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ORIGINAL RESEARCH

Feasibility of a Novel Augmented 6-Minute Incremental Step Test

A Simplified Cardiorespiratory Fitness Assessment Tool

Jeroen Molinger, MS,[a,b,c] Veraprapas Kittipibul, MD,[a,d] J. Matthew Gray, MS,[a] Vishal N. Rao, MD, MPH,[a,d] Stratton Barth, BS,[b] Ashley Swavely, MS,[a] Brian Coyne, MEd,[a] Aubrie Coburn, MS,[a] Jan Bakker, MD,[e,f] Paul E. Wischmeyer, MD,[c] Cynthia L. Green, PhD,[d,g] David MacLeod, MD,[b,c] Manesh Patel, MD,[a,d] Marat Fudim, MD, MHS[a,d]

ABSTRACT

BACKGROUND The cardiopulmonary exercise test (CPET) is considered a gold standard in assessing cardiorespiratory fitness (CRF) but has limited accessibility due to competency requirements and cost. Incorporating portable sensor devices into a simple bedside test of CRF could improve diagnostic and prognostic value.

OBJECTIVES The authors sought to evaluate the association of an augmented 6-minute incremental step test (6MIST) with standard CPET.

METHODS We enrolled patients undergoing clinically indicated supine cycle ergometry CPET with invasive hemodynamics (iCPET) for the same-day 6MIST. CRF-related variables were simultaneously recorded using a signal morphology-based impedance cardiograph (PhysioFlow Enduro) and a portable metabolic analyzer (VO_2 Master Pro) during incremental pace stationary stepping. The correlation between CPET and hemodynamic parameters from both tests was assessed using the intraclass correlation coefficient (ICC).

RESULTS Fifteen patients (mean age 60 $\pm$ 14 years, 40% female, 27% Black) were included. All patients who agreed to undergo 6MIST completed the study without any test-related adverse events. We observed good to excellent correlation between iCPET- and 6MIST-measured CPET parameters: peak heart rate (ICC = 0.60; 95% CI: 0.15-0.85), absolute peak O_2 consumption (VO_2) (ICC = 0.77; 95% CI: 0.44-0.92), relative peak VO_2 (ICC = 0.64; 95% CI: 0.20-0.86), maximum ventilation (ICC = 0.59; 95% CI: 0.13-0.84), O_2 pulse (ICC = 0.71; 95% CI: 0.33-0.89), and cardiorespiratory optimal point (ICC = 0.82; 95% CI: 0.52-0.94). No significant correlation was determined between iCPET and 6MIST in measuring cardiac index at rest (ICC = 0.19; 95% CI: −0.34 to 0.63) or at peak exercise (ICC = 0.36; 95% CI: −0.17 to 0.73).

CONCLUSIONS We demonstrate the feasibility of a novel augmented 6MIST with wearable devices for simultaneous CPET and hemodynamic assessment. 6MIST-measured CPET parameters were strongly correlated with the iCPET-derived measurements. Additional studies are needed to confirm the validity of the 6MIST compared to standard upright CPET. (JACC Adv 2024;3:101079) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

From the [a]Division of Cardiology, Department of Medicine, Duke University Medical Center, Durham, North Carolina, USA; [b]Human Pharmacology & Physiology Lab, Department of Anesthesiology, Duke University Medical Center, Durham, North Carolina, USA; [c]Division of Critical Care, Department of Anesthesiology, Duke University School of Medicine, Durham, North Carolina, USA; [d]Duke Clinical Research Institute, Durham, North Carolina, USA; [e]Department of Intensive Care Adults, Erasmus MC University Medical Center, Rotterdam, The Netherlands; [f]Department of Medicine, NYU Grossman School of Medicine, New York, New York, USA; and the [g]Department of Biostatistics & Bioinformatics, Duke University School of Medicine, Durham, North Carolina, USA.

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ABBREVIATIONS AND ACRONYMS

6MIST = 6-minute incremental step test

6MWT = 6-minute walk test

BA = Bland-Altman

CI = cardiac index

CO = cardiac output

COP = cardiorespiratory optimal point

CRF = cardiorespiratory fitness

HF = heart failure

HRR = heart rate reserve

ICC = intraclass correlation coefficient

iCPET = invasive cardiopulmonary exercise test

POC = point-of-care

RER = respiratory exchange ratio

RHC = right heart catheterization

VE = ventilation

VO_2 = oxygen consumption

Assessment of cardiorespiratory fitness (CRF) is essential to the diagnosis and longitudinal outpatient monitoring to track disease progression, as well as guide appropriate interventions in patients with cardiopulmonary conditions particularly heart failure (HF).[1] Progressive decline in exercise tolerance is a hallmark of HF, but the objective assessment of CRF is uncommon and is often restricted to one-time assessments given the time, logistics, and cost consuming nature of CRF testing. Cardiopulmonary exercise test (CPET) is the gold standard test to measure CRF, including in HF, and is endorsed by multiple societal guidelines.[2-4] Data derived from the CPET provide robust risk assessment and prognostic insight in the HF population.[4] Despite these advantages, the formal CPET is not readily accessible in every clinical setting due to the limited availability, competency requirements including specialized equipment as well as highly trained staff, and the dedicated test environment.[5] Bedside or field tests such as 6-minute walk test (6MWT) are commonly used to objectively quantify CRF and are useful for clinical prognostics. Minimally invasive tests such as the 6MWT have been shown to be valuable and complementary to bedside clinical assessment[6] but are limited in the insights gained on the underlying limitations leading to an impaired CRF and could provide false reassurance.[7,8] There is an unmet need for an enhanced bedside test that is easy to perform, can be applied at the point of care, and provides sufficient information to guide further management.

