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INCREMENTAL SHUTTLE WALKING TEST DISTANCE AND AUTONOMIC DYSFUNCTION PREDICT SURVIVAL IN PULMONARY ARTERIAL HYPERTENSION

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Key words: pulmonary arterial hypertension, exercise testing, incremental shuttle walking test, autonomic function, heart rate recovery, prognosis

Short running title ISWT and survival in PAH

ABSTRACT

Background

To ensure effective monitoring of pulmonary arterial hypertension (PAH), a simple, reliable assessment of exercise capacity, applicable over a range of disease severity is needed. The study aim was to assess the ability of the incremental shuttle walking test (ISWT) to correlate with disease severity, measure sensitivity to change and predict survival in PAH.

Methods

418 treatment-naïve patients with PAH, with baseline ISWT within 3 months of cardiac catheterization, were enrolled. The clinical validity and prognostic value of the ISWT distance was assessed at baseline and 1 year.

Results

ISWT distance was found to correlate at baseline with World Health Organisation functional class, Borg score and haemodynamics without a ceiling-effect (all $p<0.001$). Walking distance at baseline and after treatment predicted survival; the area under the receiver operator characteristic curve for the ability of the ISWD to predict mortality was 0.655 (95%CI 0.553-0,757), $p=0.004$ at baseline, and 0.737 (0.643-0.827), $p<0.001$ at 1 year following initiation of treatment. Change in ISWD also predicted survival ($p=0.04$). Heart rate (HR) and systolic blood pressure (SBP) parameters reflecting autonomic response to exercise (highest HR, change in HR, HR recovery at 1 minute>18, highest SBP, ΔSBP and 3minute SBP ratio) were significant predictors of survival (all $p<0.05$).

Conclusions

In patients with PAH the ISWT is simple to perform, allows assessment of maximal exercise capacity, is sensitive to treatment effect, predicts outcome and has no ceiling-effect. In addition, we have also shown that measures of autonomic function made post-exercise predict survival in PAH.

INTRODUCTION

Pulmonary arterial hypertension (PAH) is a life-threatening condition characterised by vascular proliferation and remodelling, leading to an increase in pulmonary artery pressure.[1] This increased afterload results in a reduction in cardiac output and decreased tissue oxygen delivery so limiting exercise capacity. Assessment of exercise capacity, therefore, has the potential to play a role in defining the severity of PAH and monitoring treatment but this is crucially dependent on the exercise test reflecting disease severity.

Due to its simplicity, the six-minute walking test (6MWT) is used to monitor patients in the clinic and assess the efficacy of new therapies. More recently the 6MWT has also been used to assess autonomic function in patients with PAH, and impaired heart rate recovery has been shown to predict an increased rate of clinical worsening.[2,3] However, concerns have been raised regarding the use of the 6MWT both in clinical practice and in trials of new therapies.[4-8] In particular, a "ceiling-effect" has been noted where 6MWT distance (6MWD) no longer reflects maximal oxygen aerobic capacity[9-11] or disease severity[12] and may, therefore, be unable to identify clinically important changes in haemodynamic parameters.[12-15] In addition, change in 6MWD does not explain a large proportion of observed treatment effect.[16-18]

The Incremental Shuttle Walk Test (ISWT) is an externally-paced symptom-limited 12-level test requiring the patient to increase their speed every minute. The incremental shuttle walking distance (ISWD) correlates with disease severity and is sensitive to change in a number of respiratory diseases.[19] The ISWT has potential advantages in assessment of cardiac dysfunction since in chronic heart failure the ISWT is a better predictor of survival than the 6MWT.[20] A small study in pulmonary hypertension also noted that ISWD correlated more closely with peak oxygen consumption than 6MWT distance.[21] The ISWT has therefore

been proposed as an alternative field walking test to the 6MWT in PAH,[22,23] however, there are no long-term data on the prognostic value of the ISWT or its sensitivity to change.

The aim of this study, was to undertake the first assessment of the ability of the ISWT to reflect disease severity, measure sensitivity to change and assess prognostic value in patients with PAH. In addition, we have assessed autonomic function during and immediately post exercise, using heart rate and blood pressure changes, and assessed the impact of autonomic function on survival in PAH.

METHODS

Data were retrieved from the ASPIRE registry (Assessing the Spectrum of Pulmonary hypertension Identified at a REferral centre) for consecutive patients diagnosed with pulmonary hypertension between 2001-10.[24] The diagnostic evaluation and clinical classification of these patients have been described previously.[24] For inclusion patients were required to have PAH and a baseline ISWT within 3 months of cardiac catheterization and prior to the introduction of targeted PAH therapy. Ethical approval was granted by the North Sheffield Research Ethics Committee (Reference No. 06/Q2308/8).

