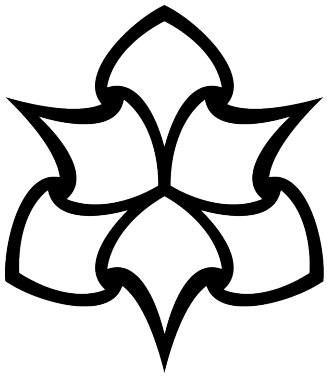

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Early View

Original research article

Pulmonary hypERtension and measurement of exerciSe caPacIty REmotely: evaluation of the 1-minute sit to stand test (PERSPIRE): a cohort study

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Pulmonary hypERtension and measurement of exerciSe caPacIty REmotely: evaluation of the 1-minute sit to stand test (PERSPIRE): a cohort study

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Abstract

Background

Multi-parameter risk assessment is recommended to aid treatment decisions in patients with pulmonary arterial hypertension. The 1-minute sit-to-stand test has been validated for use in other respiratory illnesses. The aim of this study was to evaluate its safety in the hospital setting and potential utility in remote assessment in patients with pulmonary hypertension.

Methods

In a prospective cohort study design patients performed the 1-minute sit-to-stand and Incremental Shuttle Walk tests on the same day. The primary aim of the study was to assess safety signals and correlations with other metrics used in risk assessment.

Results

Sixty patients with pulmonary arterial hypertension and 15 with chronic thromboembolic pulmonary hypertension were enrolled. No adverse events were recorded. Post-test change in physiological parameters was lower for the 1-minute sit-to-stand than for the Incremental Shuttle Walk test in heart rate (+9.4(8.0)bpm vs +38.3(25.9)bpm ($p<0.001$)), oxygen saturation (-3.8(4.0)% vs -8.9(7.3)%, ($p<0.01$)) and systolic blood pressure (+10.1(10.5)mmHg vs +17.7(19)mmHg, $p<0.001$). There were significant correlations between the 1-minute-sit-to-stand and Incremental Shuttle Walking test ($r= 0.702$, $p< 0.01$), WHO FC (-0.449, $p<0.01$), emPHAsis-10 (-0.436, $p<0.001$) and NT-proBNP (-0.270, $p=0.022$). Ninety-seven percent of patients were willing to perform the test at home.

Conclusion

This study has demonstrated the safety, sub-maximal characteristics of the 1-minute sit-to-stand test in pulmonary arterial hypertension chronic thromboembolic pulmonary hypertension in the hospital setting, its positive correlation with the Incremental Shuttle Walk test and potential role in remote risk assessment. Further evaluation of this exercise test is now warranted.

Background

Pulmonary hypertension is a chronic, progressive life-limiting condition with a number of causes.[1] An increase in pulmonary vascular resistance and right ventricular afterload arise from re-modelling of the pulmonary arterioles in pulmonary arterial hypertension (PAH), and obstruction of the vasculature by chronic clot and a variable vasculopathy in chronic thromboembolic pulmonary hypertension (CTEPH).[1] The diagnosis of pulmonary hypertension is confirmed at right heart catheterisation and is currently defined in guidelines[2] as a mean pulmonary arterial pressure of at least 25mmHg, although the 6th World symposium have proposed a new definition based on 20mmHg being the upper limit of normal.[3] Patients will typically demonstrate symptoms of breathlessness and limited exercise capacity.[1]

Drug therapies for PAH and CTEPH are focussed on slowing disease progression and minimising symptom burden. In selected patients with CTEPH, pulmonary endarterectomy offers the prospect of cure, whilst balloon pulmonary angioplasty is also associated with significant symptomatic and haemodynamic benefits.[4] Due to the progressive nature of PAH, guidelines[2] recommend regular multiparameter risk assessment and stratification, which may prompt change in treatment.[2] A number of risk assessments exist - all include measures of World Health Organisation functional class (WHO-FC), exercise capacity and right ventricular function. Hospital-based objective measures of exercise capacity used in risk assessment in PAH include the sub-maximal 6-minute walking test (6MWT)[5] and maximal tests including the Incremental Shuttle Walk Test (ISWT)[6] and cardiopulmonary exercise testing (CPET).[7] In CTEPH, data has also shown that the 6MWT can be used in the risk assessment of patients.[8]

The onset of the COVID-19 pandemic has increased the use of remote clinical consultations and highlighted the need to develop and validate alternatives to hospital-based exercise testing to aid risk assessment and stratification.[9] The 1-minute sit-to-stand test (1MSTS) is a simple exercise test where patients are asked to stand up from a chair repeatedly for 1 minute. It has been evaluated in

healthy subjects and patients with cardiorespiratory conditions including chronic obstructive pulmonary disease (COPD),[10] where it has been shown to correlate with the 6MWT,[11, 12] quadriceps strength[13] and levels of physical activity.[14] 1MSTS does not rely on patients having access to equipment or infrastructure and is therefore widely accessible and suggested for use in the home setting.[15, 16]

To date, the 1MSTS has not been evaluated in patients with pulmonary hypertension. This study has investigated the safety of the 1MSTS in the hospital setting and its potential for use in remote risk assessment of patients with PAH and CTEPH.