In this study, we sought to test the feasibility of the 6-minute incremental step test (6MIST), augmented with wearable wireless sensor technology, and correlate the test with an invasive CPET (iCPET).

METHODS

STUDY DESIGN AND PATIENT SELECTION. This study was part of the prospective Congestive Heart Failure Phenotyping study enrolling patients undergoing clinically indicated right heart catheterization (RHC) as outpatient workup with suspected or established HF, aged 18 to 80 years, at a Duke University Medical Center, Durham, North Carolina, USA, between July 2020 and February 2022. Exclusion criteria included acute coronary syndrome, symptomatic hypotension, cardiogenic shock, hypertensive crisis, or end-stage renal disease on hemodialysis. This study was approved by the Duke Institutional Review Board, and all patients provided written consent.

INVASIVE CPET PROTOCOL. All patients underwent iCPET which included a RHC through the internal jugular vein (7-Fr sheath, and 6-F pulmonary arterial catheter) and radial artery (5-F sheath) to assess central venous and arterial hemodynamics, plus blood gas analysis, and CPET. No intravenous sedative or analgesic drugs were administered. Following resting hemodynamics, patients underwent supine cycle ergometry testing at a fixed workload of 20 W during a warm-up phase until patients either reached a steady state of oxygen consumption (VO_2) or up to 3 minutes. After reaching a steady state, patients continued to exercise with a stepwise increase in workload of 20 W every minute until exhaustion. Hemodynamic assessment during exercise was performed at 20 W and at peak exercise. Patients were encouraged to maintain a pedaling cadence of 55 to 65 revolutions/min. Peak exercise was defined by achieving a respiratory exchange ratio (RER) of ≥1.10 or volitional fatigue (ie, symptom limited or failure to maintain 55-65 revolutions/min).

Breath-by-breath VO_2 was measured continuously throughout the study (Vmax e29) (**Figure 1A**). The following CPET parameters were collected: absolute and relative VO_2, ventilation (VE), O_2 pulse (VO_2/HR), RER, VE/VCO_2 slope, and VE/VO_2 slope. Age-predicted maximal HR was calculated using Tanaka's formula: $208 - (\text{age} \times 0.7)$.[9] Heart rate reserve (HRR) was calculated by age-predicted maximal HR − peak HR. Cardiorespiratory optimal point (COP) which is defined as the lowest VE/VO_2 ratio in a given minute of exercise was also measured.[10] Cardiac output (CO) was assessed using the direct Fick method. The hemodynamic parameters of each patient were indexed with their body surface area. The cardiac index (CI) augmentation was defined as the ratio between CI at peak exercise/rest.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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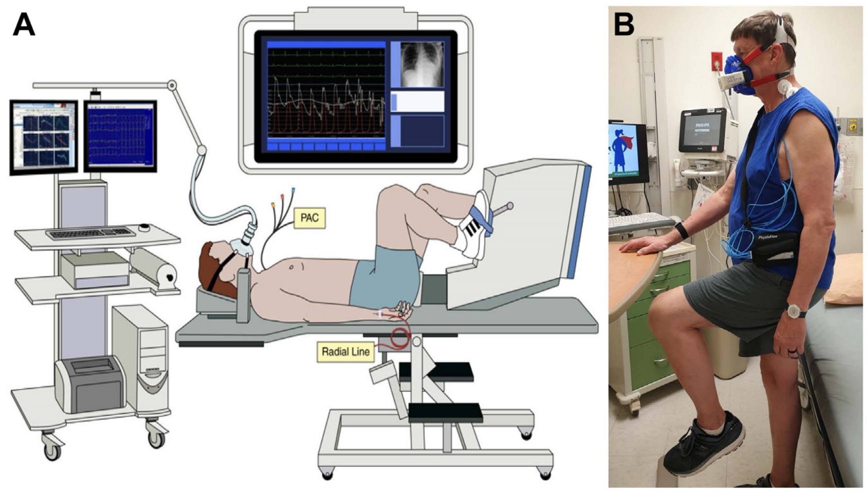
FIGURE 1 Study Arrangements



(A) iCPET with supine cycle ergometry (B) augmented 6MIST with a portable metabolic analyzer, VO_2 Master Pro (VO_2 Master Health Sensors Inc) and a wearable signal morphology-based impedance cardiograph (PhysioFlow Enduro). The figure is adapted from Fudim M, Boortz-Marx RL, Ganesh A, et al. Splanchnic nerve block for chronic heart failure. *JACC Heart Fail*. 2020;8(9):742-752. 6MIST = 6-minute incremental step test; iCPET = invasive cardiopulmonary exercise test; VO_2 = oxygen consumption.

