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A High Exercise Workload of ≥10 METS Predicts a Low Risk of Significant Ischemia and Cardiac Events in Older Adults

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Abstract

Background: Patients who achieve ≥10 METS during exercise SPECT myocardial perfusion imaging (MPI) have very low rates of significant ischemia and major adverse cardiac events (MACE). It is unknown how many older adults can achieve ≥10 METS, and if low risk extends to this subgroup.

Methods and Results: We examined the workload achieved, prevalence and predictors of ischemia, and MACE (cardiac death, nonfatal MI, late revascularization) in a cohort of 382 patients ≥65 years of age who underwent exercise ^{99m}Tc SPECT MPI. The cohort was 64.4% male and 36.9% had known coronary artery disease (CAD). All achieved ≥85% of maximum age-predicted heart rate. A workload of ≥10 METS was achieved in 25.4%; 50.3% attained 7–9 METS, and 24.4% reached <7 METS. There was a stepwise decrease in prevalence of any ischemia and significant ischemia (≥10% of the left ventricle (LV)) as workload increased (p=0.037). Patients achieving ≥10 METS had a 3.1% prevalence of ≥10% LV ischemia (1.2% in those without ST depression). Cardiac death and MACE rates in the ≥10 METS subgroup were 0.6%/year and 2.6%/year over a median 7.0 years of follow-up.

Conclusions: A substantial proportion of older adults who undergo exercise SPECT MPI can achieve ≥10 METS. This subgroup has low rates of significant LV ischemia and MACE. The favorable diagnostic and prognostic implications of achieving a high workload in an older adult population suggest it is feasible, with certain exceptions, to include this subgroup in workload-based strategies of provisional imaging.

Keywords

Coronary artery disease; Exercise stress testing; Myocardial perfusion imaging: SPECT; Outcomes research

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Exercise capacity is inversely associated with all-cause mortality and cardiovascular mortality, both in the general population and in older adults.(1–8) Among patients ≥65 years of age, attaining a high workload has been associated with a reduction in all-cause mortality and future cardiac events.(1) We previously reported 0% high-risk ischemia and low mortality and non-fatal myocardial infarction (MI) rates in a consecutive series of patients of all ages reaching ≥85% of maximum age-predicted heart rate (MAPHR) who achieved ≥10 METS with no ischemic ST segment depression.(9, 10) We concluded that exercise ECG stress testing may be sufficient in this cohort and proposed a provisional imaging protocol in which patients achieving ≥85% MAPHR and ≥10 METS without abnormal stress ECG or hemodynamic changes would not be injected with an imaging agent. Other investigators subsequently assessed such a provisional imaging protocol but excluded patients age ≥65 years.(11, 12)

As our original cohort had an inadequate sample size, we assembled a larger population to test the hypothesis that patients ≥65 years of age, achieving both ≥85% MAPHR and ≥10 METS of workload, would also demonstrate a low prevalence of high-risk ischemia and a low cardiac event rate, allowing them to qualify for a provisional imaging protocol with exercise stress testing.

Methods

Study Cohort

Prospectively collected data from the University of Virginia Nuclear Databank were analyzed in a cohort of consecutive patients who underwent exercise stress ^{99m}Tc SPECT MPI at the University of Virginia Health System between January 2006 and December 2007. The rate of exercise stress in this population was 39.4%. The study cohort for the primary analysis included 382 subjects who achieved ≥85% of their MAPHR. They were subdivided into 3 groups [<7 METs (n=93), 7 to 9 METs (n=192), and ≥10 METs (n=97)] as shown in Figure 1. The primary analysis was to determine the prevalence of a high exercise workload of ≥10 METs and the risk of high-risk LV ischemia (≥10%) at this workload in patients achieving a diagnostic stress test. Additional analysis on all-cause mortality and major adverse cardiac event (MACE) rates was performed in the subjects in the primary analysis cohort who had follow-up data available. A secondary analysis of the prevalence of any and significant ischemia was performed on 39 subjects who did not reach ≥85% of their MAPHR.

Clinical Information Collection and Management

Clinical information was collected from patients at the time of their exercise test and was entered into the University of Virginia Nuclear Databank. Exercise test parameters and SPECT results were also recorded.(13, 14) MACE, including nonfatal MI, revascularization, and cardiac death and all-cause mortality were identified thorough chart review and phone calls when needed. Protocol approval and waiver of informed consent were obtained from the University of Virginia Institutional Review Board.

Exercise Testing

All subjects underwent exercise treadmill stress with electrocardiographic monitoring using standard exercise protocols (93% Bruce or modified Bruce). Anti-ischemic medications were held at the discretion of the referring physician. Testing was symptom limited unless prematurely terminated as recommended in the exercise testing guidelines.(15) Exercise workload was defined as the total METs achieved.(16) Ischemic ST segment depression was defined as ≥1 mm horizontal or down-sloping depression of the ST-segment ≥80 ms after the J-point for 3 consecutive beats.

Radionuclide SPECT Imaging

^{99m}Tc sestamibi rest-stress, gated-SPECT MPI was performed with either a 1-day or 2-day protocol (for a body mass index ≥36 kg/m^2) as described previously.(9) With the 1-day protocol, patients first received 10 mCi of ^{99m}Tc sestamibi at rest, and images were acquired after a 60-minute delay. Patients subsequently received 30 mCi of ^{99m}Tc sestamibi at peak stress, 1 minute prior to exercise cessation, with gated-SPECT imaging performed after a 30-minute delay. The 2-day protocol differed in that the patients received 30 mCi ^{99m}Tc sestamibi (45 mCi in patients with body mass index >45 kg/m^2) before both rest and stress imaging.

