# Cardiac Effort to Compare Clinic and Remote 6-Minute Walk Testing in Pulmonary Arterial Hypertension

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**BACKGROUND:** The SARS-CoV-2 pandemic has limited objective physiologic assessments. A standardized remote alternative is not currently available. "Cardiac effort" (CE), that is, the total number of heart beats divided by the 6-min walk test (6MWT) distance (beats/m), has improved reproducibility in the 6MWT and correlated with right ventricular function in pulmonary arterial hypertension.

**RESEARCH QUESTION:** Can a chest-based accelerometer estimate 6MWT distance remotely? Is remote cardiac effort more reproducible than 6MWT distance when compared with clinic assessment?

**STUDY DESIGN AND METHODS:** This was a single-center, prospective observational study, with institutional review board approval, completed between October 2020 and April 2021. Group 1 subjects with pulmonary arterial hypertension, receiving stable therapy for > 90 days, completed four to six total 6MWTs during a 2-week period to assess reproducibility. The first and last 6MWTs were performed in the clinic; two to four remote 6MWTs were completed at each participant's discretion. Masks were not worn. BioStamp nPoint sensors (MC10) were worn on the chest to measure heart rate and accelerometry. Two blinded readers counted laps, using accelerometry data obtained on the clinic or user-defined course. Averages of clinic variables and remote variables were used for Wilcoxon matched-pairs signed rank tests, Bland-Altman plots, or Spearman correlation coefficients.

**RESULTS:** Estimated 6MWT distance, using the MC10, correlated strongly with directly measured 6MWT distance ($r = 0.99$; $P < .0001$; in 20 subjects). Remote 6MWT distances were shorter than clinic 6MWT distances: 405 m (330-464 m) vs 389 m (312-430 m) ($P = .002$). There was no difference between in-clinic and remote CE: 1.75 beats/m (1.48-2.20 beats/m) vs 1.86 beats/m (1.57-2.14 beats/m) ($P = .14$).

**INTERPRETATION:** Remote 6MWT was feasible on a user-defined course; 6MWT distance was shorter than clinic distance. CE calculated by chest heart rate and accelerometer-estimated distance provides a reproducible remote assessment of exercise tolerance, comparable to the clinic-measured value. CHEST 2022; ■(■):■-■

**KEY WORDS:** 6-min walk test; heart rate; pulmonary arterial hypertension; remote

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### Take-home Points

**Study Question:** Can a chest-based accelerometer with heart rate monitoring estimate remote 6-min walk distance, and does incorporating heart rate determination improve the test?

**Results:** Remote 6-min walk test distance was less than the clinic measurement, whereas there was no difference between clinic and remote testing after adjusting for heart rate.

**Interpretation:** Incorporation of heart rate during remote 6-min walk testing provides data comparable to clinic assessment.

The 6-min walk test (6MWT) is a submaximal exercise test[1] and a core component of therapeutic research[2] and risk assessment[3-5] in pulmonary arterial hypertension (PAH). Beyond equipment for assessing vital signs, the 6MWT requires only an unobstructed walking space (preferably 30 m). The initial 6MWT validation study,[1] as well as subsequent follow-up studies,[6,7] have shown variability in repeat 6MWT distance for stable participants whose walks were > 400 m. This variability complicates interpreting changes in walk distances and, especially, in identifying a clinically meaningful improvement (the minimal clinically important difference[8]). Variability has made some speculate about a ceiling effect in PAH therapy trials despite the fact that walks > 500 m are routinely recorded.[9] On the other hand, decrements in 6MWT distance are more readily accepted as a marker of clinical worsening and an important negative prognostic sign.[10] In an attempt to improve the reproducibility of the 6MWT, we developed "cardiac effort," the total number of heart beats needed during the 6MWT divided by the 6MWT distance. This measure was less variable than 6MWT distance and sensitive to changes in therapy; it also correlated with two different assessments of right ventricular function.[7,11]

The SARS-CoV-2 pandemic has exposed the limitations of gauging objective exercise tolerance testing in patients with PAH. The difficulty of doing in-clinic hallway walks complicated efforts to restart therapeutic research after the first wave, and the absence of 6MWT data made risk assessment in clinical practice less meaningful. Masking during the 6MWT appears to decrease walk distance in patients with PAH,[12] which makes interpreting changes in walk distance challenging. Activity trackers capable of remote monitoring seem like an appealing alternative. However, prior studies in PAH have shown high sedentary times,[13-15] and there are limited data on the correlation between activity and PAH metrics[16] or hospitalizations.[17] We recently showed the variability in measurements using two different types of activity trackers worn at the same time in patients with PAH,[18] which further emphasizes the gaps in our knowledge about activity measures in PAH. Instead of collecting large amounts of data for 7 days and relying on proprietary algorithms to calculate activity time and steps, a remote 6MWT seems like a reasonable, objective alternative to assess patients. In contrast to the novelty of activity tracking data, our long history with 6MWT data should help us to understand and interpret the results. In non-PAH cohorts, remote 6MWTs have been studied using mobile phones[19] and accelerometers[20]; a recent two-center publication sheds light on this in patients with PAH.[12] These previous studies have shown correlation with directly observed walk distance.