Methods and Materials

In this prospective cohort study, patients with PAH and CTEPH were identified from the Sheffield Pulmonary Vascular Disease Unit between June and December 2021.

Inclusion criteria required patients to be >= 18 years of age with a diagnosis of PAH or CTEPH following multimodality testing including right heart catheterization, as defined in guidelines.[2]

Patients were excluded if also presenting with significant mobility issues, uncontrolled systemic hypertension (systolic > 220mmHg or diastolic >120mmHg) or hypotension (systolic < 90mmHg or diastolic < 60mmHg), resting tachycardia (>130bpm), cognitive impairment that would prohibit informed consent. Also excluded were patients who had experienced surgery, myocardial infarction, pneumothorax or stroke within the past 8 weeks, or chest pain, haemoptysis, or syncope within the last 2 weeks. To avoid selection bias, all patients attending on days where recruitment occurred were screened for the study.

Sample size estimation

Sample size in correlation studies can be estimated by using estimates of the effect size in t-test calculations.[17] In this study, effect sizes were estimated using comparable studies in COPD which

included samples of 48 and 52 participants,[11, 18] and identified correlation coefficients between 1MSTS and 6-minute walk distance (6MWD) of between r=0.57 and r=0.67. Based on these values, assuming Type I error rate=0.05 and Type II error rate=0.2, a sample size of between n=22 (r=0.5) and n=15 (r=0.6) was indicated.[17] To capture participants with a range of exercise capabilities, a stratified sample was selected across three bands of ISWT distance: ≤ 180m, 190m – 330m, ≥ 340m.[6] To accommodate this, a total sample of 75 was sought, with a minimum of 22 participants in each of the three ISWT bands.

Exercise testing and data collection

The ISWT was conducted first, on a 10m corridor and performed using a standard protocol.[19] As per American Thoracic Society guidelines for repeat exercise testing, participants rested for at least 30 minutes before undertaking the 1MSTS test.[19]

The 1MSTS used an armless chair of 46 to 48cm height and was performed as previously described.[11] Participants were instructed to stand up and sit down as many times as they could within one minute, without using their arms. They were advised to fully stand up on each repetition, and either come fully to sitting, or tap their bottom on the chair before standing back up. They were advised to use rest periods if needed, and to stop before the end of the test if necessary. They were informed when 15s of the test time remained.[11] As the ISWT is standardly conducted in the study setting without supplemental oxygen, regardless of whether patients are on long term or ambulatory oxygen therapy,[6] the same approach was adopted for the 1MSTS.

The number of completed levels on the ISWT was recorded and expressed as metres and the number of full repetitions in the 1MSTS was recorded. Heart rate, blood pressure and oxygen saturations were captured before and after both tests, along with a patient reported measures of dyspnoea.[20] Adverse events e.g. dizziness, syncope or the participant becoming unwell were also recorded. Where participants stopped the test within 1 minute, the reason for stopping was

captured. Routine clinical assessments recorded on the day of testing were also captured, including N-terminal pro b-type natriuretic peptide (NT-proBNP), emPHasis10 (patient reported outcome measure in pulmonary hypertension)[21] and WHO-FC.

Survey

On completion of testing a short survey was conducted to assess the potential for a future study assessing the 1-minute sit-to-stand performed by patients at home. Participants were asked if they would be happy to perform the test at home, and if they had access to device to measure physiological parameters – blood pressure, weight, heart rate, oxygen saturations.

Statistics

Descriptive statistics were used to describe demographics and key characteristics at diagnosis and at the time of testing. Spearman's rank correlations were used to compare the two tests. Paired t-tests were used to examine difference in physiological characteristics of the tests. Where data is normally distributed, results are presented as mean (standard deviation), otherwise as median (interquartile range).

Patients identified and approached by PHA UK (the UK patient charity for patients with pulmonary hypertension) were consulted in the study design, involved in the development of study materials, and participated in the study steering committee.

The study protocol was approved by the National Health Service Health Research Authority (protocol reference number: 21/EE/0074). The study was registered at ClinicalTrials.gov (NCT04903704). Written informed consent was obtained.

Results

Participant characteristics

Of 75 participants, 60 (80%) had a diagnosis of PAH. 15 (20%) were diagnosed with CTEPH, of whom 6 had residual pulmonary hypertension following pulmonary endarterectomy (PEA) surgery, 3 had residual pulmonary hypertension following balloon pulmonary angioplasty (BPA), 3 were ineligible for PEA or BPA, and 3 had declined these interventions. 58 (77%) of participants were female.