Images were acquired with a dual-head GE Infinia camera (GE Medical Systems, Milwaukee, Wisconsin) with low-energy, high-resolution collimators. Each camera head rotated through 60 projections at 30 to 40 seconds/projection to acquire 180° of data with a standard ^{99m}Tc energy window. The data from the 2 heads were combined to give 360° of coverage. No scatter or attenuation correction was used.

Nuclear Imaging Interpretation

Experienced nuclear cardiology specialists performed visual and quantitative image analysis of the perfusion images according to a 17-segment model.(13) All borderline and abnormal studies were reclassified by the consensus of 2 additional readers blinded to all other clinical patient information, including data from the exercise study and the exercise ECG. Readers were aware that all patients had undergone exercise stress. Each segment was given a score from 0 to 4, with 0 representing normal perfusion and 1–4 representing mild, moderate, severe defects, and absent tracer uptake. Segmental scores were categorized by each reader who chose a score based on both quantitative perfusion data and a qualitative visual assessment. The semi-quantitative summed stress, rest, and difference values were calculated from these segmental scores. The 5 apical segments were weighted at 40% of the value of non-apical segments to so that each unit of myocardial volume was equal.(9) The percent myocardial ischemia, representing the extent and severity of LV inducible ischemia, was obtained by dividing the difference between the summed stress and summed rest scores by the maximum possible difference.(17, 18) Systolic and diastolic volumes and body surface area normalized volumes were also calculated.(13)

Outcomes

The primary outcome for this study was the prevalence of a high exercise workload of ≥10 METs and high-risk LV ischemia (≥10%) at this workload among patients 65 and older. The prevalence of varying degrees of LV ischemia was determined in the subgroups of patients achieving either <7, 7 to 9, or ≥10 METs. Secondary endpoints included predictors of ischemia and the prevalence of MACE (cardiac death, nonfatal MI, and late revascularization) amongst all patients and subdivided by exercise workload achieved, <10 versus ≥10 METs. Cardiac death was defined as any death with a demonstrable cardiac cause or without a clear non-cardiac cause. Nonfatal MI was designated if a patient presented with a history consistent with an acute coronary syndrome and had a troponin ≥2 times the upper limit of normal, with or without typical ischemic ECG changes. Late revascularization (or late invasive coronary angiography) was defined as >90 days post-MPI study unless the event was explicitly linked to the results of the MPI study.

Statistical Analysis

Continuous variables were described as medians with 25th and 75th percentiles and were compared by *t* tests with Satterthwaite approximations for unequal variances. Categorical variables were given as numbers of subjects with percentages and were compared with Pearson chi-square or Fisher's exact testing. Event rates were calculated through person-years analysis. The total events in a subgroup over the entire study period were divided by the sum of the years of follow-up for all patients in that subgroup. This value was adjusted for one person-year of follow-up to give an annualized rate. The alpha level of significance was 0.05 for all analyses.

Univariable logistic regression analysis of possible predictors of LV ischemia was performed. Variables with p values <0.10 were entered into a multivariable logistic regression model predicting any LV ischemia. The C-statistic represents the discriminative power of the logistic equation (1.0 represents perfect prediction). Key assumptions for logistic regression validity were met. Kaplan-Meier survival analysis was performed to assess cardiac death and cardiac events over the 7-year median survival free of events. Cox proportional hazards analysis was performed to examine the relationship of ischemia and 10% LV ischemia to cardiac events. All statistics were performed with SAS version 9.4 (SAS Institute, Cary, North Carolina).

Results

Study Population Characteristics

A substantial number of the 382 older adult subjects reaching target heart rate were able to achieve ≥10 METS of exercise capacity (97/382, 25.4%). The majority reached 7–9 METS (192/382, 50.3%), and 93/382 (24.4%) achieved a low workload of <7 METS. The median age of the entire cohort was 70.5 (25th, 75th: 67, 74). There were 161 subjects age 65–69 (42.2%), 131 age 70–74 (34.3%), and 90 subjects age 75 or greater (23.5%). The study population was 64.4% male and 36.9% had known CAD; 61.0% had chest pain, and 22.0% presented with dyspnea. The baseline characteristics related to workload achieved are provided in Table 1. The likelihood of achieving a high exercise workload was higher in younger adults and in men. Those with hypertension, diabetes mellitus, and elevated BMI ≥30 were less likely to achieve a high exercise workload. The presence of prior CAD and its sequelae did not appear to impact the likelihood of achieving a high workload.

Stress Findings

Exercise testing and stress electrocardiographic variables are presented by workload achieved in Table 2. There were no differences in percentage MAPHR achieved, maximum systolic and diastolic blood pressures, rate-pressure product, ischemic ST-depression, or chest pain during stress among the 3 workload groups. The median workload achieved decreased significantly for each age decile (8.5 METS for age 65–69, 8.0 METS for age 70–79, and 6.6 METS for age ≥80, p<0.001).