We aimed to evaluate whether a chest-based accelerometer with ECG heart rate monitoring could be used to (1) estimate 6MWT distance in the clinic and at home through two different methods (counting laps and calculating vector sum); (2) evaluate the safety of remote 6MWT in PAH; (3) evaluate whether cardiac effort is a better remote measure than 6MWT distance by correcting for effort or shorter walk courses with extra turns; and (4) compare ECG heart rate monitoring vs. wrist-based photoplethysmography during 6MWT in PAH.

## Study Design and Methods

This was a single-center, prospective, observational study with institutional review board approval; it was completed between October 2020 and April 2021. Subjects with World Health Organization group 1 PAH[21] were recruited from our Pulmonary Hypertension Association-accredited comprehensive care center. Participants were eligible if they were stable in New York Heart

Association Functional class I-III without adjustment to vasodilator therapy for > 90 days; in addition, we required that they complete the 6MWT without stopping in an effort to decrease variability between clinic and remote 6MWT. All clinic 6MWTs were performed according to the American Thoracic Society criteria[22] without masks to minimize confounders between in-clinic and remote walks. As previously described,[7] two BioStamp nPoint sensors (MC10) were placed on the chest to record acceleration and

heart rate (by ECG) during all 6MWTs. During the 6MWT in the clinic, subjects also wore a model 3150 pulse oximeter (Nonin) on their wrist to measure continuous heart rate and pulse oximetry, using photoplethysmography (PPG). Remote 6MWTs were performed on at least a 9.14 m unobstructed and flat walking space. A picture of the walking space with a 30.48 m tape measure was sent to the study team to review for course safety and acceptability. Two orange cones were used to mark the space. During remote 6MWT, subjects wore the two chest sensors in the same anatomic location as during the clinic walk. We provided a smartphone that included the BioStamp nPoint (MC10) app. At the start of the 6MWT participants would hit "start" within the app, and the device would record and timestamp the 6MWT. Participants were instructed not to hold the phone during the walk, and at the end of 6 min an alarm on the phone would sound. On a provided sheet, the participant reported the Borg Dyspnea Index score (rating scale provided) after the walk and reported the number of laps completed on their walking space. The subject calculated a distance by multiplying the number of laps by the walking space distance; this calculation was independent of the separately collected accelerometry data. A physically present support person was encouraged but not required.

Participants completed two 6MWTs in the clinic (first and last) and two to four remote 6MWTs depending on the individual's schedule. All walks were completed within 2 weeks. Only one walk was allowed per day. All 6MWT distances (clinic and remote) were estimated by two blinded reviewers counting the number of laps based on a graph of acceleration data recorded by the MC10 BioStamp nPoint sensor during the 6MWT (Fig 1). The accelerometer-derived count of laps multiplied by the measured walking distance yielded an estimate for 6MWT distance; we compared these values with what was directly observed in the clinic or reported remotely. A second approach was taken to objectively quantify the raw acceleration data using vector magnitude counts and mean amplitude deviation. The MC10 BioStamp nPoint is a triaxial accelerometer gathering data at 31.25 Hz. Python was used for data analysis. Vector magnitude counts were obtained $[(x^2 + y^2 + z^2)^{1/2}]$[23] during the 6MWT, and the data were summarized by taking mean amplitude deviations[24] in epoch lengths of 5 s. Vector magnitude counts were reported without a unit, similar to a recent report.[16] Cardiac effort was calculated as previously described.[7] Adhesive reaction, falls, syncope, and other injuries were recorded during this 3-week observation period. We also collected baseline demographic and clinical information.

### Statistics

Wilcoxon matched-pairs signed rank tests, Spearman correlation coefficients, and Bland-Altman plots were used for comparisons. Estimated 6MWT distances using MC10 accelerometer data were compared with what was directly measured in the clinic. The average accelerometer-estimated 6MWT distance from the clinic was compared with accelerometer-estimated remote 6MWT distance. If subjects did four remote walks, only the middle two 6MWT distances were averaged. We used the same walks to calculate distance and cardiac effort. The same comparisons were made with vector magnitude counts and mean amplitude deviation from the accelerometry data.

