

The Digital 1-Minute Walk Test: A New Patient-centered Cardiorespiratory Endpoint

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Contributorship statement

LR and JN are joint first authors of this manuscript. LR, JN and MT conceived and designed the study. LR and JN acquired, analysed and curated the data. LR and JN drafted the initial manuscript and produced the figures. SC, MF and IA assisted with the co-design of this research with patient input. EFM and EHD oversaw the development of the digitalisation of the 1MWT and 6MWT on Aparito's Atom5™ platform. All authors reviewed and edited the manuscript.

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To the Editor:

The 6-Minute Walk Test (6MWT) is widely used in cardiorespiratory clinical trials and practice. The original study that defined the six-minute timeframe concluded that this was a “*sensible compromise*” when durations from two to twelve minutes were all comparable[1]. This set a precedent which has rarely been challenged. As many clinical endpoints are transferring from the clinic to the community, a shorter walk would be technically easier and more practical for patients. It can be challenging for patients to find spaces that allow an appropriate unimpeded, flat 6MWT track indoors or outdoors. Our previous patient engagement initiative showed that patients are enthusiastic about digital and community measures of exercise capacity[2]. We set out to design a community digital exercise capacity test that was acceptable to and practical for patients across two different cardiorespiratory diseases with well-established evidence-bases for the 6MWT: pulmonary hypertension (PH) and interstitial lung disease (ILD). Some of the results of these studies have been previously reported in the form of an abstract[3].

Methods

Consecutive adult outpatients who undertook a routine clinical 6MWT[4] with an established diagnosis of PH or ILD were included. During a standardised specialist centre-based 6MWT, distance walked was recorded at 1,2,3,4 and 6 minutes (October 2019 to January 2020). Three-year mortality data was captured prospectively from electronic health records. PH patients had quality-of-life data collected via a validated disease-specific Patient-Reported Outcome Measure (CAMPHOR)[5]. The primary aim was to establish the extent to which shorter timed walk distances correlate with

the 6MWD whilst not losing important and established prognostic associations with mortality. This study was approved by Royal Papworth Hospital research governance committee.

A subsequent prospective study of the optimal defined timeframe (the digital 1MWT or d1MWT) was conducted. Patients were recruited from The National Cohort Study of Idiopathic and Heritable PAH (IRAS-123349) with Research Ethics Committee approval from the East of England (13/EE/0203). For a correlation coefficient of 0.80 for d1MWT vs ground truth distance, α of 0.05, 80% power and a potential dropout rate of 20%, the minimum estimated sample size was $n=12$. Following a rest period, patients were asked to walk as far as possible in one minute on a flat, even, firm, dry and uninterrupted outdoor surface (January to September 2023). Patients chose the route and self-paced without the need to complete laps or circuits. Patients wore a provisioned Garmin Venu 2 smartwatch on their non-dominant wrist, paired with a customised digital walking module on the Atom5™ (Aparito Ltd) mobile application on the patients' own smartphone (iOS or Android). The d1MWT platform was co-designed with patients in partnership with Pulmonary Hypertension Association UK and tested for usability and technical aspects. Data captured included distance (via GPS, GLONASS and Galileo), heart rate, step count and Borg scores. The outdoor ground truth distance was directly measured using an analogue trundle measuring wheel (SKU-1-77-17). After resting for an hour, patients completed the gold standard indoor 6MWT[4] supervised by a physiologist blinded to the d1MWD. Having completed both tests, patients were asked to qualitatively score their preferences on test duration and modality by an independent researcher on 5-point Likert scales.

Results

192 patients (102 PH; 91 ILD) performed a 6MWT (Table 1). The shorter duration walk tests (1/2/3/4 minutes) strongly correlated with the 6MWD in both the PH and ILD cohorts (Figure 1A & 1B). There was a moderate correlation between the 1MWD in the PH cohort and CAMPHOR scores across all three domains: activity, symptoms and quality of life ($r=-0.57$, $r=-0.53$, $r=-0.39$, all $p<0.01$), consistent with the 6MWT ($r=-0.62$, $r=-0.59$, $r=-0.45$, all $p<0.01$). There was equivalent 3-year mortality prediction for 1MWT and 6MWT within each cohort (Figure 1C). The Youden index determining the optimal discriminatory threshold for mortality prediction was similar in both cohorts: 59 metres in the PH cohort (Log-rank $p<0.001$) and 60 metres in the ILD cohort (Log-rank $p<0.01$)(Figure 1D).