AUGMENTED 6-MINUTE INCREMENTAL STEP TEST PROTOCOL. The augmented 6MIST consisted of incremental pace stationary stepping (increasing pace by 5 steps every 30 seconds using a metronome) for a maximum of 6 minutes while clinical CRF-related variables were simultaneously recorded (Figure 1B). A portable metabolic analyzer, VO_2 Master Pro (VO_2 Master Health Sensors Inc),[11] was used to assess VO_2 and VE (tidal volume and respiratory rate). The VO_2 Master Pro has 3 user pieces for different ranges of VE. The medium user piece which measures minimal flow of 15L was used for 6MIST, therefore the resting VO_2 could not be accurately measured. The VO_2 Master Pro does not have a CO_2 sensor, therefore RER and VE/VCO_2 could not be obtained. A portable, signal morphology-based impedance cardiograph with real-time wireless monitoring (PhysioFlow Enduro, PhysioFlow Inc)[12,13] was used to estimate CO. Variations in the impedance to an alternating high-frequency and low-magnitude current across the thorax results in a characteristic waveform used to calculate stroke volume and subsequently CO (average stroke volume over 30 seconds × HR). Similarly CI and the degree of augmentation were calculated. All sensors (VO_2 Master and PhysioFlow Enduro) were simultaneously connected to the SplendoMonitor (Apple iPad) App (SplendoHealth, USA) to continuously collect all VO_2 kinetics, HR, and hemodynamic data. SplendoMonitor, powered by a multimodal real-time cloud-based platform, synchronized all the data between the 2 devices. All patients completed the upright 6MIST after supine CPET with an approximately 1-hour rest period between tests.

STATISTICAL ANALYSIS. Continuous variables are presented using the mean ± SD; and categorical variables are presented using the frequency and percentage. Correlation between cardiopulmonary exercise parameters as well as exercise hemodynamics obtained from iCPET and 6MIST were determined using the intraclass correlation coefficient (ICC) to measure the degree of consistency rather than absolute agreement, as the measures were not expected to be the same. Each ICC was derived using a 2-way mixed effects model and is presented with 95% CI. ICC values >0.75, >0.60 to 0.74, 0.40 to 0.59, and <0.40 represent excellent, good, fair, and poor correlation, respectively.[14] Estimates were not adjusted for multiple comparisons, thus CIs should be interpreted with caution. A Bland-Altman (BA) analysis was performed to illustrate the discrepancy between iCPET and 6MIST by comparing the mean difference of each pair to their mean. BA plots were used to show the mean bias and limits of agreement. Statistical analyses were performed using SAS, version 9.4 (SAS Institute, Inc).

TABLE 1 Baseline Characteristics (N = 15)

Demographics	
Age (y)	60 ± 14.1
Female	6 (40)
Body mass index (kg/m^2)	28.9 ± 4.4
Black race	4 (27)
Comorbidities	
Left ventricular EF (%)	43.6 ± 21.6
Heart failure	10 (67)
Reduced EF	6 (60)
Preserved EF	4 (40)
Hypertension	7 (47)
Diabetes	3 (20)
Chronic kidney disease	5 (33)
COPD	1 (7)

	iCPET		6MIST		Difference
Cardiopulmonary exercise parameters		N Miss		N Miss	
Peak HR (beats/min)	119.7 ± 20.8	0	132.7 ± 22.5	0	−13.1 ± 19.3
Heart rate reserve (beats/min)	46.3 ± 16.3	0	34.2 ± 21.3	0	12.1 ± 17.7
RER	1.07 ± 0.10	0	-	-	-
Absolute peak VO_2 (mL/min)	1,125 ± 398	0	1,241 ± 496	0	−115 ± 306
Relative peak VO_2 (mL/kg/min)	13.4 ± 4.1	0	14.6 ± 4.8	0	−1.2 ± 3.8
VE (L/min)	46.0 ± 13.6	0	56.2 ± 25.9	0	−10.2 ± 18.7
VE/VO_2	35.0 ± 8.4	2	49.1 ± 15.7	2	−14.1 ± 14.2
COP	26.3 ± 5.1	2	27.2 ± 7.4	2	−0.90 ± 3.81
VE/VCO_2	35.4 ± 5.7	0	-	-	-
O_2 pulse (mL/beats)	9.5 ± 3.4	0	9.4 ± 3.9	0	0.08 ± 2.78
Exercise hemodynamics					
RAP rest (mm Hg)	7.6 ± 3.6	0	-	-	-
RAP peak (mm Hg)	11.7 ± 7.4	1	-	-	-
PASP rest (mm Hg)	32.9 ± 12.6	0	-	-	-
PASP peak (mm Hg)	56.9 ± 18.4	0	-	-	-
PCWP rest (mm Hg)	14.8 ± 7.7	0	-	-	-
PCWP peak (mm Hg)	24.8 ± 13.5	0	-	-	-
CI rest (L/min/m^2)	2.7 ± 0.7	1	2.4 ± 0.7	3	0.42 ± 0.84
CI peak (L/min/m^2)	5.6 ± 2.6	1	5.3 ± 1.4	3	0.70 ± 2.36
CI augmentation during peak exercise	2.2 ± 0.8	3	2.3 ± 0.6	3	−0.13 ± 0.97

Values are mean ± SD or n (%).