## Results

We enrolled 20 participants; most were women with connective tissue disease and receiving combination therapy (Table 1). Eighteen subjects (90%) underwent paired clinic walks. Two individuals did not complete the second clinic walk because of surging SARS-CoV-2 cases. Participants demonstrated a wide range of clinic walk distances (220-570 m) with a median of 391 m.

Safety was a key concern. No participant or study team member tested positive for SARS-CoV-2 during the study activity period.

### 6MWT in the Clinic

There were no significant differences between directly observed in-clinic walks ($P = .44$) (Fig 2A), with a median difference of 6 (–9 to 12) m. We also found no
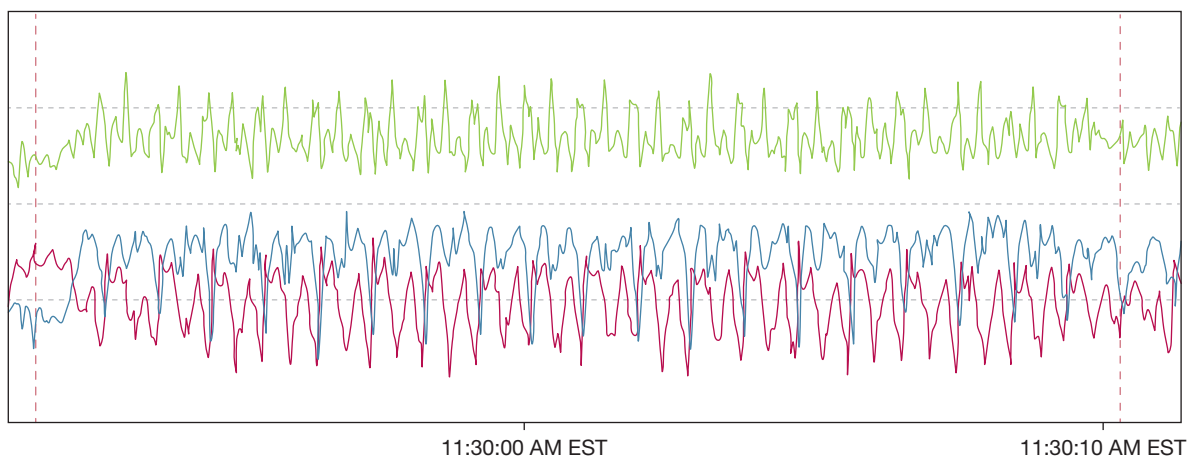


Figure 1 – Accelerometry data from BioStamp nPoint sensors (MC10) worn on the chest during a 6-min walk test. Shown are representative tracings of how laps were counted. The flat areas at the beginning and end signify turns, when no acceleration occurred. The area between the two red dashed lines represents one completed lap. The red, blue, and green tracings indicate acceleration in the x, y, and z axes. There is no ECG recording with this tracing.

TABLE 1 ] Baseline Demographics: n = 20 Patients

| Demographic | Value |
|---|---|
| Age, median (IQR), y | 59 (44-67) |
| Sex, female, No. (%) | 16 (80%) |
| BMI, median (IQR), kg/m$^2$ | 29.6 (23.9-35.2) |
| PAH etiology, No. (%) | |
|   Idiopathic | 6 (30%) |
|   Associated with: | |
|     Connective tissue disease | 12 (60%) |
|     Repaired congenital heart disease | 2 (10%) |
| PAH vasodilator therapy, No. (%) | |
|   None | 2 (10%) |
|   Monotherapy | 3 (15%) |
|   Ambrisentan/tadalafil | 13 (65%) |
|   Oral combination + treprostinil | 2 (10%) |
| REVEAL 2.0 Lite, median (IQR) | 4 (3-7) |
| French noninvasive, No. of low risk criteria, median (IQR) | 2 (1-3) |
| NT-proBNP, median (IQR), pg/mL | 166 (95-1,056) |
| Functional class (I/II), No. (%) | 2 (10%)/18 (90%) |
| Chronic hypoxic respiratory failure requiring supplemental oxygen, No. (%) | 2 (10%) |

IQR = interquartile range; NT-proBNP = N-terminal pro-brain natriuretic peptide; PAH = pulmonary arterial hypertension; REVEAL = Registry to Evaluate Early and Long-Term PAH Disease Management.

difference between the two clinic 6MWT mean amplitude deviation ($P = .17$) (Fig 2B). Using 38 clinic walks, we found that walk distance estimated by counting laps with MC10 BioStamp data (Fig 1) correlated very well with directly observed walk distance laps ($r = 0.99$; $P < .0001$) (Fig 2C). A Bland-Altman plot showed relatively narrow limits of agreement and little bias between directly observed and accelerometry-estimated 6MWT distance in the clinic (Fig 2D). To explore the possibility of using mean amplitude deviation as an objective measure of total activity during 6MWT, we found that mean amplitude deviation correlated quite well with directly observed walk distance ($r = 0.90$; $P < .0001$) (Fig 2E).