SPECT Imaging Results and Predictors

The prevalence of any reversible ischemia in the overall cohort of older adult patients achieving target heart rate was 22.8%, and 18.1% had a fixed defect with prior known infarction or wall-motion abnormality. The prevalence of significant LV ischemia (≥10%) in the entire cohort was 6.5%, and 0.8% had ≥20% LV ischemia. The median LVEF was 64% (25^{th}, 75^{th} percentiles: 58%, 70%). There were 34 subjects (8.9%) with a LVEF <50%. The prevalence of different levels of LV ischemia (mild or equivocal (1–4%), moderate (5–9%), and significant (≥10%)) are given by workload achieved in Figure 2. There is a significant stepwise decrease in all degrees of ischemia as workload increases (p=0.037). Significant LV ischemia (≥10%) was more prevalent in those with a lesser degree of workload achieved (11.8% for <7 METS versus 3.1% for ≥10 METS, p=0.042). Additional SPECT MPI results are analyzed by workload achieved in Table 3. Both the prevalence of a fixed perfusion defect and any reversible ischemia decreased by more than half as workload increased (p=0.005 and p=0.002, respectively). Similarly, the prevalence of significant LV ischemia (≥10%) decreased by almost three-quarters with increased workload (p=0.042). There were trends towards increased end-systolic and end-diastolic volume indices and decreased LVEF, but the differences were not significant. As shown in figure 3, subjects who had stress-induced ischemic ST depression ≥1mm had a higher prevalence of ≥10% LV ischemia both for those achieving <10 METS (18.0% versus 4.9%, p<0.001) and ≥10 METS (12.5% versus 1.2%, p=0.017).

The predictors of any LV ischemia in univariable and multivariable analyses are given in Table 4. Results were similar when the dichotomous <10 or ≥10 METS variable was replaced with the trilevel METS variable (<7, 7–9 and ≥10). METS as a continuous variable was highly predictive of ischemia (HR 1.22, 95% CI 1.08–1.37, p=0.002) and for ≥10% LV ischemia (HR 1.32, 95% CI 1.06–1.66, p=0.014).

Long-Term Events and Relationship of Ischemia

Follow-up for all-cause mortality and MACE were available in 372 (97.4%) and 359 (94.0%) of the entire cohort. The rate of 10-METS exercise capacity was not significantly different in those with and without follow-up (25.3% versus 22.2%, p= 0.83). The median follow-up was 7.7 years for all-cause mortality and 7.1 years for MACE. Early invasive coronary angiography was performed in 27 of the 359 patients (7.5%). The rate of early angiography was significantly lower in those reaching ≥10 METS: 3/88 (3.4%) versus 29/271 (10.7%), p=0.037. Of the three reaching ≥10 METS, 2 had known CAD and all had ≥5% LV ischemia. Subjects with early revascularization were excluded from subsequent outcomes analysis. Kaplan-Meier curves for cardiovascular death and MACE are provided in Figure 4 stratified by achievement of < or ≥10 METS. Yearly event rates are provided in Table 5 stratified by achievement of < or ≥10 METS. The annualized rate of cardiac death and nonfatal MI in patients achieving ≥10 METS were 0.6%/year and 0.8%/year, respectively. The rate of late revascularization was 1.4%/year. In those achieving ≥10 METS, neither ischemia (p=0.83) nor 10% LV ischemia (p=0.99) were significant predictors of MACE by Cox proportional hazards analysis. Eleven of the 13 subjects (84.6%) with MACE who had reached ≥10 METS had no ischemia during baseline imaging. Of the two with baseline ischemia, the median time to event was 3.9 years. There were no cardiac deaths or nonfatal MIs in the first 7 years of follow-up in those without known CAD who achieved ≥10 METS. Similarly, METS as a continuous variable was not a significant predictor of cardiac death (p=0.69) nor of MACE, though there was a trend (p=0.08).

Secondary Analysis in Subjects Failing to Reach Target Heart Rate

The 39 subjects who received an inadequate exercise stress of <85% MAPHR had a 12.8% rate of a positive stress ECG versus 20.2% for the study cohort with ≥85% MAPHR, p=0.27. There was a significant increased prevalence of ischemia, 46.2% versus 22.8% for those reaching target heart rate, p=0.001. However, there was no difference in the prevalence of significant ≥10% LV ischemia (5.1% for <85% MAPHR versus 6.5% for ≥85% MAPHR, p=0.73).

Discussion

Prior studies have shown that workload achieved on exercise stress testing is a good prognostic indicator of mortality and future cardiac events.(1, 2, 4, 10, 14, 19–22) We previously showed that patients achieving ≥85% of MAPHR, and ≥10 METS of workload on treadmill testing, had a low 0.4% prevalence of high-risk ≥10% LV ischemia on SPECT MPI.(9). Those achieving <7 METS had an 18-fold higher prevalence of high-risk ischemia, compared to those reaching ≥10 METS. A follow-up study of this cohort attaining ≥10 METS of exercise workload revealed a cardiac death rate of 0.1%/year and a nonfatal MI rate of 0.7%/year.(10) From these observations, we concluded that a provisional imaging protocol could be established in which low-risk patients reaching 85% MAPHR and ≥10 METS without ischemic ST depression would not be injected with an imaging agent at peak exercise unless other adverse exercise test endpoints were present (e.g. typical angina chest pain, exercise hypotension, serious arrhythmias).