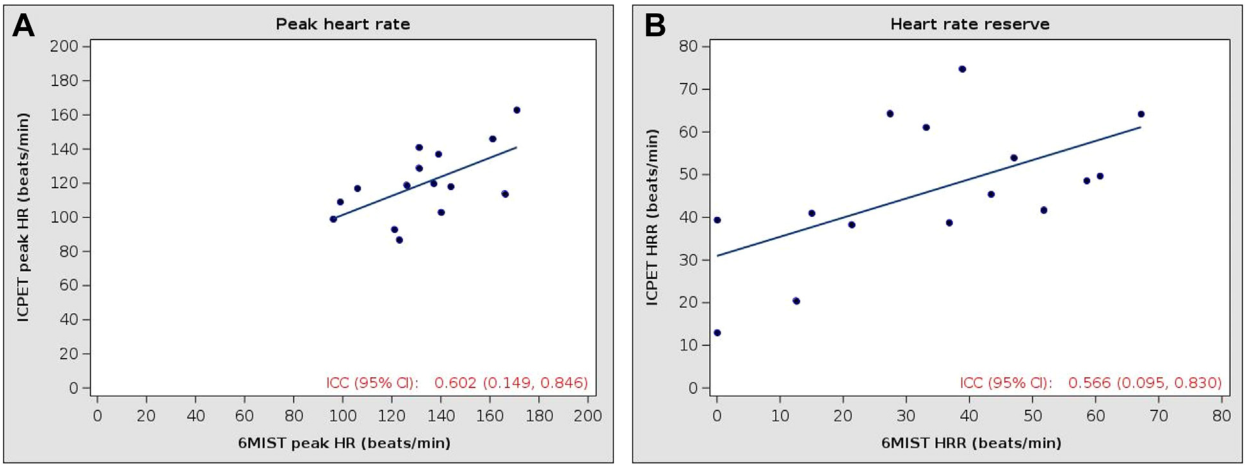
6MIST = 6-minute incremental step test; CI = cardiac index; CO = cardiac output; COP = cardiorespiratory optimal point; COPD = chronic obstructive pulmonary disease; EF = ejection fraction; HR = heart rate; iCPET = invasive cardiopulmonary exercise test; PASP = pulmonary systolic pressure; PCWP = pulmonary capillary wedge pressure; RAP = right atrial pressure; RER = respiratory exchange ratio; VCO_2 = carbon dioxide production; VE = ventilation; VO_2 = oxygen consumption.

RESULTS

BASELINE CHARACTERISTICS. A total of 15 patients were included, with a mean age of 60 ± 14.1 years, 40% women, 27% Black, and a mean body mass index of 28.9 ± 4.4 kg/m^2 (Table 1). The majority of patients (67%) had HF: 6 with reduced ejection fraction and 4 with preserved ejection fraction. Mean left ventricular ejection fraction was 43.6% ± 21.6%. Other comorbidities included 47% hypertension, 20% diabetes, 33% chronic kidney disease, and 7% chronic obstructive pulmonary disease.

CARDIOPULMONARY EXERCISE PARAMETERS. All patients completed the 6MIST without complications. All patients were in sinus rhythm throughout both iCPET and 6MIST. Peak HR achieved during the exercise was 120 ± 20.8 beats/min in iCPET and 132.7 ± 22.5 beats/min in 6MIST (Table 1). HRR was 46.3 ± 16.4 and 34.2 ± 21.3 beats/min in iCPET and 6MIST, respectively. Absolute and relative VO_2 during peak exercise were 1,126 ± 398 and 1,241 ± 496 mL/min, and 13.4 ± 4.1 and 14.6 ± 4.8 mL/kg/min in iCPET and 6MIST, respectively. VE was 46.0 ± 13.6 L/min in iCPET and 56.2 ± 25.9 L/min in 6MIST. O_2 pulse

FIGURE 2 **Correlation Between HR Parameters Measured During 6MIST and iCPET**

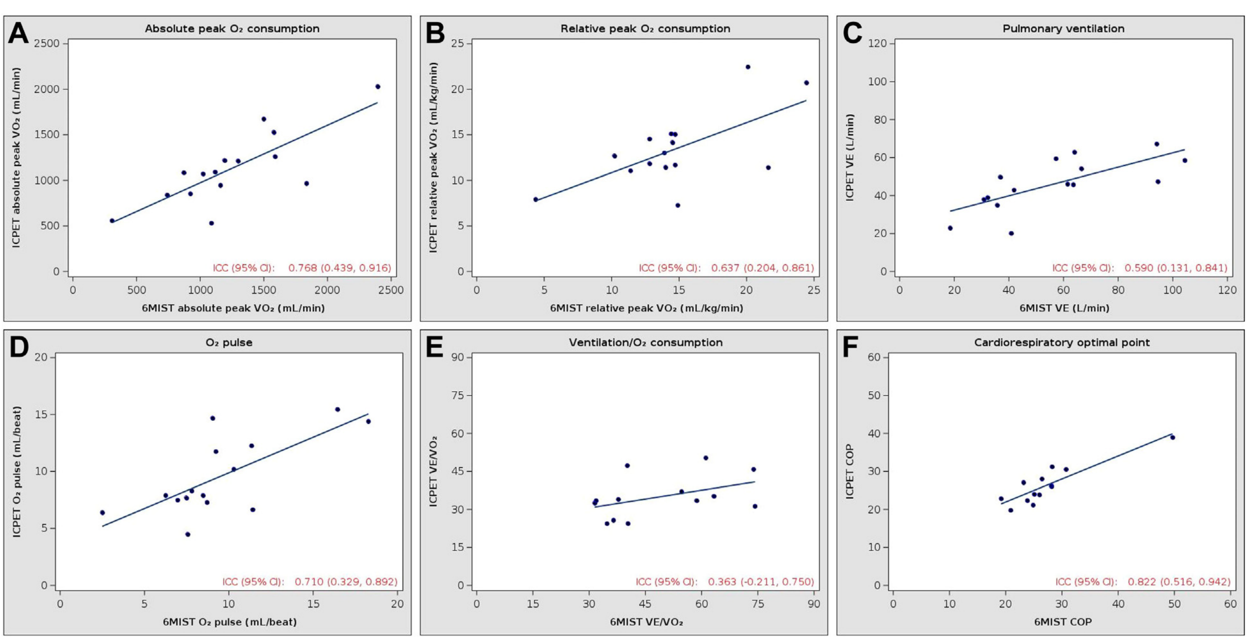


(A) peak HR, (B) HRR. HRR = heart rate reserve; other abbreviations as in Figure 1.