### Remote 6MWT

There were no episodes of syncope, falls, or skin irritation. The remote walking space was about one-half the distance of the clinic walking space (Table 2). We could not reliably count laps (and thus estimate remote distance) in one subject (5%) because of an abnormal gait in combination with a short walking space. That subject had an average step count of 261 steps in the clinic and 247 remotely (during the 6MWT). One 74-year-old did not record remote walk distances but did use the device appropriately, allowing for distance to be

calculated. For the two subjects with only one clinic walk, the single value was used for comparison.

In total, 65 of 69 remote walks were analyzed by counting laps (Fig 1) and compared with participant-reported walk distance, and 69 of 69 were analyzed to calculate the mean amplitude deviation during the 6MWT. A Bland-Altman plot showed less agreement between MC10 BioStamp nPoint-estimated remote 6MWT distance and what was measured by the participant (Fig 3A). The average difference between reported and estimated remote 6MWT distance was 2.8% ± 12.9%. This could reflect participant counting error on short walking spaces or premature turns. The correlation between reported and estimated remote 6MWT remained strong at $r = 0.81$, $P < .0001$ (Fig 3B). The median MC10-estimated clinic 6MWT distance was longer than the remote 6MWT distance: 405 (330-464) m vs 389 (312-430) m ($P = .002$) (Fig 3C). Using accelerometry-derived mean amplitude deviation, we found that the clinic 6MWT mean amplitude deviation was significantly higher than what was measured remotely: 188 (119-213) vs 154 (113-203) ($P = .005$) (Fig 3D). Mean amplitude deviation correlated with estimated remote walk distance, but not as well as in the clinic ($r = 0.75$; $P < .0001$) (Fig 3E).
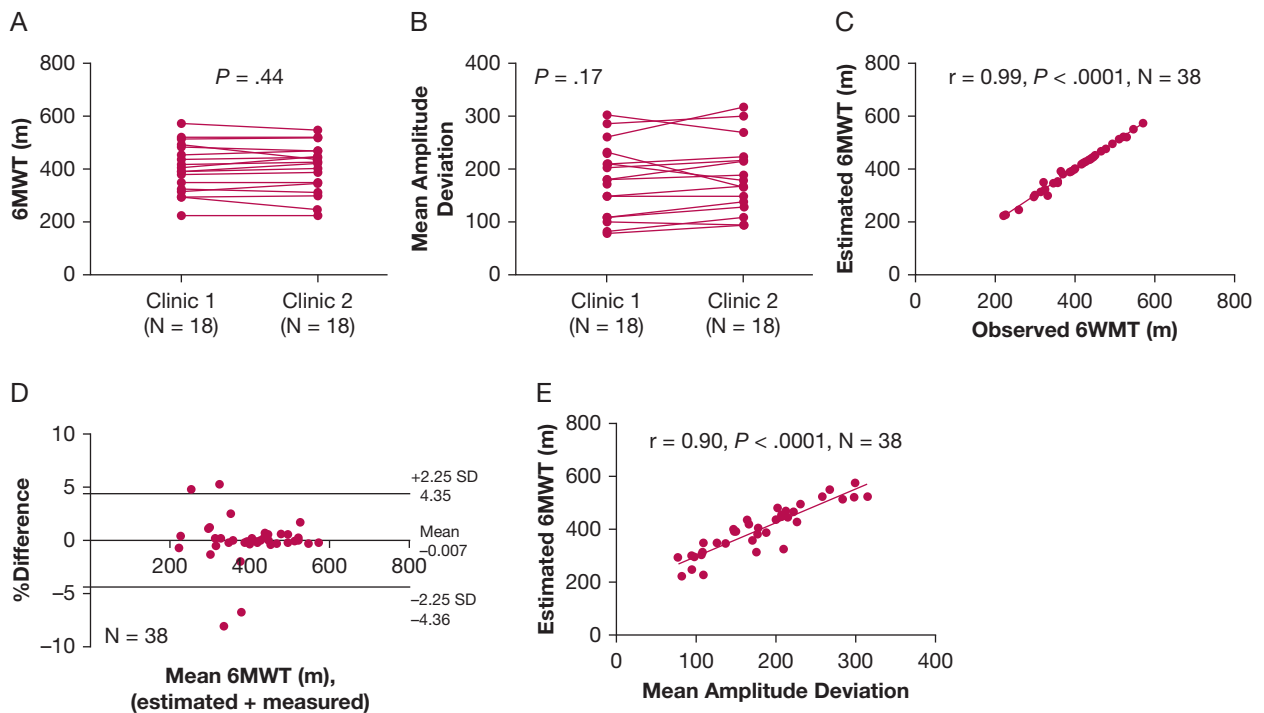
Figure 2 – Comparisons between the two observed clinic 6-min walk tests (6MWTs). A, There was no difference between the two in-clinic 6MWTs completed within 2 weeks. B, Accelerometry-derived mean amplitude deviation between the two walks appeared reproducible. C, There was a very strong correlation between directly observed and accelerometry-estimated 6MWT distances, using the MC10 BioStamp nPoint data (n = 38). D, Bland-Altman plot showed high agreement between directly observed and accelerometry-estimated 6MWT distance. E, Accelerometry-derived mean amplitude deviation had a strong correlation with estimated 6MWT distance from the clinic (n = 38).