At diagnosis, the mean age was 52 (16.8) years, 95% of participants were in WHO FC III or IV with a mean pulmonary arterial pressure (mPAP) of 48mmHg (13.3), PAWP 10 (5) mmHg and PVR of 764 (388) dynes/m^2 (Table 1). A detailed breakdown of PAH subgroups is in the supplementary material (Table S1). On the day of testing, patients were on average 4.3 (4.2) years post-diagnosis. 68% were in WHO FC III or IV, with an ISWT of 281m (174.4), NT-proBNP 339ng/L (120-723) and an emPHasis10 score of 27 (19 – 34) (Table 2).

Safety and adverse events

75 hospital-based 1MSTS tests were conducted with no adverse events. One participant reported feeling anxious at the end of the 1MSTS test, recovering after less than 5 minutes of rest. Two participants terminated the test before the end of 1 minute, after 50 and 55 seconds, due to shortness of breath and leg pain (Table S2).

Comparison of exercise tests

Compared to the 1MSTS, patients undergoing the ISWT had a significantly greater fall in oxygen saturation from baseline when compared to post-test measures (3.8(4.0) % vs 8.9(7.3) %, $p<0.01$) and a greater rise in heart rate (9.4 (8.0) bpm vs 38.3 (25.9) bpm, $p<0.001$), systolic blood pressure (10.1 (10.5) mmHg vs 17.7 (19) mmHg, $p<0.001$), diastolic blood pressure (2.9(7.8) vs 10.3(15.1), $p<0.01$), and Borg breathlessness score (2.8 (1.7) vs 3.7 (2.2), $p<0.001$) (see Table 3).

There were significant correlations between the 1MSTS and the ISWT (r= 0.702, p < 0.01). Correlations within the risk stratification bands were: high risk (r=0.391, p=0.044, n=27), intermediate risk (r=0.300, p=0.165, n=23), low risk (r=0.667, p<0.01, n=25). The 1MSTS correlated significantly with WHO FC (-0.503, p<0.01), emPHAsis-10 (-0.436, p<0.001) and NT-proBNP (-0.262, p=0.028). There were also significant correlations between the ISWT and WHO FC, emPHasis-10 and NT-proBNP (Table 4). Scatterplots of 1MSTS versus Incremental Shuttle Walk Distance (ISWD), WHO FC, NT-proBNP and emPHAsis-10 scores are shown in Figure 1. Figure 2 shows Box plots of 1MSTS in each of the risk stratification bands.

Survey Results

97% of participants surveyed (n=67) indicated that they would conduct a 1MSTS at home as part of a remote assessment, with 90% having access to weighing scales, 45% an oxygen saturation monitor, and 40% a sphygmomanometer at home (Table S3).

Discussion

To our knowledge this is the first study to examine the 1MSTS test in patients with PAH and CTEPH. We have demonstrated that it is a safe, sub-maximal test, that correlates strongly with ISWT distance and other metrics used to assess disease severity and has the characteristics of an exercise test that could be performed by patients remotely in the home.

Safety

No adverse events occurred in 75 hospital-based 1-minute sit-to-stand. This is consistent with an acceptable safety profile, supporting further exploration of the 1MSTS for remote assessment of exercise capacity in the home setting. Two patients undergoing hospital-based testing stopped before the end of the test due to leg pain and shortness of breath, in accordance with the test protocol.[19]

Test characteristics

Our study demonstrates the sub-maximal nature of the 1MSTS when compared to the ISWT in PAH and CTEPH, with lower post-test changes from baseline in heart rate, oxygen saturation, systolic blood pressure and Borg score when compared to changes observed with the ISWT. This is in accordance with the findings of Ozalevli et al.[12] who compared the 1MSTS to the 6MWT in patients with COPD.

This study also shows a strong correlation between the 1MSTS and ISWT ($r=0.702$, $p<0.001$). The 1MSTS also correlates significantly with other measurements used to assess patients with PAH and CTEPH, namely WHO-FC ($r=-0.449$), NT-pro BNP ($r=-0.270$) and emPHasis10 ($r=-0.436$). Furthermore, these correlations were similar to those of the ISWT with the same parameters. Comparable studies in COPD, with smaller sample sizes, identified correlation coefficients between 1MSTS and 6MWD of between 0.57 and 0.67[11, 18] as well as an association with age, quality of life and muscle strength.[11, 12, 18]

The 1MSTS test comprises an activity commonly performed in daily life. This functional feature, along with the sub-maximal characteristics of the test, absence of adverse events in this study, its positive correlation with the ISWT, scatter and distribution of values, suggests there is potential for its use as an exercise test conducted by patients at home, as a surrogate for hospital-based exercise testing. This is an important finding in the context of the increased use of remote consultations in the management of patients with PAH and CTEPH. The advantages of remote consultation include the potential for more frequent monitoring whilst reducing patient travel, stress and fatigue, improved access for patients with disabilities and potential cost savings.[22] This approach can also empower patients to take a more active role in their own monitoring and can support patient-initiated follow-up. Increasingly, pulmonary hypertension centres are offering hybrid care models which incorporate both remote and face-to-face clinical consultations, structured to meet the needs of patients.[9]