was 9.5 ± 3.4 mL/beat in iCPET and 9.4 ± 3.9 mL/beat in 6MIST. VE/VO2 slope was 35.0 ± 8.4 in iCPET and 49.1 ± 15.7 in 6MIST. COP was 26.3 ± 5.1 in iCPET and 27.2 ± 7.4 in 6MIST. RER of 1.07 ± 0.10 and VE/CO_2 production (VCO_2) slope of 35.4 ± 5.7 were only able to be measured in iCPET.

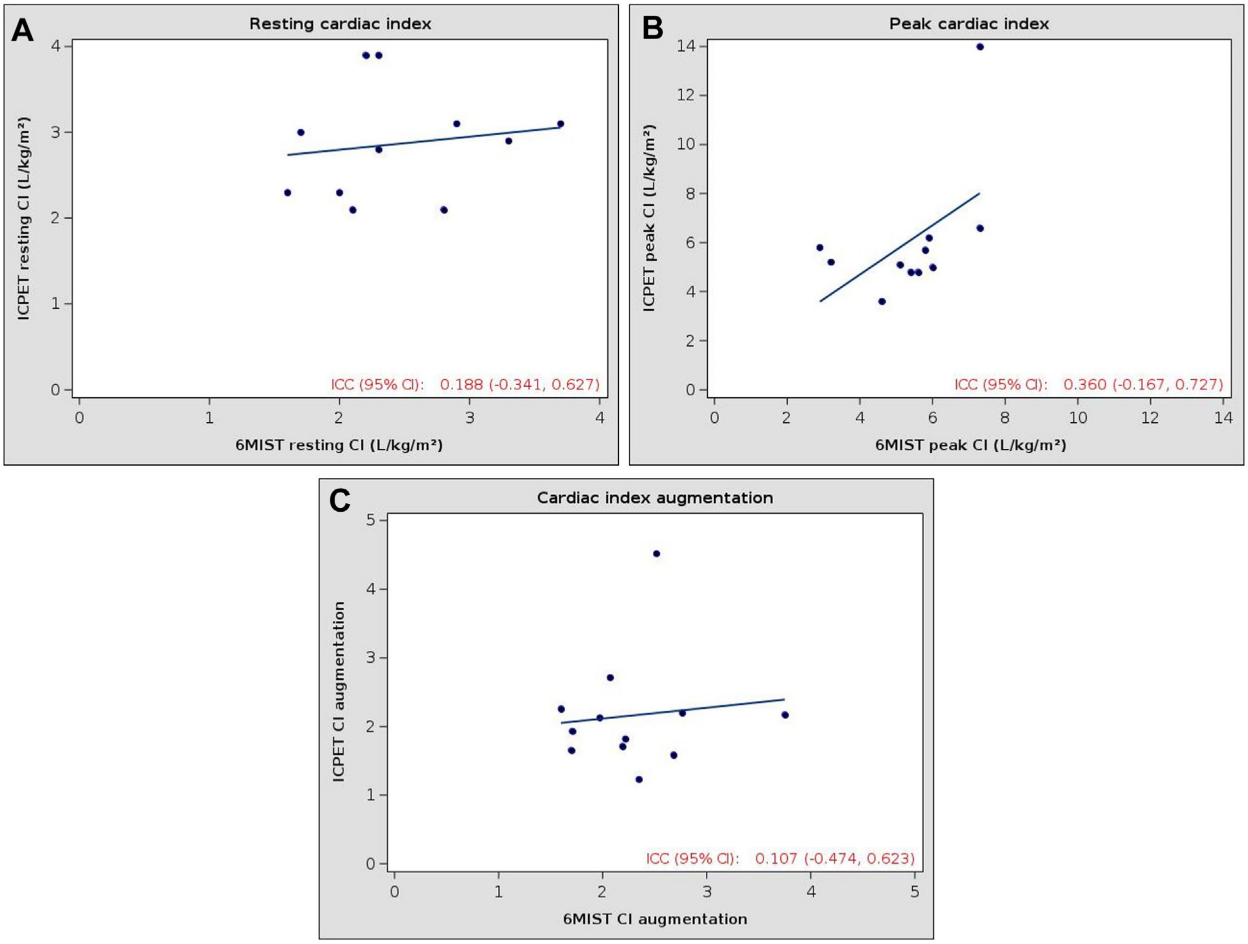
We observed a good to excellent correlation between iCPET- and 6MIST-measured HR and metabolic parameters (Figures 2 and 3): peak HR (ICC = 0.60; 95% CI: 0.15-0.85), HRR (ICC = 0.57; 95% CI: 0.10-0.83), absolute peak VO_2 (ICC = 0.77; 95% CI: 0.44-0.92), relative peak VO_2 (ICC = 0.64; 95% CI:

FIGURE 3 **Correlation Between CPET Parameters Measured During 6MIST and iCPET**



(A) absolute peak VO_2, (B) relative peak VO_2, (C) VE, (D) O_2 pulse, (E) VE/VO_2, (F) COP. COP = cardiorespiratory optimal point; VE = ventilation; other abbreviations as in Figure 1.