### Heart Rate Monitoring

Thirty-one 6MWTs were performed in the clinic, during which subjects wore both MC10 BioStamp nPoint sensors (electrocardiography) and the Nonin 3150 (photoplethysmography) to measure continuous heart rate during the 6MWT. Seven walks had incomplete Nonin data. Peak heart rate [129 (119-144) beats/min vs 119 (109-129) beats/min; $P < .0001$], heart rate at 6 min [126 (116-136) beats/min vs 114 (90-124) beats/min; $P < .0001$], and total heart rate expenditure [730 (662-813) beats vs 658 (538-721) beats; $P < .0001$]

were significantly lower when measured by PPG. In addition to the large bias favoring the more accurate ECG measurement, Bland-Altman plots also showed wide limits of agreement between the two devices (Figs 4A-4C). We were unable to access the raw PPG data and relied on the algorithm for reporting heart rate (an additional limitation; in contrast, we were able to visualize the MC10 BioStamp nPoint data and verify the data quality).

Sixteen subjects (80%) had both clinic and remote heart rate data and walk distance estimated by MC10. Three

**TABLE 2 ]** Comparison Between Observed and Remote 6MWT

| Parameter | Clinic | Home | P Value |
|---|---|---|---|
| 6MWT walking course, m | 27.432 | 12.19 (10.66-12.80) | … |
| Peak HR,[a] beats/min | 129 (122-141) | 125 (117-136) | .07 |
| HR, end of 6MWT, beats/min | 123 (117-133) | 124 (111-131) | .41 |
| Heart rate expenditure,[b] beats | 731 (662-775) | 710 (624-768) | .15 |
| 6MWT distance,[a] m | 405 (330-464) | 389 (312-430) | .002 |
| Cardiac effort,[b] beats/m | 1.75 (1.48-2.20) | 1.85 (1.57-2.14) | .14 |
| Borg dyspnea index | 3.5 (2-5.4) | 3.4 (2.1-6.1) | .35 |