Incremental Shuttle Walk Test

The ISWT was performed according to the method of Singh et al.[25] No practice walk was performed and no supplemental oxygen used. Patients usually receiving supplemental oxygen performed the test breathing room air. Breathlessness and blood pressure were measured at rest and at the end of the test. Heart rate was measured throughout the test. To assess autonomic function, change in heart rate, heart rate recovery at 1 minute post-exercise (HRR1), change in systolic blood pressure (SBP), and the systolic blood pressure three minute ratio were calculated. Predicted ISWD (ISWD%pred) was calculated using the equation described by Probst et al.[26] (See online supplementary data , available online at www.jhltonline.org).

Follow-up

Treatment of PAH was in accordance with UK national commissioning policy based on international guidelines. Mortality was ascertained at the census point via the NHS enhanced reporting service. Data were collected for patients at 12 months (+/-2 months) post-diagnosis.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics v19 (SPSS, Chicago, IL, USA). Continuous variables were described by mean±standard deviation. Pearson's correlation test was used to assess correlations between incremental shuttle walk test distance and haemodynamic parameters and was tested for 2-sided significance. Multiple comparisons between groups were performed using ANOVA for parametric data. Event (death or transplantation)-free survival from date of diagnosis was estimated using the Kaplan–Meier method with comparison between groups performed by the log-rank test. The accuracy of the prognostic parameters was estimated using receiver operating curves ROC. A p-value of <0.05 was deemed statistically significant.

Stratification of patients

The ISWT has 12 levels. We used a model with 5 pre-specified Bands based on walking distance/maximal walking speed that were the best fit for a Gaussian distribution. Band 1: Level 1, 0-30m, equivalent to 0.50 m/s, 14% of patients; Band 2:Level 2 and 3, 40-120m, 0.67-0.84 m/s, 28% of patients; Band 3:Level 4 and 5, 130-250m, 1.01-1.18 m/s, 28% of patients ; Band 4: Level 6 and 7, 260-420m, 1.35-1.52m/s, 22% of patients ; Band 5: Level 8-12, 430-1020m, 1.69-2.37 m/s, 8% of patients. ISWD%pred was also stratified into 5 Bands. To ensure the ISWT bands did not result from over-fitting of the data, resampling techniques were used to validate the utility of ISWT distance as a predictor of mortality using sub-samples. At follow-up improvement was defined as increase >40m, decline decrease >20m and the remaining patients defined as stable.[27,28]

RESULTS

Between 2001-10, 418 patients had a diagnosis of PAH and a baseline ISWT within 3 months of cardiac catheterization and prior to the introduction of targeted-therapy. Baseline characteristics are presented in table1. There were high levels of data completeness for all parameters studied (>90%). Median distance walked at baseline was 150m and median time to complete the walk was 3.67 minutes. The ISWT was found to be a safe test with no major adverse event (death, need for cardiopulmonary resuscitation, arrhythmia, causing collapse) reported (n=10,979 tests completed during this study period).

Baseline ISWD and clinical correlates

Absolute baseline ISWT distance correlated significantly with haemodynamic parameters including, right atrial pressure (RAP), pulmonary vascular resistance (PVR), cardiac output, cardiac index and mixed venous oxygen saturation, (p all<0.001). ISWT distance also correlated with baseline resting Borg score and World Health Organization (WHO) functional class, (p all ≤0.001). One-way ANOVA demonstrated a highly significant relationship (p<0.001) for ISWD Band (Figure 1) with WHO functional class, baseline resting Borg score, and baseline pulmonary haemodynamic parameters across all Bands. There were significant differences in haemodynamics even between the top two bands with Band 5 having significantly lower PVR (mean±sd 6.2±3.0 vs 8.9±4.7 Wood unit, p=0.04) and mRAP (5.5±3.3 vs 8.3±4.4 mmHg, p=0.002) than Band 4.

Baseline ISWD and survival

Kaplan-Meier survival analysis demonstrated that baseline ISWT distance predicted survival with no ceiling-effect across the 5 Bands (p<0.001), (Figure 2A). This pattern was also evident in PAH subgroups: IPAH (p<0.001); PAH-SSc (p<0.001), and older PAH patients

>60 years of age (<0.001) (Figure 3). Internal validation of the banding model found that ISWD band significantly predicted survival in patients diagnosed at different times and in all random subgroups examined, (p all <0.05). A similar pattern with no ceiling-effect was seen across the 5 bands of ISWD%pred bands (p<0.001). ISWD%pred was not a better predictor of survival than absolute distance walked with an area under the Receiver Operator Characteristic curve (AUROC) of 0.646 (95%CI 0.594-0.699) and 0.690 (0.639-0.740) respectively, p>0.05. The sensitivity and specificity of different ISWD cut-off points to predict mortality are shown in table 2.