FIGURE 4 Correlation Between CI Measured During 6MIST and iCPET



(A) CI at rest, (B) CI at peak exercise, (C) CI augmentation. CI = cardiac index; other abbreviations as in Figure 1.

0.20-0.86), VE (ICC = 0.59; 95% CI: 0.13-0.84), O_2 pulse (ICC = 0.71; 95% CI: 0.33-0.89), and COP (ICC = 0.82; 95% CI: 0.52-0.94). A statistically significant correlation between iCPET- and 6MIST-measured VE/VO_2 slope (ICC = 0.36; 95% CI: −0.21 to 0.75) was not determined. The BA plots for each CPET parameter are illustrated in Supplemental Figure 1.

EXERCISE HEMODYNAMICS. Intracardiac pressures during iCPET were mean right atrial pressure of 7.6 ± 3.6 mm Hg at rest and 11.7 ± 7.4 mm Hg at peak exercise, mean pulmonary artery systolic pressure 32.9 ± 12.6 mm Hg at rest and 56.9 ± 18.4 mm Hg at peak exercise, and mean pulmonary capillary wedge pressure 14.8 ± 7.7 mm Hg and 24.8 ± 13.5 mm Hg at peak exercise. CI at rest and peak exercise were 2.7 ± 0.7 and 2.4 ± 0.7 L/min/m^2, and 5.6 ± 2.6 and 5.3 ± 1.4 L/min/m^2 in iCPET and 6MIST, respectively. CI augmentation during peak exercise was 2.2 ± 0.8 times in iCPET and 2.3 ± 0.6 times in 6MIST.

No statistically significant correlation between iCPET and 6MIST was found in measuring CI at rest (ICC = 0.19; 95% CI: −0.34 to 0.63), CI at peak exercise (ICC = 0.36; 95% CI: −0.17 to 0.73), or CI augmentation (ICC = 0.11; 95% CI: −0.47 to 0.62) (Figure 4). The BA plots for each hemodynamic parameter are illustrated in Supplemental Figure 2.

DISCUSSION

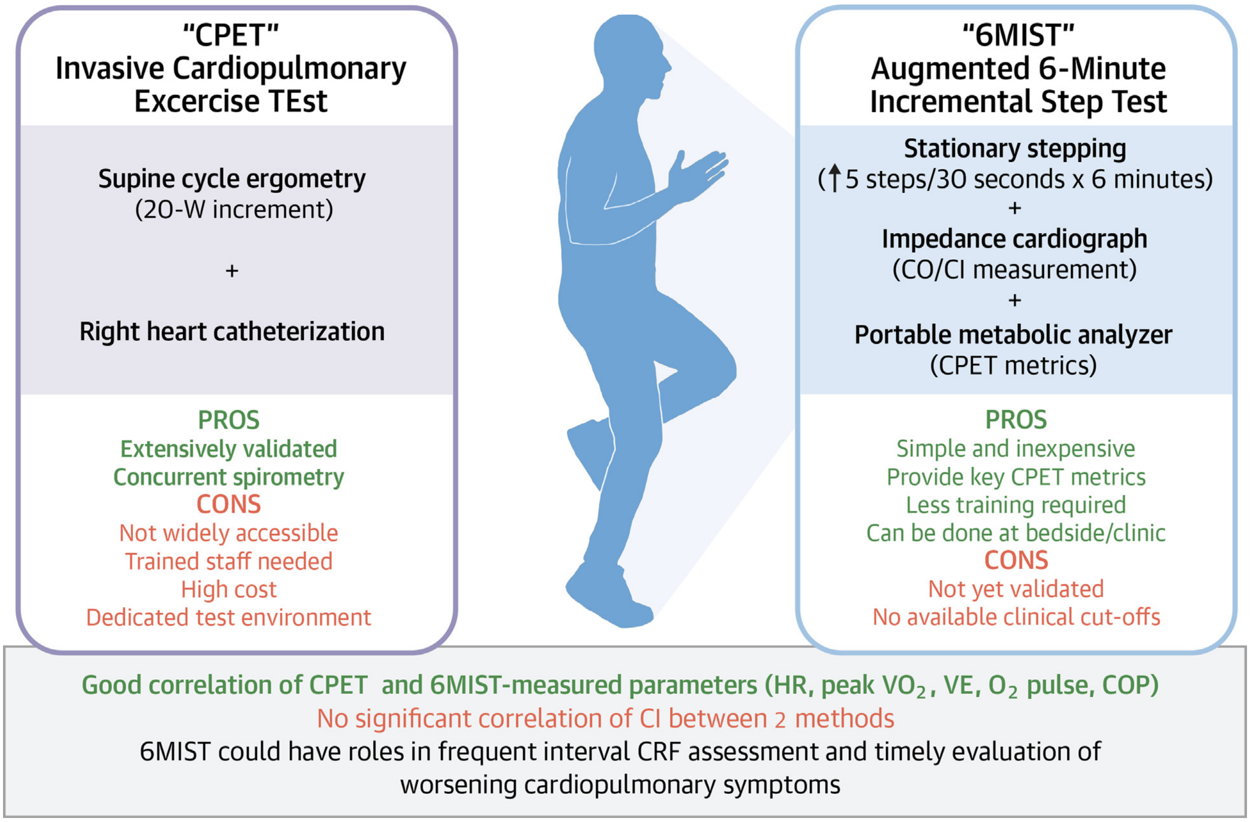
We present the feasibility of a novel bedside augmented 6MIST utilizing multimodal wearable technology as a simple, inexpensive, and potentially scalable alternative to current traditional form of CRF assessment in selected settings. The key CPET metrics including peak VO_2, VE, O_2 pulse, and COP obtained during the 6MIST strongly correlate with those obtained from iCPET. However, the 6MIST-measured CI at rest and peak exercise was not significantly correlated with iCPET-derived values.