Values reported as median (IQR). 6MWT = 6-min walk test; HR = heart rate; IQR = interquartile range.
[a]Nineteen subjects had remote 6MWT distance estimated.
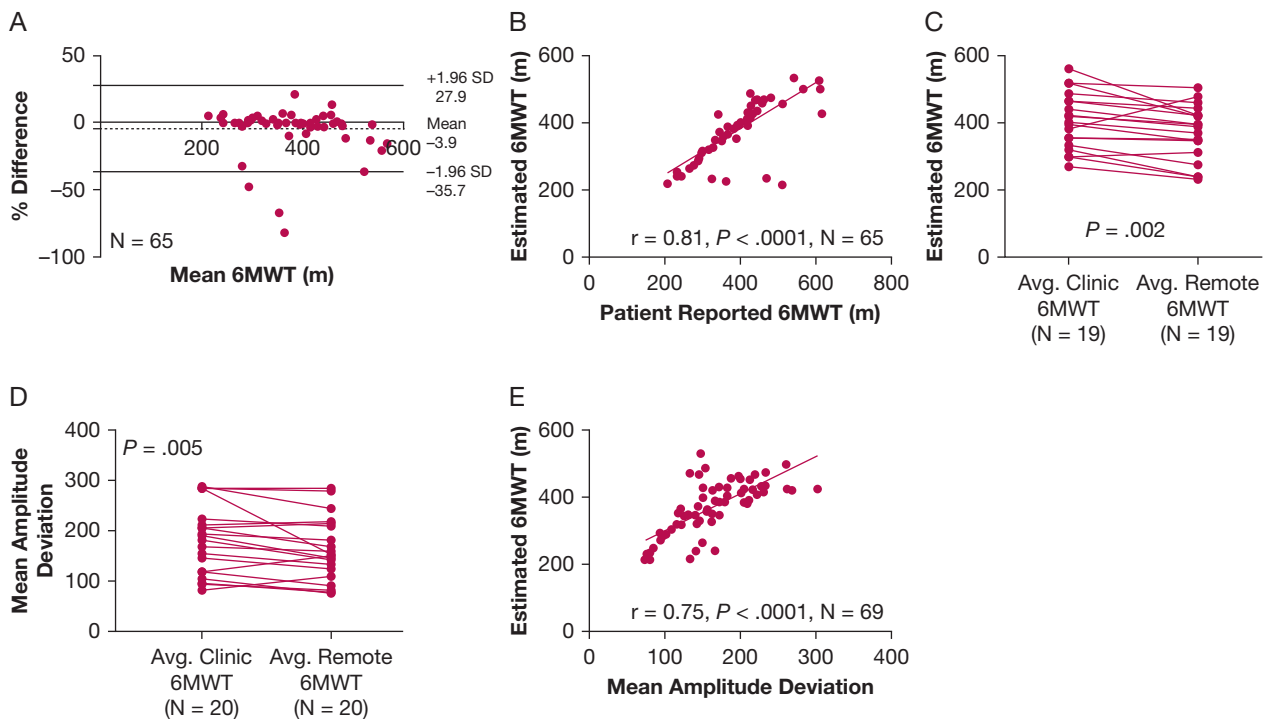[b]Sixteen subjects underwent complete remote heart rate monitoring.

Figure 3 – Remote 6-min walk test (6MWT). A, Compared with directly observed 6MWT in the clinic, a Bland-Altman plot showed wider variability between accelerometry-estimated and patient-reported 6MWT distance. This difference may reflect participant error in counting laps on a short distance. B, Correlation between accelerometry-estimated and patient-reported remote 6MWT distance was reasonably strong, but not as good as in the clinic. C, Participants walked farther during in-clinic 6MWT as compared with remote 6MWT (shorter course and no direct supervision). D, Similarly, accelerometry-derived mean amplitude deviation was lower remotely than in clinic. E, There was a reasonable correlation with accelerometry-derived mean amplitude deviation and estimated remote 6MWT distance, but not as tight as in-clinic measures.
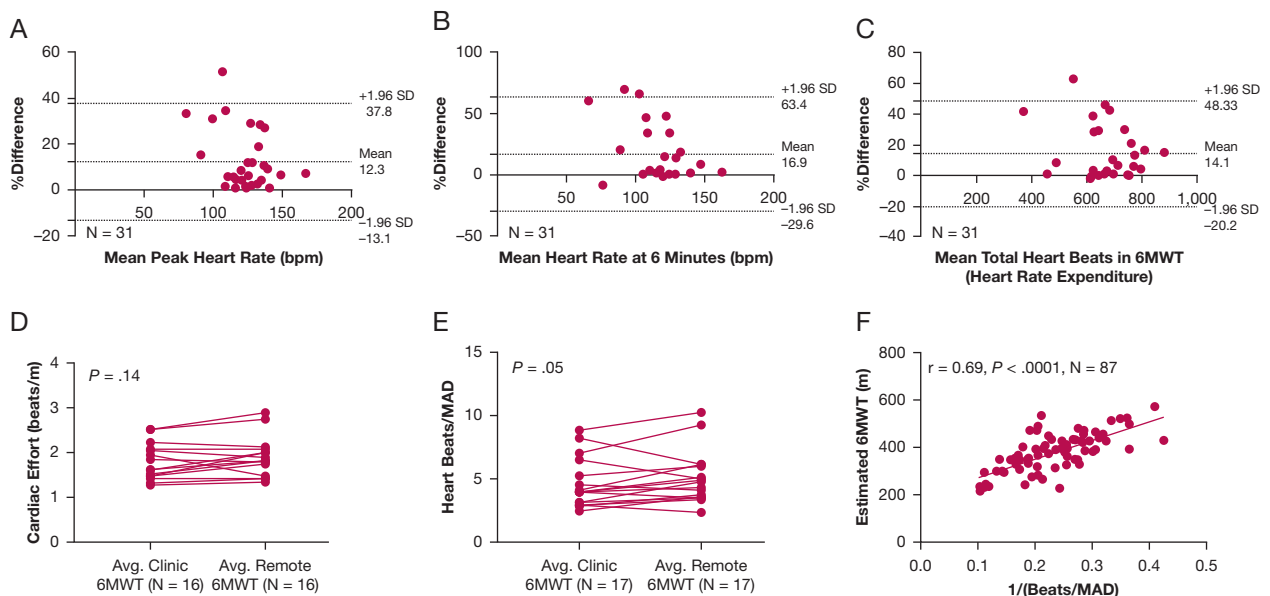