Risk assessment

Due to the progressive nature of PAH and the high risk for rapid deterioration, international guidelines[2] recommend regular risk assessment in PAH to aid treatment decisions. Risk assessment incorporates parameters including exercise testing, NT-proBNP, and WHO functional class. Remote consultation without exercise testing diminishes the effectiveness of risk assessment.[9]

Investigators have evaluated the of use of device-based applications to measure 6MWD as a substitute for hospital-based exercise, using smart phone or physical activity monitors; to date, these studies have been inconclusive.[23, 24] Furthermore, this approach is limited to patients who own a smart phone, have reliable internet access[25] and who can confidently walk outdoors. In contrast, these restrictions do not apply in the 1MSTS.

This study was not designed to look at thresholds that could be used to risk stratify patients with PAH. Nonetheless, it has a strong correlation with the maximal exercise test that it was benchmarked against (ISWT), and strong-moderate correlations within each of the risk stratification bands, where sample sizes were lower. It also correlates with other measurements that can be used to risk stratify patients with PAH, namely WHO-FC, NT-proBNP and emPHasis 10 score.

Limitations

This pragmatic study was designed to collect data with minimal disruption to clinical services and patients during the COVID-19 pandemic. To this end, all participants conducted their ISWT before the 1MSTS, which may have contributed to fatigue in the second test. Additionally a practice test was excluded from the protocol - all participants had conducted at least one ISWT prior to their testing in this study, but none had previously completed the 1MSTS. The 1MSTS has been shown to have a learning effect in patients with COPD,[11] and this may therefore have impacted on outcomes.

Further work

While this study supports the safety of the 1MSTS in the hospital setting and illustrates its potential role in risk assessment of patients with PAH and CTEPH, further examination of this exercise test is required. Future studies should compare the 1MSTS with the 6MWT and the results of CPET testing. A larger data set collected across multiple sites with a longer period of follow-up, including testing of home-based safety, would further inform the potential for use in remote risk assessment, along with inclusion of mortality data. Test and re-test to examine the learning effect of the 1MSTS in this patient group would be of value, as would studies to establish minimal clinically important difference of 1MSTS in PAH and CTEPH and its value in measuring response to treatment.[18] The survey results in this study suggest patients would be happy to conduct the 1-minute sit-to-stand test at home, but it would be important to ascertain patients' perspectives on the wider use of remote assessment and patient initiated follow-up. It would also be of interest to explore clinicians' perceptions of patient recorded assessments, in comparison to the results of hospital-based testing.

Conclusion

This study has demonstrated the sub-maximal characteristics of the 1-minute sit-to-stand test in PAH and CTEPH, its safety in the hospital setting, , its positive correlation with the Incremental Shuttle Walk test and potential role in remote risk assessment. Further evaluation of this exercise test is now warranted.

Financial conflict of interest statement

David G Kiely has received payment for participation in advisory boards, speaker fees and support to attend educational meetings from Acceleron, Janssen, GSK and Ferrer. He has received grant funding from GSK and Janssen.

Carol Keen has received payment for participation in advisory boards, speaker fees and grant funding from Janssen.

There are no conflicts for interest to declare for Dr Hashmi-Greenwood, Ian Smith or Professor Sage.