Compared to traditional laboratory tests, field tests are generally more utilized as an adjunctive objective assessment during clinic visits due to their simplicity, cost, and time efficiency; however, the data obtained from these tests are limited. Therefore, the concept of augmented point-of-care (POC) CRF assessment using various wearable technology could offer advantages of both testing strategies. One of the challenges of the augmented POC CRF assessment concept is whether measurements represent peak exercise capacity as would CPET. This becomes more clinically relevant as the POC testing with wearable devices, at least in this study, was unable to determine the anaerobic threshold using RER, thus making analysis challenging to ascertain if patients reached their maximum exercise capacity. However, in the present study, we found a strong correlation between peak HR (as a surrogate of physical demands and intensity)[4] of both testing strategies; and a numerically higher peak HR achieved during the 6MIST which could be from greater recruitment of involved muscle groups due to the upright nature of exercise. Moreover, a recent study using a wearable CPET device during a 6MWT demonstrated that VO_2 achieved during the 6MWT was 98% $\pm$ 20% of the peak VO_2 of standard CPET studies in HF patients.[15] Up to 40% of patients with advanced HF (defined as peak VO_2 <12 mL/kg/min) had 6MIST-peak VO_2 >110% of measured standard CPET-peak VO_2. Interestingly, the proportion of patients achieving >110% of standard CPET-peak VO_2 during 6MWT was lower in HF patients with less impaired exercise capacity and lowest in healthy subjects. Moreover, some parameters not requiring maximal exercise determination such as COP could still be obtained. This observation suggests clinicians could substitute the relatively inconvenient CPET-derived data with simple POC CRF assessment when clinically indicated.

To our knowledge, this is the first study to describe the use of a stationary 6MIST especially in conjunction with the CPET-capable wearables. The 6-minute step test as equivalent to the standard 6MWT using a portable 20-cm-high step without a protocolized increment in the exercise intensity has been previously described and validated in HF population.[16] A prolonged (patient-terminated, up to 15 minutes) incremental step test using a similar portable step has also been tested in patients with chronic obstructive pulmonary disease.[17] Compared to other exercise protocols, we find the stationary 6MIST to be the most appealing protocol to be coupled with the wearable CPET equipment. The 6MIST, in contrast to the 6MWT, more closely simulates the standard CPET as the 6MIST entails a more physiologic ramp exercise protocol. The implementation of incremental workload increases during the 6MIST would also theoretically help patients attain a maximal or submaximal exercise effort in a shorter period. Stepping exercise in general requires less space (ie, can be performed in the clinic room after the patient's visit) and allows closer monitoring during the test. A stationary stepping protocol on the flat surface rather than up and down the stepping stool is also safer with a lower fall risk. Furthermore, limiting the test duration to 6 minutes improves time efficiency without disrupting clinic workflow should the 6MIST be implemented into routine interval evaluation.

Although we have demonstrated the feasibility of incorporating a wearable CPET device into a basic 6MIST, the challenge remains how accurate and clinically relevant these POC CRF assessments are. Several portable devices or operating systems for CRF assessment have been developed as well as validated for different clinical scenarios. Two different wearables were utilized during the augmented 6MIST in this study: the VO_2 Master Pro and the PhysioFlow Enduro. The VO_2 Master Pro is a breath analyzer used to assess VO_2 utilizing the same concept as a traditional CPET; therefore, the results were acceptably comparable across most CPET parameters.[11] On the other hand, the PhysioFlow Enduro operates using the noninvasive impedance cardiograph to estimate stroke volume and subsequently CO/CI,[12] in contrast to the direct Fick's method that estimates CO directly. PhysioFlow has been shown to overestimate CO/CI compared to the direct Fick's method in HF patients which could account for a lack of correlation between CI at rest and exercise measured by both methods.[13] Although we hypothesized that incorporating noninvasive hemodynamic assessment could still be helpful to estimate relative changes or CI augmentation during exercise which is an important indicator for good CRF in addition to evaluating CI at rest or exercise individually,[18] there was also no significant correlation between CI augmentation measured during 6MIST or iCPET. Additionally, we noted that 6MIST-measured CI at rest and peak exercise appears to be lower than iCPET-measured counterparts which are opposite to the metabolic trends that are higher during the 6MIST. The reasons for lower CI in the 6MIST group are still unclear but should not be due to differences in body position during the tests. Upright

CENTRAL ILLUSTRATION Feasibility of Augmented 6-Minute Incremental Step Test (6MIST) in Cardiorespiratory Functional Assessment



Molinger J, et al. JACC Adv. 2024;3(8):101079.