Figure 4 – Chest heart rate measurements significantly outperform photoplethysmography pulse measurements during the 6-min walk test (6MWT). A-C, Bland-Altman plots show wide limits of agreement between heart rate measured using electrocardiography and photoplethysmography during clinic 6MWT, with photoplethysmography nearly always biased toward an underestimate, sometimes markedly so. D, In 16 subjects who had data to calculate both in-clinic and remote cardiac effort, we found this physiologic assessment was reproducible between the in-clinic and remote measurements. E, in 17 subjects with accelerometry-derived mean amplitued deviation (MAD), we made a similar measurement by dividing total heart beats during 6MWT (heart rate expenditure) into the MAD; this physiologic adjustment of the MAD sum made the in-clinic and remote values more comparable. F, There was a reasonable correlation between heart rate expenditure (HRE)/MAD and accelerometry-estimated 6MWT, using MC10 BioStamp data (considering all walks, in clinic and remote).

subjects who had poor remote heart rate tracings were > 60 years old and had scleroderma. There was no difference between cardiac effort measured in the clinic vs what was obtained remotely [1.75 (1.48-2.20) beats/m vs 1.85 (1.57-2.14) beats/m; $P = .14$] (Fig 4D). Performing the same analysis using heart rate and mean amplitude deviation (beats/mean amplitude deviation), we found no difference between in-clinic and remote measurement (Fig 4E). In 87 clinic and remote walks with complete heart rate data, we found a reasonable correlation between 1/(beats/mean amplitude deviation) and estimated 6MWT distance ($r = 0.69$, $P < .0001$) (Fig 4F). Five subjects wearing the MC10 (25%) had atrial tachyarrhythmia identified during at least one 6MWT.

## Discussion

This single-center report demonstrates the benefit of incorporating accelerometry and continuous heart rate monitoring in a remote 6MWT to assess distance objectively in the home setting and to measure "cardiac effort" (heart beats per meter walked). The data confirm and extend our previous finding that cardiac effort is less variable than distance walked by showing that it "levels the field" between in-clinic and remote 6MWT, correcting for multiple factors, including extra turns with a shorter walking space and/or reduced effort (no staff). Like LaPatra et al,[12] we found that remote 6MWT in the home was safe and feasible for motivated patients with functional class II PAH, but we did ours without a team member supervising the walk. Our study was conducted during inclement weather months in Rochester, New York, and relied on modified walking spaces indoor, which increases the generalizability. Finally, our data make it clear that electrocardiographic heart rate monitoring is superior to photoplethysmography to measure heart rate and to calculate "cardiac effort" in PAH; there was also more data loss with photoplethysmography, and both of these observations confirm our previous report. Remote cardiac effort appears to be an easily obtained, objective physiologic assessment that can complement telemedicine and potentially facilitate therapeutic research.

The SARS-CoV-2 pandemic exposed the limitations of gauging objective exercise tolerance: either 6MWT could not be performed with telehealth visits or required a mask in routine clinic visits. All of the PAH risk assessments have 6MWT distance as a core component,[3-5] and thus much clinical care was done with incomplete risk assessment calculations. There is growing excitement in using wearable accelerometers to help improve care in PAH.[16,17] However, we recently showed significant variability in what different accelerometers measure when worn at the same time on different parts of the body,[18] and further studies are needed to determine the optimal device, wear time, and body location (hip vs wrist) before they are incorporated into routine clinical care.