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Tables

Table 1 - Participant characteristics at diagnosis

Characteristics	PAH (n = 60)	CTEPH (n = 15)	All (n= 75)
Age, mean (SD), y	49.1 (16.4)	64.0 (13.8)	52 (16.8)
Female, no., (%)	47 (78.3)	11 (73.3)	58 (77.3)
BMI, mean (SD), kg/m^2	28.8 (7.3)	30.4 (8.7)	29.2 (7.6)
WHO FC, no., (%)			
Class II	4 (6.7)	0 (0)	4 (5.3)
Class III	49 (81.7)	15 (100)	64 (85.3)
Class IV	7 (11.7)	0 (0)	7 (9.3)
ISWT, mean (SD), m	222 (161)	192 (155.9)	216 (159)
Haemodynamics			
mRAP, mean (SD), mmHg	10 (6.2)	10 (5.5)	10 (6.1)
mPAP, mean (SD), mmHg	49 (13.7)	42 (11.1)	48 (13.3)
PAWP, mean (SD), mmHg	10 (4.6)	12 (6.4)	10 (5.0)
CO, mean (SD), l/min	4.49 (1.60)	4.26 (1.33)	4.44 (1.54)
CI, mean (SD), l/min/m^2	2.54 (0.94)	2.21 (0.58)	2.46 (0.87)
PVR, mean (SD), dynes/m^2	796 (401)	645 (322)	764 (388)
Mixed venous SpO_2 %	64.3 (10.7)	63.0 (7.64)	64.0 (10.0)
Pulmonary Function			
FEV_1, mean ± SD (% predicted), litres	2.09 ± 0.72 (77)	2.09 ± 0.82 (82)	2.09 ± 0.73 (78)
FVC, mean ± SD (% predicted), litres	2.82 ± 1.1 (88)	3.08 ± 1.3 (96)	2.87 ± 1.1 (90)
TL_{CO}, mean ± SD (% predicted), mmol/min/kPa	4.41 ± 1.9 (51)	4.96 ± 1.9 (64)	4.51 ± 1.8 (54)
emPHasis10, median (IQR), score out of 50	33 (25-41)	29 (22-36)	31 (23-39)
Co-morbidities			
Systemic hypertension, no., (%)	8 (13.3)	5 (33.3)	13 (17.3)
Atrial Fibrillation, no., (%)	5 (8.3)	2 (13.3)	7 (9.3)
Diabetes, no., (%)	6 (10)	2 (13.3)	8 (10.7)
Ischaemic Heart Disease, no., (%)	2 (3.3)	1 (6.7)	3 (4.0)
COPD, no., (%)	1 (1.7)	1 (6.7)	2 (2.7)
Interstitial Lung Disease, no., (%)	7 (11.7)	0 (0)	7 (9.3)
Chronic Kidney Disease, no., (%)	1 (1.7)	0 (0)	1 (1.3)

Definition of abbreviations: PAH=pulmonary arterial hypertension; CTEPH=chronic thromboembolic pulmonary hypertension; BMI=body mass index; WHO-FC = World Health Organisation Functional Classification; ISWT=Incremental Shuttle Walk Test; mRAP=mean right atrial pressure; mPAP=mean pulmonary arterial pressure; PAWP=pulmonary arterial wedge pressure; CO=cardiac output; CI=cardiac index; PVR=pulmonary vascular resistance; SpO2=oxygen saturations; FEV=forced expiratory volume; FVC=forced vital capacity; TL_{CO}=lung carbon monoxide transfer factor; emPHasis10=patient reported outcome measure; COPD=chronic obstructive pulmonary disease

Table 2 - Participant characteristics on day of testing

Characteristics	PAH (n = 60)	CTEPH (n = 15)	All (n = 75)
Age, mean (SD), years	53.9 (14.9)	68.1 (12.5)	56.7 (15.5)
Years since diagnosis, mean, (SD)	4.4 (4.4)	3.9 (3.1)	4.3 (4.2)
BMI, mean (SD), kg/m^2	29.4 (8.0)	29.7 (5.7)	29.5 (7.5)
WHO FC, no., (%)			
Class I	0 (0.0)	2 (13.3)	2 (2.7)
Class II	18 (30.0)	4 (26.7)	22 (29.3)
Class III	41 (68.3)	9 (60.0)	50 (66.7)
Class IV	1 (1.7)	0 (0.0)	1 (1.3)
ISWT mean (SD), m	278 (174)	291 (184)	281 (174)

NT-proBNP, median (IQR), pg/mL	437 (111-830)	219 (127-378)	339 (120-723)
emPHasis10, median (IQR), score out of 50	29 (20-35)	22 (9-27)	27 (19-34)
Definition of abbreviations: PAH=pulmonary arterial hypertension; CTEPH=chronic thromboembolic pulmonary hypertension; BMI=body mass index; WHO-FC = World Health Organisation Functional Classification; ISWT=Incremental Shuttle Walk Test; NT-proBNP=N-terminal pro b-type natriuretic peptide; emPHasis10=patient reported outcome measure			

Table 3 - Change in physiological parameters in response to 1-minute sit-to-stand and Incremental Shuttle Walk tests