Duvall et al. proposed such a provisional injection protocol for patients with chest pain in the emergency department, but excluded patients ≥65 years of age.(11) They performed a retrospective analysis of their existing stress test population data applying the hypothetical provisional protocol and found that only 5.9% of the patients qualifying for the provisional protocol had an abnormal MPI with a low 5-year all-cause mortality of 1.1%. This protocol could have avoided imaging in 29% of their patient population. This same group then undertook a prospective, non-randomized study in 965 low to low-intermediate risk patients age ≤65 years, with no known CAD and an interpretable ECG who were deemed able to exercise.(12) Patients who achieved target heart rate and ≥10 METS with no ST depression or exercise-induced anginal symptoms were not injected with a radioisotope (n=192). This provisional injection group had a similar all-cause mortality rate at an average follow-up of 42 months compared to those who had exercise imaging and achieved ≥10 METS (n=773). Only 1 cardiac death in the entire cohort was documented. Importantly, 22% of the original population of patients were not considered for the provisional protocol because of age >65 years.(12)

In our expanded study, we surmised that a provisional injection protocol for stress MPI might also be applied to a substantial number of patients ≥65 years of age. Approximately 25% of patients ≥65 years of age achieved ≥85% of their MAPHR and ≥10 METS on exercise testing. Those patients achieving ≥10 METs with no ischemic ST depression had a very low prevalence (1.2%) of high-risk ischemia on MPI and low rates of cardiac death (0.6%/year) and MACE (2.6%/year) over a median 7.0 years of follow-up. The MACE rate was similar in those with and without known CAD. Most patients achieving a high workload who had events did not have any ischemia on MPI. Of note, event rates were low for the entire population, with no difference in event rates between those achieving ≥10 METS vs <10 METS, possibly attributed to the lower risk of contemporary stress testing populations, particularly for patients able to exercise.

The favorable prognosis in this analysis for patients of advanced age achieving ≥10 METS is consistent with other groups (1, 6–8). Morise et al. showed that each 1-MET increment in peak treadmill workload was associated with an 18% reduction among those >65 years of age.(1) In a study of male veterans aged 65–92, every 1-MET increase in exercise capacity conferred a 12% lower risk of mortality.(8) Compared to the least fit veterans (≤4 METS), the adjusted hazard for death declined by 61% in those achieving >9 METS.

Certain limitations of employing a provisional imaging protocol in the clinical setting have been identified.(23) Referral physicians would have to agree to a provisional strategy. The costs of IV insertion and the imaging agent (even if not used) would need to be covered by insurance but would be offset by the cost savings related to not performing MPI. Pharmacologic stress imaging could be performed for patients requiring imaging for ST changes or angina symptoms during recovery. Potentially useful data on fixed perfusion defects and LV volumes and ejection fraction are not obtained. In addition, some high-risk patients undergoing stress ECG without imaging could benefit from CT coronary calcium imaging for further risk assessment as suggested previously.(24–27) The demonstration of a zero or very low coronary calcium score would provide further evidence of a low risk test result.

There are limitations to this study. First, it is a single-center study with a small cohort for assessing hard cardiac events. However, it is a valid patient population for determination of the percentage of older adult patients reaching target heart rate who can achieve ≥10 METS of exercise workload. A larger cohort of patients would be required to better ascertain event rates related to workload achieved.

Summary and Conclusions

In conclusion, this study shows that patients who are ≥65 years of age but achieve ≥85% of MAPHR and ≥10 METS on exercise stress testing have a very low prevalence of high-risk ischemia (≥10% LV ischemia) on MPI and low rate of MACE. Such patients, comprising approximately 25% of older adult patients who have a diagnostic exercise test, could avoid MPI for risk assessment. We suggest a larger study to evaluate the worth of a provisional imaging protocol for exercise testing, that includes patients ≥65 years of age, who are able to exercise to ≥10 METS without manifesting ST depression or exhibiting other adverse exercise test endpoints. The additional role of coronary calcium imaging in certain patients with a high pretest risk of CAD should also be evaluated in such a study design.

New Knowledge Gained

This analysis demonstrates that a substantial proportion of patients age ≥65 years undergoing stress testing can achieve ≥10 METS. This subgroup has a low prevalence of significant LV ischemia and early rate of subsequent MACE. These findings should facilitate the extension of the concept of a provisional imaging protocol to older adults, who make up a significant proportion of the population undergoing stress testing but have previously been excluded from such protocols.

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Abbreviations

CAD	coronary artery disease
CV	cardiovascular
ECG	electrocardiography
LV	left ventricular
MAPHR	maximum age-predicted heart rate
METS	metabolic equivalents
MI	myocardial infarction
MPI	myocardial perfusion imaging
SPECT	single photon-emission computed tomography

