*. 2014;5(1):17.
5. Vinik AI, Erbas T, Casellini CM. Diabetic cardiac autonomic neuropathy, inflammation and cardiovascular disease. *J Diabetes Investig*. 2013 Jan;4(1):4-18.
6. Maser RE, Lenhard JM, DeCherney SG. Cardiovascular autonomic neuropathy: the clinical significance of its determination. *Endocrinologist*. 2000;10(1):27-33.
7. Kaze AD, Fonarow GC, Echouffo-Tcheugui JB. Cardiac autonomic dysfunction and risk of silent myocardial infarction among adults with type 2 diabetes. *J Am Heart Assoc*. 2023 Oct 17;12(20):e029814.
8. Israel O, Pellet O, Biassoni L, De Palma D, Estrada-Lobato E, Gnanasegaran G, Kuwert T, la Fougère C, Mariani G, Massalha S, Paez D, Giammarile F. Two decades of SPECT/CT - the coming of age of a technology: an updated review of literature evidence. *Eur J Nucl Med Mol Imaging*. 2019 Sep;46(10):1990-2012.
9. Slomka PJ, Patton JA, Berman DS, Germano G. Advances in technical aspects of myocardial perfusion SPECT imaging. *J Nucl Cardiol*. 2009 Mar-Apr;16(2):255-76.
10. Serdarova M, Dimova R, Chakarova N, Grozeva G, Todorova A, Tankova T. Relationship between cardiac autonomic neuropathy and cardio-metabolic risk profile in adults with type 1 diabetes. *Diabetes Res Clin Pract*. 2021 Apr;174:108721.
11. Abdul Manan H, Chishti HR, Hewlett FD. Prevalence and predictors of silent myocardial ischemia in diabetic patients. *Cureus*. 2025 Apr 16;17(4):e82407.

Table 1. Demographic characteristics and MPI findings in patients with MetS and CAN (n=268)

Variable	n	%
Male	83	31.0
Female	185	69.0
Myocardial ischemia	97	36.2
Transient ischemic dilation (TID)	21	7.8
Increased RV uptake	20	7.5
Increased lung uptake	11	4.1

Table 2. MPI secondary findings by presence or absence of myocardial ischemia

Finding	Ischemia present (n=97)	Ischemia absent (n=171)	p-value
TID, n (%)	15 (15.5%)	6 (3.5%)	0.001
Increased RV uptake, n (%)	15 (15.5%)	5 (2.9%)	0.001
Increased lung uptake, n (%)	7 (7.2%)	4 (2.3%)	0.053

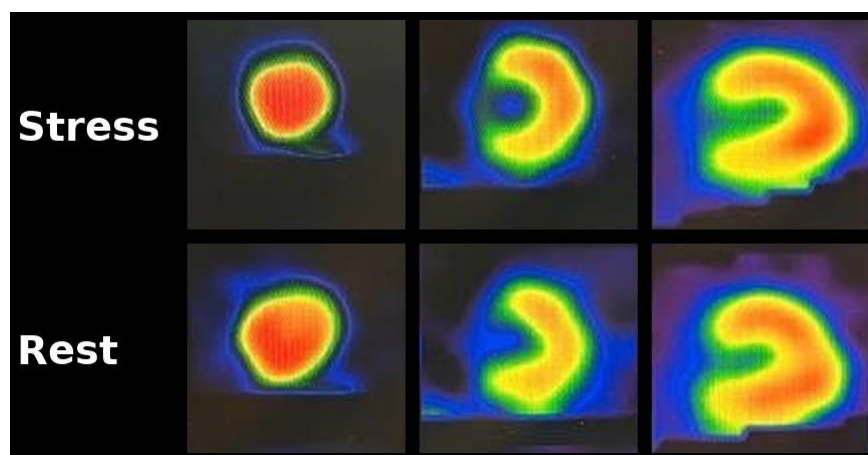


Figure 1. Representative short-axis, vertical long-axis, and horizontal long-axis stress/rest MPI slices from a patient in the cohort with elevated TID (TID = 1.12) and a significant reversible perfusion defect (summed stress score 5, summed difference score 5), illustrating combined TID and myocardial ischemia. Patient-identifying information has been removed

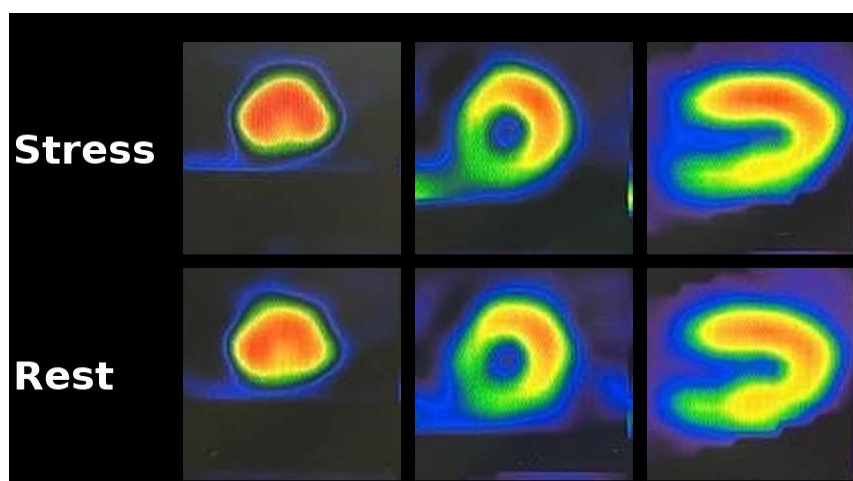


Figure 2. Representative short-axis, vertical long-axis, and horizontal long-axis stress/rest MPI slices from a second patient with mildly elevated TID (TID = 1.02) and a small reversible perfusion defect (summed stress score 2, summed difference score 2), illustrating a milder combined TID/ischemia pattern. Patient-identifying information has been removed