	1MSTS Mean (SD)	ISWT Mean (SD)	Mean difference	CI	p value
Oxygen Saturations SpO2 (%)					
Baseline	95 (3.4)	94 (4.1)	1.0	(0.4 - 1.8)	0.002*
Post-test	91 (6.2)	85 (8.9)	6.2	(4.6 - 7.7)	<0.001*
Change from baseline	-3.8 (4.0)	-8.9 (7.3)	5.0	(3.5 - 6.7)	<0.001*
Heart Rate (bpm)					
Baseline	79 (13.1)	80 (13.3)	-5.2	(-2.5 - 1.4)	0.593
Post-test	89 (14.9)	118 (24.3)	-29.4	(-34.9 - -23.9)	<0.001*
Change from baseline	9.4 (8.0)	38.3 (25.9)	-28.8	(-34.8 - -22.9)	<0.001*
Systolic blood pressure (mmHg)					
Baseline	126 (19.1)	119 (17.9)	7.1	(3.9 - 10.2)	<0.001*
Post-test	136 (21.4)	136 (28.2)	0.0	(-4.9 - 4.9)	0.995
Change from baseline	10.1 (10.5)	17.7 (19.0)	-7.6	(-12.0 - -3.2)	<0.001*
Diastolic blood pressure (mmHg)					
Baseline	75 (11.1)	74 (14.8)	1.4	(-1.4 - 4.3)	0.32
Post-test	78.8 (13.0)	84.4 (17.6)	-5.6	(-8.8 - -2.4)	<0.001*
Change from baseline	2.9 (7.8)	10.3 (15.1)	-7.4	(-10.7 - -4.0)	<0.001*
Borg Breathlessness (Scale 0-10)					
Baseline	0.85 (1.1)	0.92 (1.1)	-0.1	(-0.24 – 0.09)	0.34
Post-test	3.6 (1.8)	4.6 (2.0)	-1.0	(-1.37 - -0.62)	<0.001*
Change from baseline	2.8 (1.8)	3.7 (2.2)	-0.9	(-1.3 - -0.6)	<0.001*
* indicates p < 0.05					

Table 4 - Correlation of outcomes for 1MSTS test and ISWT

	1MSTS		ISWT	
	Correlation coefficient (r)	p value	Correlation coefficient (r)	p value
1MSTS			0.702	<0.001*
High risk			0.391	0.044*
Intermediate risk			0.300	0.165
Low risk			0.667	<0.001*
WHO FC	-0.503	<0.001*	-0.592	<0.001*
NT-proBNP	-0.262	0.028*	-0.286	0.012*
emPHasis10	-0.436	<0.001*	-0.479	<0.001*
Age	-0.393	<0.001*	-0.445	<0.001*
r - Spearman's rank correlations coefficient * indicates p < 0.05				
Definition of abbreviations: 1MSTS=1-minute sit-to-stand; ISWT=Incremental Shuttle Walk Test; WHO-FC=World Health Organisation Functional Classification; NT-proBNP=N-terminal pro b-type natriuretic peptide; emPHasis10=patient reported outcome measure				

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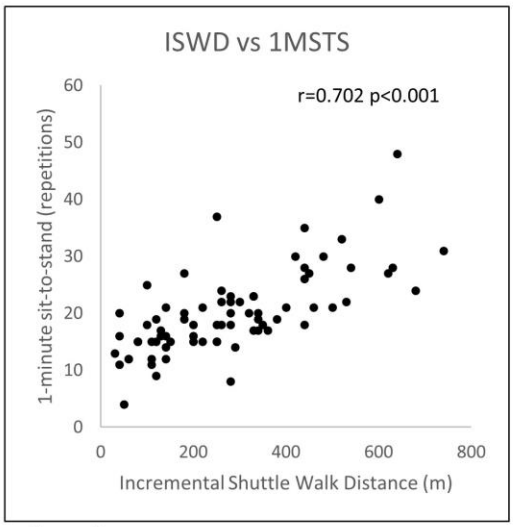