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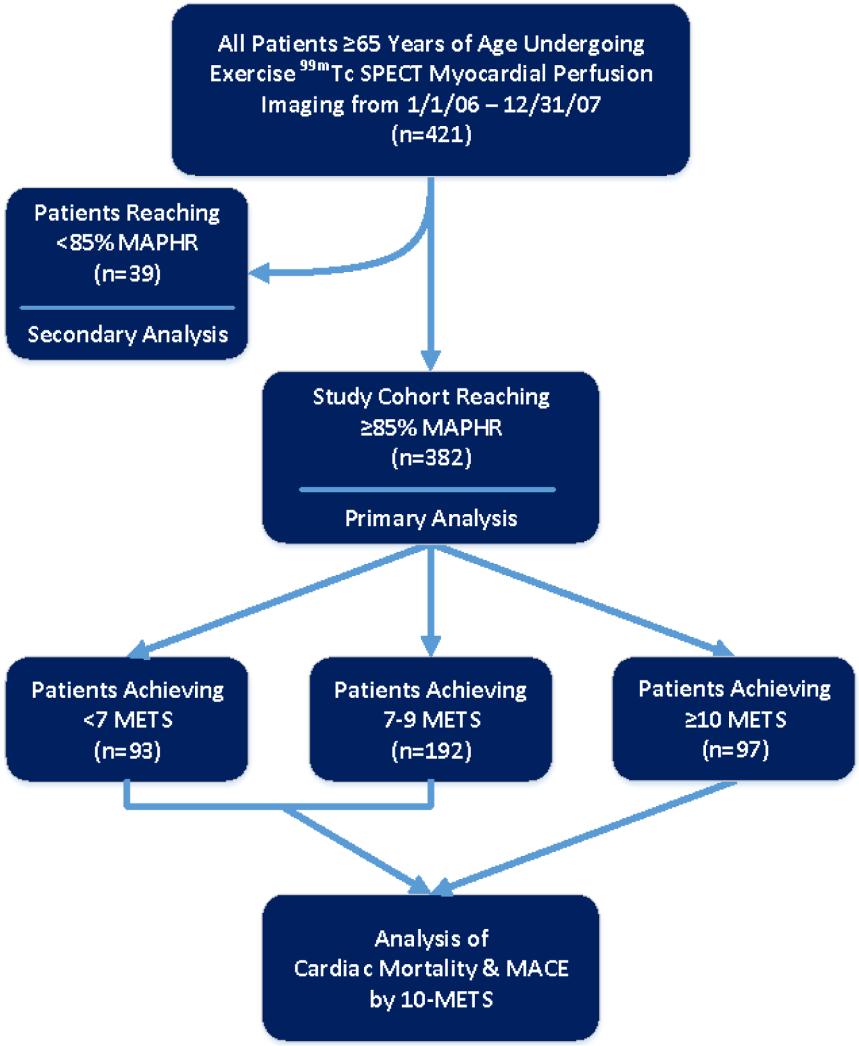

Figure 1.

Patient flow diagram showing derivation of the study cohort. The final study cohort for the primary analysis included 382 subjects. Additional analysis of cardiac mortality and major adverse cardiac events (MACE) was subsequently performed in those with follow-up available comparing those achieving < and ≥10 METS. A secondary analysis of the prevalence of positive ECG and ischemia was performed in the 39 subjects who achieved <85% MAPHR.

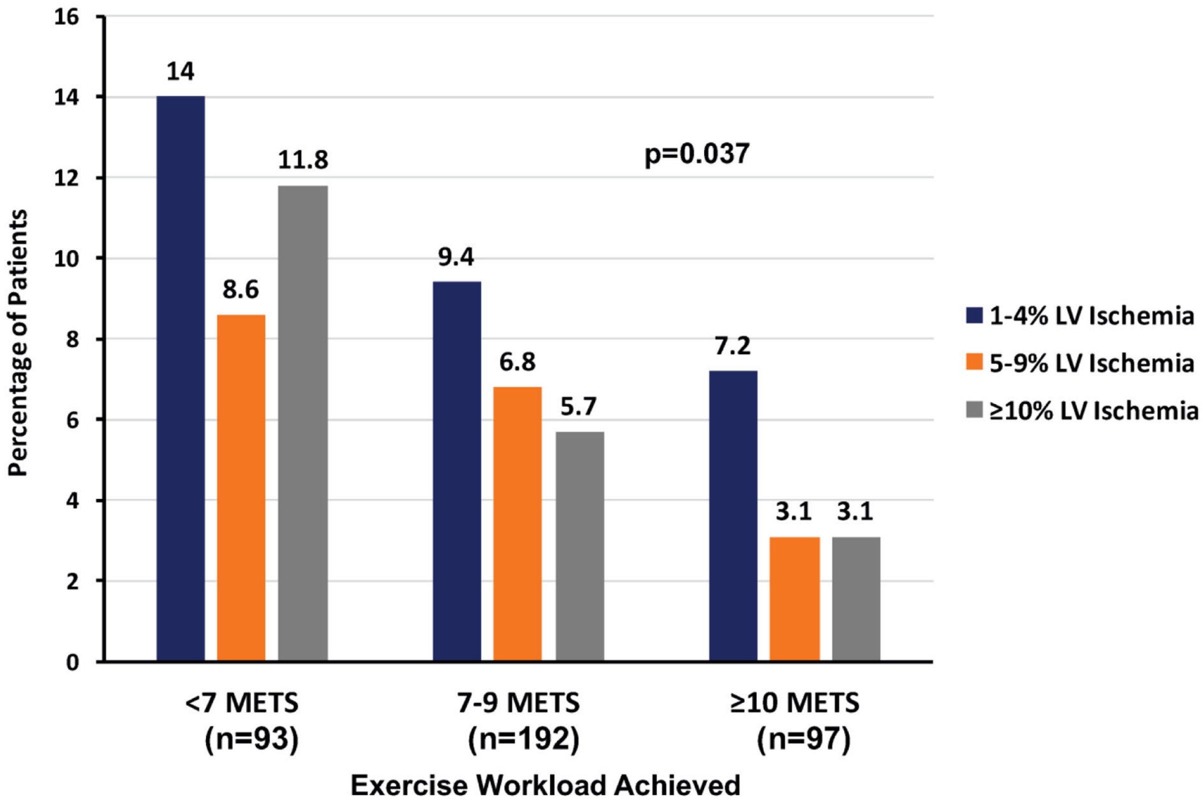

Figure 2.