Combining cardiopulmonary exercise and hemodynamic assessment using wearable technologies with a simple bedside 6-minute incremental step test is feasible and more informative. Cardiopulmonary exercise parameters (heart rate, peak oxygen consumption, oxygen pulse and cardiorespiratory optimal point) obtained from 6MIST are strongly correlated with those obtained from the standardized invasive cardiopulmonary exercise test. 6MIST has the potential to serve as a scalable addition to the formal cardiopulmonary exercise test, enabling more frequent and convenient point-of-care assessments. CO = cardiac output; CRF = cardiorespiratory fitness; other abbreviations as in Figures 1, 3, and 4.

exercise in 6MIST has been shown to have higher CO/CI at rest and during exercise.[19] However, the higher VO_2 in the 6MIST group is consistent with previously described observation that VO_2 is higher in the upright position compared to supine or semi-supine positions.[19]

Despite the strong correlation between 6MIST and iCPET measurements, we do not imply or encourage the interchangeable use of these distinctive parameters. The observed correlations only imply that the augmented 6MIST strategy might be able to capture similar trends of physiological responses to exercise. The next crucial step will be to validate the 6MIST against the standard upright CPET whose measurements represent the most physiological state and have been extensively validated in various cardiopulmonary conditions. Nonetheless, a traditional CPET remains the gold standard test to assess CRF with numerous highly standardized exercise protocols tailored to patients.[5] In addition to well-known metabolic parameters, a formal CPET usually provides an extremely helpful understanding of the interplay of cardiovascular, pulmonary vascular, pulmonary, and skeletal muscle physiology during exercise as a mean of determining the limiting system and often root cause of symptoms.[20] In addition to basic parameters that can be obtained during portable CPET study, a formal CPET performed and interpreted by experienced personnel also provides complementary data on specific patterns of O_2 kinetics and VE such as exercise oscillatory ventilation which is a strong prognostic indicator of increased morbidity and mortality in HF.[21,22] However, in common clinical practice, peak VO_2 is the most important and clinically significant parameter clinicians need from any CPET. The peak VO_2 which has been considered a key and, on most occasions, sole parameter in quantifying CRF. It accurately determines disease progression and prognosis and evaluates the need for advanced HF therapies particularly heart transplant. As demonstrated in our study, VO_2 could be reliably measured during 6MIST and is well correlated with the standard measurements, we believe that the augmented 6MIST, even after being validated, would not replace but rather fill in the gap in the current clinical practice. The traditional in-lab CPET would still be a comprehensive test for evaluation of patients with suspected cardiopulmonary disease, unknown cause of dyspnea, or determination of the need for advanced HF therapies. The proposed roles of augmented 6MIST would be to allow more frequent interval assessment of CRF in patients with HF or other cardiopulmonary conditions and to timely evaluate patients with worsening cardiopulmonary symptoms, and objectively quantify worsening functional capacity (**Central Illustration**). Because the diagnostic and prognostic values of CPET parameters have been established using traditional CPET settings, the common cutoff values should not be extrapolated to bedside CPET measurements. However, these 6MIST-measured CPET parameters could be extremely useful to help clinicians understand relative changes or trends over more frequent intervals. These simple and less expensive tests could also be considered as screening tools in the clinic in stable patients that are doing well to avoid the inconvenience of in-lab CPET.

This study has some limitations. First, the study sample size is small due to exploratory nature of the study. PhysioFlow data were also not available in some patients. Additionally, the methods of exercise were different between 2 CPET measurement strategies which could influence the interpretation of differences in CPET parameters. Nonetheless, the exact exercise setup is not feasible as the stepping test is not routinely performed during the traditional CPET. An upright cycling or treadmill test without simultaneous RHC, although not perfect, would be better for future comparison and validation. Given the notable potential practical benefits and additional information of the 6MIST over standard 6MWT, we chose not to compare these 2 tests. As the main goal of this pilot study was to demonstrate the feasibility in terms of safety and practicality of performing the 6MIST and incorporating 2 wearables as a new POC CRF testing strategy, we did not intend to determine the accuracy or validity of the 6MIST-derived CPET or hemodynamic measurements. Moreover, we acknowledged the inherent physiological differences between upright (6MIST) and supine (iCPET) exercise and did not expect the interchangeable values between these 2 tests. Therefore, our primary aim was to assess the degree of consistency (ICC) rather than absolute agreement (BA plots). Finally, 6MIST was performed on the same day after iCPET which could have led to underperformance of the former due to fatigue. However, all patients rested for approximately an hour following iCPET prior to the augmented 6MIST.

In conclusion, we demonstrate the feasibility of a novel augmented 6MIST with wearable devices for simultaneous CPET and hemodynamic assessment. 6MIST-measured CPET parameters were strongly correlated with the iCPET-derived measurements, but the correlation of CI was not observed. Incorporating wearable devices into bedside CRF assessment may serve as a viable alternative to a standard CPET for certain indications. Additional studies are needed to confirm the validity of the 6MIST compared to standard upright CPET.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

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ADDRESS FOR CORRESPONDENCE: Dr Marat Fudim, Duke University Medical Center, 2301 Erwin Road, Durham, North Carolina 27710, USA. E-mail: Marat.fudim@duke.edu.

PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Augmented 6MIST with simultaneous portable metabolic breath analyzer and signal morphology-based impedance cardiograph is a feasible bedside test and could provide additional cardiopulmonary exercise parameters and exercise CO as a promising alternative to a formal CPET for certain clinical scenarios. Strong correlation of cardiopulmonary exercise metrics including peak VO_2 between 2 functional assessment strategies is demonstrated.

TRANSLATIONAL OUTLOOK: Further studies examining diagnostic and prognostic values of an augmented 6MIST would help further delineate the complementary roles of 6MIST to the standard CPET. Larger-scale studies are warranted to determine the feasibility of integrating 6MIST into routine clinical practice.

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KEY WORDS 6-minute incremental step test, cardiopulmonary exercise test, cardiorespiratory fitness, wearable devices

APPENDIX For supplemental figures, please see the online version of this paper.