Figure 1a

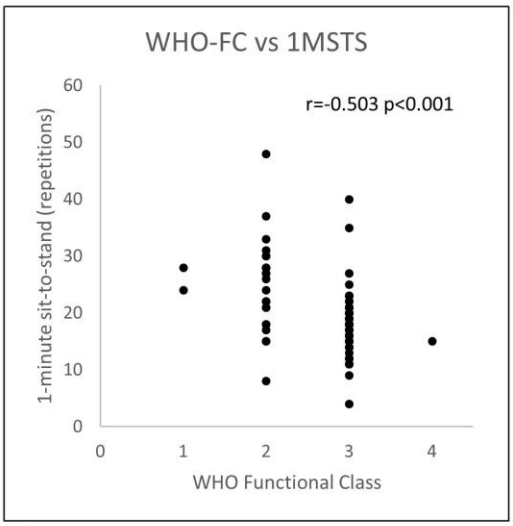

Figure 1b

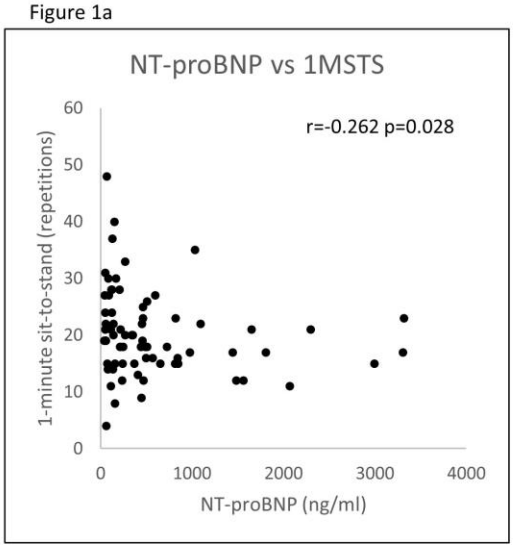

Figure 1c

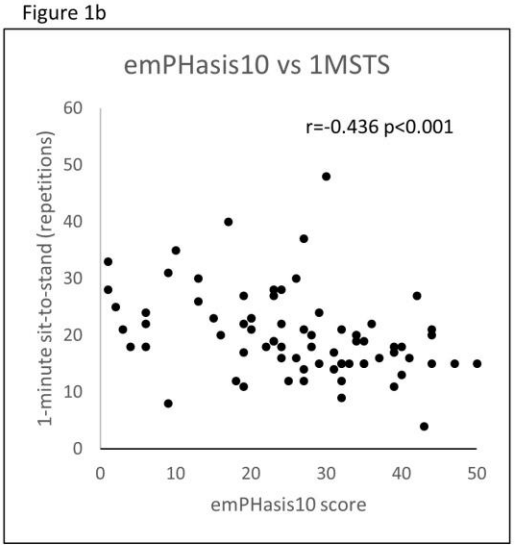

Figure 1d

Figure 1 - Scatter plots of 1MSTS against a) ISWD b) WHO-FC c) NT-proBNP d) emPHasis10