Until we can better correlate activity measures with our established metrics in PAH, it would be desirable to incorporate remote 6MWT into routine PAH care. Standardized methods for remote 6MWT would allow spot objective testing to be done as a complement to telehealth or between clinic visits to guide decisions (eg, prostacyclin dose titration or the timing of an echocardiogram). The traditional 6MWT is staff supervised within an unobstructed 30-m hallway[22]; especially indoors, most patients will not be able to replicate this hallway at home. Others have reported different strategies for remote 6MWT including algorithms developed to estimate walk distance based on wearables[20,25] or smartphones[19,25-28]; global positioning system (GPS)-enabled devices can estimate walk distance outdoors,[19,29] and LaPatra et al[12] used remote observation. These different approaches were tested in a wide variety of individuals including healthy control subjects[27] and patients with strokes,[29] pulmonary hypertension,[12] peripheral vascular disease,[26] and coronary artery disease[26]; the courses were also variable. All of the different methods showed high agreement between estimated and directly measured 6MWT distance, performed at about the same time. Algorithms that estimate 6MWT may not perform as well in disease states with altered gaits (eg, neurologic disease, using a walker, pulling an oxygen tank); algorithms can also be influenced by how well the device is secured, subject age or height, performance of turns, and walking speed.[20,30] GPS-based strategies are limited to outdoor walking, may suffer interference in dense urban areas with buildings, and will be influenced by weather. Wevers et al[29] also found that > 10% of patients felt uncomfortable with a neighbor observing them doing a 6MWT outdoors. Patient motivation, especially in those with cardiopulmonary disease, may fall in an unsupervised walk and thus might make interpreting walk distance difficult. We found that our indoor strategy accommodated a variety of different hallway lengths, was easy and reproducible for motivated participants (over a wide range of 6MWT distances), and was not overly susceptible to gait alterations.

Specifically, in a PAH cohort, we observed that participants in an unsupervised, shorter walking space walked less compared with direct supervision in the longer clinic hallway. LaPatra et al[12] measured no systematic difference in a cohort of patients with PAH/chronic thromboembolic pulmonary hypertension who had similar walking distances in the clinic and remotely. We think two key methodologic differences likely explain the different observations. We allowed greater flexibility in defining a walking space (9.14 m of unobstructed space), as opposed to LaPatra et al,[12] who required that participants find a 30-m remote walking space. A 30-m unobstructed indoor walking space would be difficult for many patients to find. In addition, our participants did their 6MWT without assistance, whereas LaPatra et al[12] dedicated a study team member to be involved with all of the walks; this supervision may have increased motivation and may not be a sustainable or generalizable strategy.

Our data strongly suggest that using cardiac effort (number of heart beats per walk distance) is a reliable way to account for any differences in course construction or motivation during a remote 6MWT. Conceptually, it is also a more direct interrogation of a patient's cardiac physiology with structured physical activity. Moreover, unlike activity measures, which are heavily influenced by intrinsic patient traits, the standardized instructions of the walk with continuous ECG monitoring could provide a measure that is relatively independent of motivation. We think our strategy has two key advantages over previous reports: (1) no specific hallway length is required; and (2) it is more comfortable for those who don't want to be observed outside. The MC10 is a single device capable of objective confirmation of number of laps (accelerometry) along with continuous heart rate monitoring to calculate cardiac effort more accurately than photoplethysmography. Importantly, in our 20-patient cohort we did not observe any safety concerns, although only functional class I/II patients chose to enroll.

There are limitations to our study. This was completed in a small and very motivated cohort in the winter months during the COVID pandemic. Only stable functional class I/II subjects were enrolled. We cannot comment on the safety or reproducibility of remote 6MWT in a functional class III cohort or in the setting of medication titration. Further studies are needed in those instances. Three older patients with scleroderma had poor remote heart rate recordings that prevented cardiac effort from being calculated. The challenge was likely related to them having difficulty adequately securing the adhesive to their skin, as their clinic and remote resting heart rate recordings were usable. Two patients completed only a single clinic 6MWT because of a second COVID surge. Our method for calculating distance relies on knowing the hallway length, and in one case, a sufficiently aberrant gait prevented us from recognizing turns in the data. Our data analysis was labor intensive, but we are currently working on automating several features of the analysis.

## Interpretation

Using MC10 nPoint accelerometry and heart rate data provided a relatively easy, safe, and reproducible way to perform an indoor, remote 6MWT. By incorporating heart rate measures during the 6MWT and calculating cardiac effort, we extended our previous finding that cardiac effort reduces between-test variability as compared with walk distance, this time reducing the variability between clinic and remote testing. This reduced variability should make the cardiac effort measure more sensitive to real change (in either direction) and perhaps allow direct comparison between remote and in-clinic measurements. Further studies are needed to validate cardiac effort in multicenter cohorts and to evaluate its relation to outcomes over time.

## Acknowledgments

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