Chart of the percentage of patients who had 1–4%, 5–9%, and ≥10% LV ischemia divided by exercise workload achieved during stress testing. There was a stepwise decrease in all degrees of ischemia as exercise workload achieved increased (p=0.037).

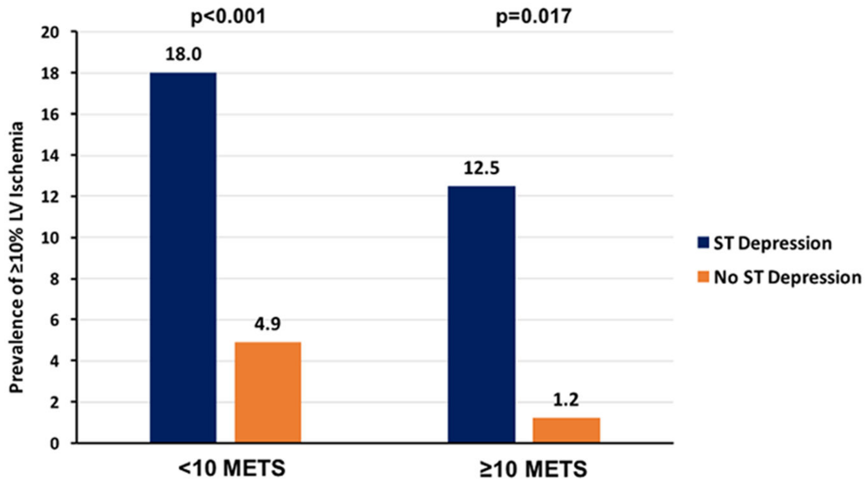

Figure 3.

Chart of the percentage of patients with significant (≥10%) left ventricular ischemia divided by workload achieved (<10 versus ≥10 METS) and presence or absence of diagnostic ST depression on stress electrocardiography. The prevalence of significant ischemia is very low in the group achieving ≥10 METS with no ST depression.

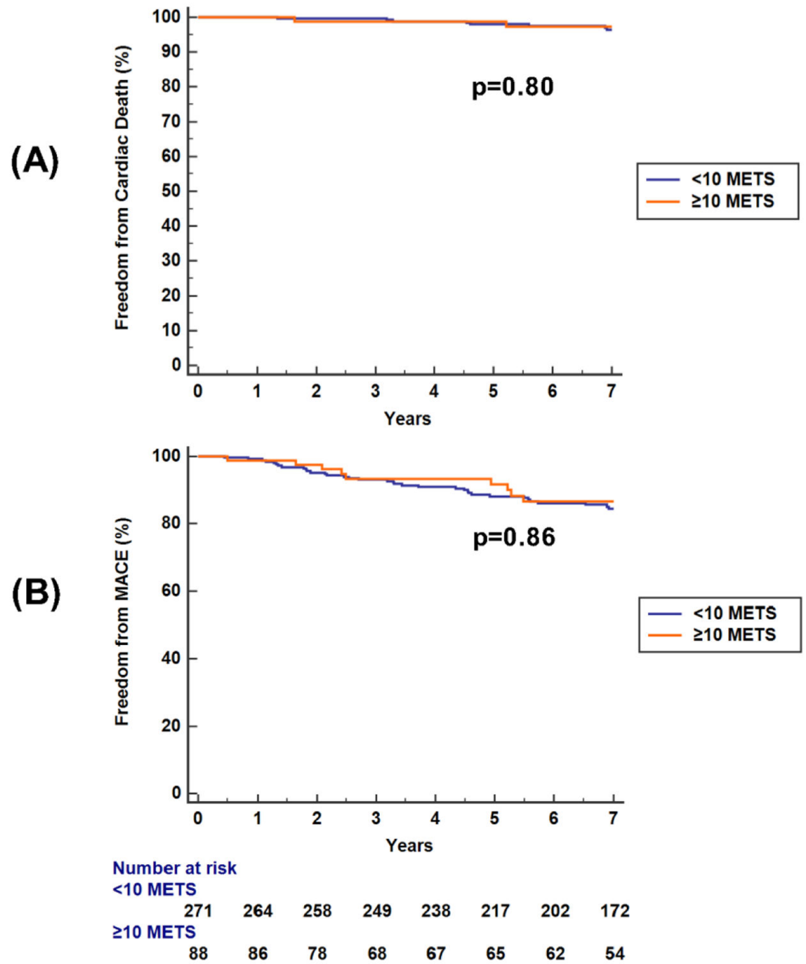

Figure 4.

Graphs of Kaplan-Meier survival analysis for freedom from cardiac death (panel A) and freedom from cardiac events (panel B) over the 7-year median follow-up stratified by achievement of < or ≥10 METS in the 359 subjects with follow-up data on cardiac events available. The rate of both cardiac death and MACE was low in this older adult subgroup irrespective of exercise capacity.