26 patients with Group 1 PAH were enrolled in the d1MWT study (77% (20/26) female; mean age 51 years (SD 15.0)). There were no adverse events. There was a strong correlation of $r=0.92$ ($p<0.001$) between the d1MWD and the ground truth 1MWD with good agreement (Figure 1E). There was a strong correlation between the d1MWD and both the distance walked in the first minute of the 6MWT ($r=0.91$, $p<0.001$) and the 6MWD ($r=0.86$, $p<0.001$) (Figure F). As a measure of test-retest repeatability for independent community-based d1MWTs, the intraclass correlation coefficient (ICC) was 0.86 (95% CI 0.40-0.97) comparable to an ICC of 0.95 (0.72-0.99) for d6MWTs. Patients expressed a preference for shorter timed walk tests and remote testing via smart technology (Figures 1G & 1H).

Discussion

Walk tests of shorter duration correlate strongly with the 6MWT, CAMPHOR scores (especially symptomatology and activity) and mortality at three years. These are comparable findings across two distinct disease cohorts – PH and ILD. The d1MWT showed technical accuracy relative to the ground truth distance, construct validity relative to the 6MWT and excellent patient acceptability.

Shorter walk tests have cost-saving and feasibility implications, with reduced burden on patients. In an outdoor setting, patients are more likely to find appropriate uninterrupted routes when walking for shorter durations. Not only do these self-directed naturalistic routes more meaningfully reflect patients' real world function, but they are also more accurately measured by GPS compared to outdoor 6MWTs[6] or by inertial measurements[7,8], and correlate with peak VO_2 on cardiopulmonary exercise testing (CPET)[9].

The d1MWT can be deployed more frequently and conveniently than snapshot in-centre measures. This will improve trial data granularity and likely decrease signal-to-noise ratio. Decentralised endpoints are more patient-centred in reducing travel and invasive testing, and hold the promise of enhancing patient recruitment and retention – common barriers to trial completion[10].

A notable strength of the digital study is the co-design with patients. Participant-centric designs with input from patients as partners throughout the entire research cycle have been shown to improve retention and engagement in longer term digital health studies[11]. Limitations include the possible effect of topographical and meteorological

factors in outdoor testing, but this is offset by the shorter time period of the 1MWT. Future research will include deriving reference equations for the interpretation of the d1MWT beyond the illustrative prognostic thresholds shown here – 59 metres (PH) and 60 metres (ILD).

In conclusion, this novel digital 1MWT co-developed with patients is safe and shows technical accuracy, construct validity, repeatability and patient preference. It could provide a solution to the need to innovate endpoints in clinical trials of cardiopulmonary disease as they become increasingly decentralised and patient-centred.

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Figure 1 legend:

Figure 1. Correlation analyses for the distance walked in the first 1, 2, 3 and 4 minutes of the 6MWT against the total 6MWD for the n=102 PH cohort (A) and n=91 ILD cohort (B). (C) Receiver operating characteristic (ROC) curves showing the ability of the 1MWT and 6MWT to predict 3-year mortality in the PH and ILD cohorts. (D) Kaplan-Meier survival curves for patients above and below the 1MWD thresholds of 59 metres for the PH cohort (grey lines) and 60 metres for the ILD cohort (black lines). (E) A Bland-Altman plot of average of against difference between n=26 digital 1MWDs and ground truth 1MWDs. (F) A correlation analysis of the n=26 digital 1MWD against the gold standard 6MWD. (G & H) Bar charts of the independently captured patient-reported Likert scale responses from n=26 patients in the digital study regarding preference of walk test modality and duration having completed both a gold standard in-centre 6MWT and outdoor digital 1MWT.

Table 1 legend:

Table 1. Table of patient demographics, anthropometrics and disease classification for the pulmonary hypertension (PH) and interstitial lung disease (ILD) cohorts who were followed up for 3-years following the in-centre 6MWT.

¹Pulmonary hypertension as defined by the haemodynamic values described in the 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension.

**CTD = connective tissue disease*

†HIV = human immunodeficiency virus

‡LHD = left heart disease

§CHD = congenital heart disease

***CTEPH = chronic thromboembolic pulmonary hypertension*

††CTEPD = chronic thromboembolic pulmonary disease (without PH)

‡‡COP = cryptogenic organising pneumonia

§§CTD-ILD = connective tissue disease ILD

****HP = hypersensitivity pneumonitis*

†††IPF = idiopathic pulmonary fibrosis

‡‡‡LCH = Langerhans cell histiocytosis

§§§NSIP = non-specific interstitial pneumonia

Table 1:

Disease cohort	Pulmonary hypertension ¹ (n=102)	Interstitial lung disease (n=91)
Sex		
Female	54 (53%)	27 (30%)
Male	48 (47%)	64 (70%)
Age (years)		
Mean (SD)	58.6 (15.3)	69.5 (12.7)
Min-max	18-82	22-94
Height (cm)		
Mean (SD)	168 (8.8)	169 (9.4)
Min-max	147-188	151-192
Weight (kg)		
Mean (SD)	79 (20.7)	82.3 (16.8)
Min-max	46.6-131	46-135
BMI (kg/m ²)		
Mean (SD)	27.9 (6.5)	28.8 (5.4)
Min-max	18.6-46.2	16.7-42.6
PH classification		
Group 1	36 (35%)	-
Idiopathic	28 (27%)	-
CTD*	5 (5%)	-
HIV [†]	1 (1%)	-
Portal hypertension	2 (2%)	-
Group 2	2 (2%)	-
PH due to LHD [‡]	1 (1%)	-
PH due to CHD [§]	1 (1%)	-
Group 4	61 (60%)	-
CTEPH** - pre-operative	5 (5%)	-
CTEPH** - post-operative	35 (34%)	-
CTEPH** - inoperable	21 (21%)	-
Other	3 (3%)	-
CTEPD ^{††}	3 (3%)	-
ILD classification		
COP ^{‡‡}	-	6 (7%)
CTD-ILD ^{§§}	-	2 (2%)
HP ^{***}	-	7 (8%)
IPF ^{†††}	-	52 (57%)
LCH ^{‡‡‡}	-	1 (1%)
Mixed ILD	-	1 (1%)

NSIP\$\$\$	-	3 (3%)
Sarcoidosis	-	15 (16%)
Unspecific ILD	-	4 (4%)

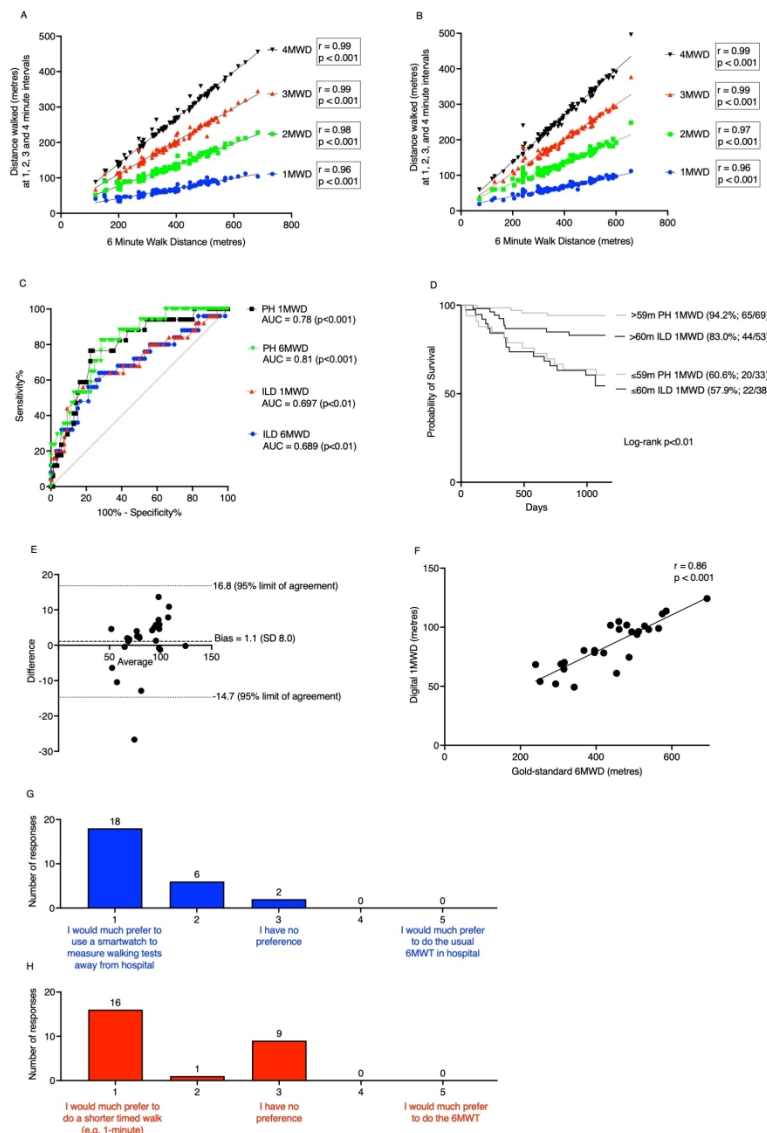


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