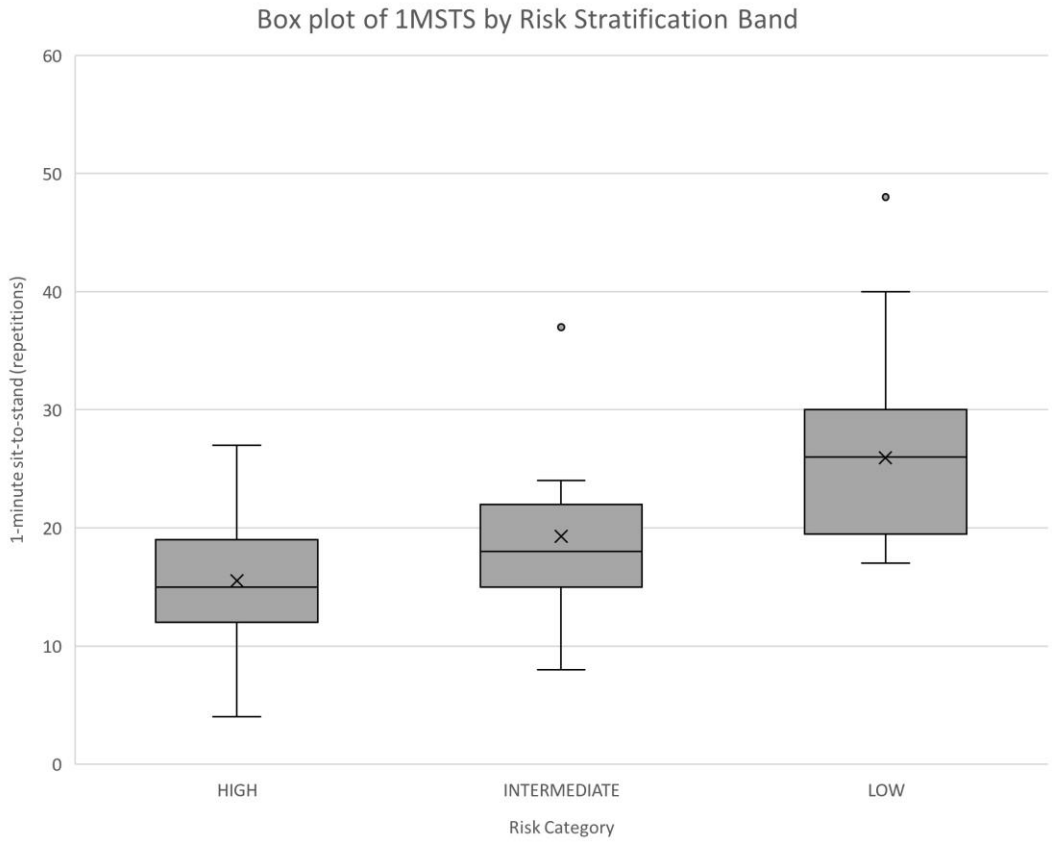

Figure 2 - Box plot of 1MSTS against risk stratification bands

Supplementary Material

Patient demographics at diagnosis for PAH patient by sub-classification				
	IPAH and HPAH (n = 28)	PAH-CTD (n = 18)	PH-CHD (n = 11)	PoPH (n=3)
Age, mean (SD), y	47.2 (17.1)	57.2 (13.0)	44.4 (16.8)	35.7 (6.0)
Female, no., (%)	21 (75.0)	16 (88.9)	9 (81.8)	1 (33.3)
BMI, mean (SD), kg/m^2	30.9 (8.1)	25.5 (5.0)	28.9 (7.67)	28.8 (3.5)
WHO FC, no., (%)				
Class II	1 (3.6)	1 (5.6)	2 (18.2)	0 (0)
Class III	21 (75.0)	16 (88.9)	9 (81.8)	3 (100)
Class IV	6 (21.4)	1 (5.6)	0 (0)	0 (0)
ISWT, mean (SD), m	218 (181)	173 (132)	310 (119)	220 (220)
Haemodynamics				
mRAP, mean (SD), mmHg	12 (6.5)	7 (4.9)	9 (5.0)	10 (13)
mPAP, mean (SD), mmHg	53 (13.0)	40 (12.1)	52 (11.7)	28 (1.4)
PAWP, mean (SD), mmHg	9 (3.8)	10 (6.0)	11 (3.1)	10 (5.0)
CO, mean (SD), l/min	4.14 (1.68)	4.60 (1.40)	5.75 (1.77)	4.5 (0.91)
CI, mean (SD), $l/min/m^2$	2.24 (0.88)	2.76 (0.88)	3.55 (0.82)	2.25 (0.85)
PVR, mean (SD), $dynes/m^2$	979 (364)	582 (355)	664 (442)	852 (111)
Mixed venous SpO_2 %	62.9 (11.9)	64.9 (6.4)	75.7 (6.33)	61.0 (15.2)
Pulmonary Function				
FEV_1, mean ± SD (% predicted), litres	2.25 ± 0.75 (81)	1.85 ± 0.61 (78)	1.99 ± 0.68 (70)	2.33 ± 1.19 (58)
FVC, mean ± SD (% predicted), litres	2.95 ± 1.03 (91)	2.45 ± 0.96 (86)	3.13 ± 1.01 (93)	3.11 ± 2.06 (65)
TL_{CO}, mean ± SD (% predicted), mmol/min/kPa	4.83 ± 1.99 (53)	3.06 ± 1.04 (41.5)	5.69 ± 1.15 (71)	4.53 ± 2.34 (41)
emPHasis10, median (IQR), score out of 50	34 (27-41)	32 (24-40)	19 (8-30)	37 (-)
Co-morbidities				
Systemic hypertension, no., (%)	4 (14.3)	3 (16.7)	1 (9.1)	0 (0)
Atrial Fibrillation, no., (%)	1 (3.6)	3 (16.7)	1 (9.1)	0 (0)
Diabetes, no., (%)	6 (21.4)	0 (0)	0 (0)	0 (0)
Ischaemic Heart Disease, no., (%)	0 (0)	2 (11.1)	0 (0)	0 (0)
COPD, no., (%)	0 (0)	0 (0)	1 (9.1)	0 (0)
Interstitial Lung Disease, no., (%)	0 (0)	7 (38.9)	0 (0)	0 (0)
Chronic Kidney Disease, no., (%)	1 (3.6)	0 (0)	0 (0)	0 (0)

Definition of abbreviations: PAH=pulmonary arterial hypertension; CTEPH=chronic thromboembolic pulmonary hypertension; BMI=body mass index; WHO-FC = World Health Organisation Functional Classification; ISWT=Incremental Shuttle Walk Test; mRAP=mean right atrial pressure; mPAP=mean pulmonary arterial pressure; PAWP=pulmonary arterial wedge pressure; CO=cardiac output; CI=cardiac index; PVR=pulmonary vascular resistance; SpO2=oxygen saturations; FEV=forced expiratory volume; FVC=forced vital capacity; TL_{CO}=lung carbon monoxide transfer factor; emPHasis10=patient reported outcome measure; COPD=chronic obstructive pulmonary disease

Table S1 – Participant characteristics separated by subgroup

n = 75	Serious Adverse Event n, %	Adverse Event n, %	Early Termination n, %
Syncope	0 (0)	0 (0)	0 (0)
Pre-syncope	0 (0)	0 (0)	0 (0)
Chest pain	0 (0)	0 (0)	0 (0)
Elevated BP, not returning to baseline	0 (0)	0 (0)	0 (0)
Shortness of breath	0 (0)	0 (0)	1 (1.3)
Anxiety	0 (0)	1 (1.3)	0 (0)
Leg pain	0 (0)	0 (0)	1 (1.3)
Requiring treatment	0 (0)	0 (0)	0 (0)
Requiring admission	0 (0)	0 (0)	0 (0)

Table S2 - Safety outcomes

n = 67	Y n (%)	N n (%)	Other n (%)
Would you be happy to do 1MSTS at home as part of a non-face-to-face assessment in the future?	65 (97.0)	0 (0)	2 (3.0)
Do you have weighing scales at home?	60 (89.6)	7 (10.5)	0 (0)
Do you have an oxygen saturation probe at home?	30 (44.8)	37 (55.2)	0 (0)
Do you have a blood pressure machine at home?	27 (40.3)	40 (59.7)	0 (0)

Table S3 – Survey results