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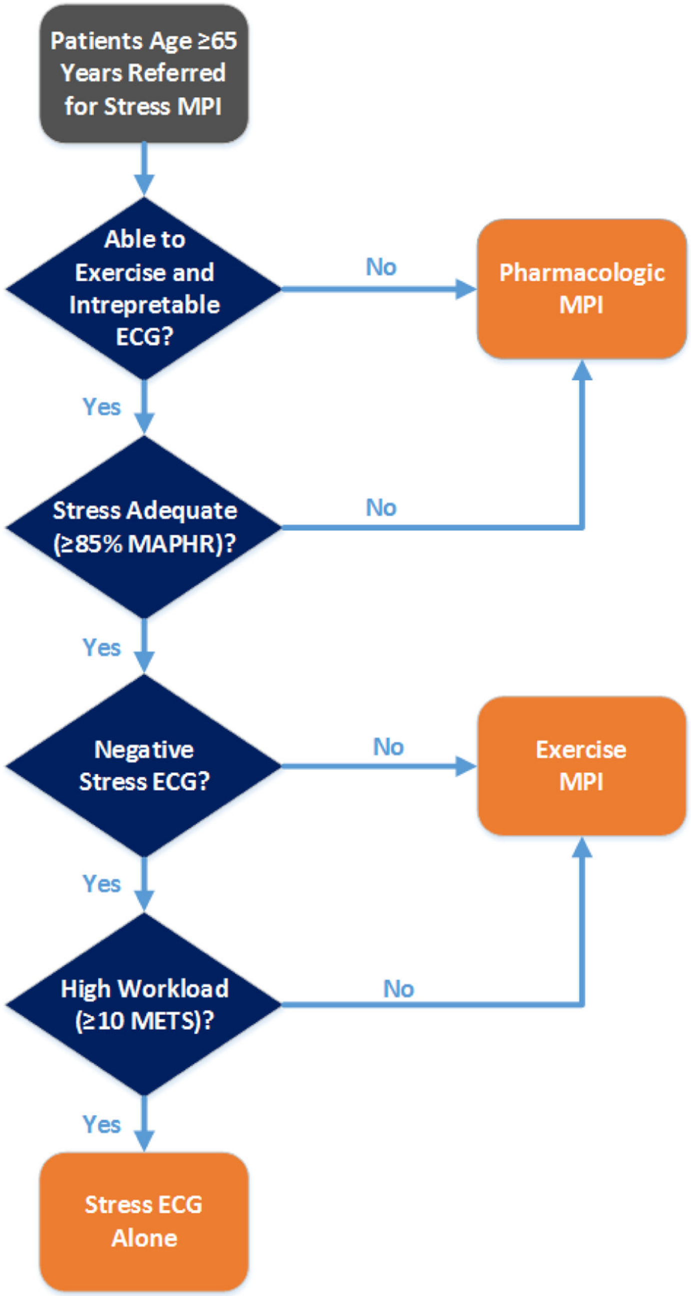

Figure 5.

Diagram of proposed provisional imaging algorithm. Older adult subjects ≥65 years of age who can exercise, have an interpretable ECG, reach target heart rate, have no concerning ECG changes, and reach a high exercise workload of ≥10 METS are appropriate for stress ECG alone due to a low risk of ischemia and subsequent MACE.

Table 1.

Baseline Characteristics in Patients Achieving ≥85% of Their MAPHR Relative to Workload Attained.

Characteristic	<7 METS* Achieved (n (%))	7-9 METS Achieved (n (%))	≥10 METS Achieved (n (%))	P-value
Total number of patients	93 (24.4)	192 (50.3)	97 (25.4)	-
Age (median, 25th, 75th percentiles)	73.0 (68.0, 77.0)	70.5 (67.0, 74.0)	70.0 (67.0, 73.0)	<0.001
Male	55 (59.1)	112 (58.3)	79 (81.4)	<0.001
Chest pain	54 (58.1)	117 (60.9)	62 (63.9)	0.71
Hypertension	71 (76.3)	143 (74.5)	59 (60.8)	0.026
Diabetes mellitus	23 (24.7)	34 (17.7)	9 (9.3)	0.019
Hyperlipidemia	61 (65.6)	140 (72.9)	65 (67.0)	0.37
Current tobacco use	29 (31.2)	45 (23.4)	20 (20.6)	0.21
BMI ≥30	20 (21.5)	34 (17.7)	8 (8.3)	0.034
Known CAD*	29 (31.2)	71 (37.0)	41 (42.3)	0.29
History of MI*	15 (16.1)	38 (19.8)	16 (16.5)	0.68
Prior revascularization	23 (24.7)	64 (33.3)	33 (34.0)	0.28
Abnormal resting ECG*	21 (22.6)	26 (13.5)	11 (11.3)	0.07
Same-day beta-blocker use	5 (5.4)	15 (7.8)	4 (4.1)	0.44

*CAD=coronary artery disease; ECG=electrocardiogram; METS=metabolic equivalents; MI=myocardial infarction.

Table 2.

Exercise Test Variables in Patients Achieving ≥85% of Their MAPHR Relative to Workload Attained.

Exercise Test Parameter	<7 METS* Achieved (n= 93)	7-9 METS Achieved (n= 192)	≥10 METS Achieved (n= 97)	P-value
Exercise Duration (min) (median (25th, 75th percentiles)*	5.5 (5.2, 6.2)	8.0 (7.0, 8.5)	11.0 (10.1, 12.0)	-
Percentage of MAPHR Achieved*	95.4 (90.3, 102.0)	95.3 (89.7, 100.7)	97.9 (92.4, 103.3)	0.15
Maximum Systolic BP (mmHg)	194 (178, 216)	196 (169, 215)	194 (180, 213)	0.63
Maximum Diastolic BP (mmHg)	84 (76, 96)	83 (73, 97)	83 (73, 97)	0.87
Rate Pressure Product ($\times 10^3$)	27.2 (24.4, 30.9)	27.5 (24.1, 30.8)	28.6 (25.0, 31.8)	0.08
≥1mm ST-depression on ECG* (n (%))	19 (20.4)	42 (21.9)	16 (16.5)	0.56
Chest pain during stress (n (%))	16 (17.2)	25 (13.0)	10 (10.3)	0.37

*BP=blood pressure; ECG=electrocardiogram; HR=heart rate; MAPHR=maximum age-predicted heart rate; METS=metabolic equivalents; min=minutes.

Table 3.

Myocardial SPECT Imaging Results Versus Exercise Capacity in Patients Achieving ≥85% of Their MAPHR.

Characteristic	<7 METS* Achieved (n= 93)	7-9 METS Achieved (n= 192)	≥10 METS Achieved (n= 97)	P-value
Perfusion				
Fixed Perfusion Defects†	27 (29.0)	30 (15.6)	12 (12.4)	0.005δ
Any Reversible Ischemia	32 (34.4)	42 (21.9)	13 (13.4)	0.002
Percentage LV Ischemia (mean ± SD)	2.7±5.2	1.7±4.3	0.9±3.1	
LV Ischemic burden				0.037
0% Ischemic	61 (65.6)	150 (78.1)	84 (86.6)	
1-4% Ischemic	13 (14.0)	18 (9.4)	7 (7.2)	
5-9% Ischemic	8 (8.6)	13 (6.8)	3 (3.1)	
≥10% Ischemic	11 (11.8)	11 (5.7)	3 (3.1)	
Volumes & Function				
ESVI* (median (25th, 75th percentiles)	12 (9, 20)	11 (8, 17)	15 (11, 19)	0.07
ESVI ≥25	14 (15.2)	19 (10.1)	12 (12.5)	0.45
EDVI*	45 (38, 55)	43 (38, 51)	46 (39, 56)	0.053
Ejection fraction	65 (57, 69)	65 (59, 71)	63 (58, 68)	0.07

*EDVI=end-diastolic volume index; ESVI=end-systolic volume index; METS=metabolic equivalents.

†All fixed perfusion defects had either known prior infarction in the affected territory or an associated wall-motion abnormality.

δP-values are two-tailed with values <0.05 considered statistically-significant.

Table 4.

Uni- and Multivariable Logistic Regression Analysis Predicting Any Ischemia of the Left Ventricle (Global Wald X^2 = 68.3, c=0.84).

	Univariable			Multivariable		
Predictors	**X^2**	**Hazard Ratio (95% CI)***	**p-value**	**X^2**	**Hazard Ratio (95% CI)**	**p-value**
LVEF (5% decrements)*	53.4	1.76 (1.51-2.04)	<0.001†	37.1	1.68 (1.42-1.99)	<0.001
Male gender	25.6	6.6 (3.17-13.56)	<0.001†	12.6	4.54 (1.97-10.47)	<0.001
<10 METS achieved	6.3	2.27 (1.19-4.30)	0.012†	12.5	3.76 (1.80-7.84)	<0.001
ST-Depression ≥1mm	8.0	2.21 (1.28-3.81)	0.005†	6.9	2.42 (1.25-4.68)	0.009
Known CAD*	21.7	3.22 (1.97-5.29)	<0.001†	4.2	1.84 (1.02-3.31)	0.041
Prior MI*	21.7	3.74 (2.15-6.53)	<0.001†			
Prior revascularization	20.5	3.14 (1.92-5.16)	<0.001†			
Hypertension	6.8	2.25 (1.22-4.12)	0.009†			
Age (5-year increments)	2.9	1.24 (0.97-1.58)	0.086			
Hyperlipidemia	0.8	1.28 (0.75-2.19)	0.37			
Chest pain	0.6	0.83 (0.51-1.34)	0.44			
Body mass index ≥30	0.5	0.78 (0.40-1.55)	0.48			
Diabetes mellitus	0.4	1.22 (0.66-2.25)	0.53			
Tobacco use	0.0	1.05 (0.60-1.82)	0.87			

*CAD=coronary artery disease; CI=confidence interval; LVEF=left ventricular ejection fraction; METS=metabolic equivalents; MI=myocardial infarction.

†P-values are two-tailed with values <0.05 considered statistically-significant.

Table 5.

Follow-up events by workload achieved

Event	<10 METS* Achieved n (%/year)	≥10 METS Achieved n (%/year)	P-value†
Total patients	For Mortality: 278 For Cardiac Events: 271	For Mortality: 94 For Cardiac Events: 88	
All-cause mortality	32 (1.7%/year)	8 (1.3%/year)	0.65
Cardiovascular death	12 (0.7%/year)	3 (0.6%/year)	0.68
Nonfatal MI*	14 (0.9%/year)	4 (0.8%/year)	0.82
Late revascularization	23 (1.4%/year)	7 (1.4%/year)	0.88
Total MACE*	41 (2.5%/year)	13 (2.6%/year)	0.94

*MACE=major adverse cardiac events; METS=metabolic equivalents; MI=myocardial infarction.

†P-values were determined using Chi-Square analysis.