Follow-up and change in ISWD

Follow-up ISWT distance was a significant predictor of survival at 1 year (Figure 2B). Analysing data only from patients who had repeated tests at 1 year, AUROC (95%CI) was 0.655 (0.553-0,757), p=0.004 at baseline, and 0.737 (0.643-0.827), p<0.001 at 1 year following initiation of treatment. Compared to ISWD at baseline, ISWD at one year was a significantly better predictor of long term outcome (p<0.05) and the sensitivity and specificity of death at 2 years post-diagnosis associated with walking ≤120m at baseline was 15/93 compared to 19/95 associated with walking ≤120m at 1 year.

Mean ΔISWD was +12.2m at 1 year (p<0.001, paired t test). ΔISWD differed significantly across the bands (p<0.001) with an overall mean ΔISWD at 1 year in Band 1 of +71m compared with an overall mean ΔISWD in Band 5 of -23m. However, analysis of individual data showed that response to therapy was varied. Approximately 30% had an improved walking distance of >40m, 40% remained stable and 30% declined by more than 20m. This pattern of response was seen across the Bands. The median ΔISWD for improvers was similar across the Bands. However, for decliners, the median ΔISWD varied significantly across the Bands, increasing with increasing baseline distance (p<0.05), (table 3).

ΔISWD was found to correlate significantly with changes in highest HR, highest SBP and resting Borg score at 1 year. Univariate Cox survival analysis demonstrated that absolute change from baseline was a significant predictor of survival and KM survival curves showed significant survival differences between groups. However, multivariate Cox proportional hazards analysis demonstrated that although ΔISWD predicted survival even when adjusted for baseline ISWD ($p<0.001$), when adjusted for follow-up ISWD, ΔISWD was no longer a significant predictor ($p=0.75$). Survival difference between improvers and decliners was reflected by mean distance walked at 1 year (304m/152m) ($p<0.001$). Greatest percentage change from baseline distance (%ΔISWD) occurred in patients with a low baseline ISWD (Supplemental Table 1). Examining the relationship between %changeISWD and follow-up ISWD (Supplemental Figure 1), survival was again found to reflect distance walked at follow-up, rather than a linear relationship with %change. Cox proportional hazards analysis also showed that %ΔISWD from baseline was not predictive of survival ($p>0.05$).

Autonomic response to exercise

Univariate Cox analysis demonstrated that parameters reflecting autonomic response to exercise (highest HR, ΔHR, HRR1>18, Highest SBP, ΔSBP and 3minute SBP ratio) were significant predictors of survival and Kaplan-Meier analysis using thresholds derived from ROC analysis also showed significant survival benefit for improved chronotropic and blood pressure response (p all<0.05) (Figure 4). All these parameters correlated significantly with ISWD, and when corrected for ISWD the chronotropic and blood pressure responses were no longer significant independent prognostic predictors. Multivariate Cox analysis including haemodynamic data showed that ISWD remained an independent predictor of survival ($p<0.001$)

DISCUSSION

We have demonstrated in patients with pulmonary arterial hypertension that distance walked using the incremental shuttle walking test correlates with pulmonary haemodynamics, WHO functional class and resting Borg score and predicts prognosis both at baseline and at subsequent follow-up, all without a ceiling-effect. Furthermore, we have also shown that measures of autonomic function made immediately post exercise predict survival in PAH. These attributes of the incremental shuttle walking test make it an attractive field walking test in PAH.

Currently two exercise tests are used in PAH: the 6MWT which is an un-encouraged test and CPET which is an incremental maximal test. Because of the sub-maximal nature of the 6MWT it loses its ability to reflect maximal oxygen aerobic capacity[9-12] and pulmonary haemodynamic severity[11,12] in patients with milder disease. Furthermore, changes in haemodynamic parameters may not be reflected by alteration in 6MWT distance.[12-15] Nonetheless the 6MWT has been useful in clinical trials and clinical practice having the benefit of being evaluated over several decades. CPET provides information on the aetiology of exercise limitation,[29] provides prognostic information,[230] reflects haemodynamic severity and unlike the 6MWT reflects maximal oxygen uptake even in mild disease. However, routine use of CPET is challenging and when used in a randomised controlled trial it was unable due to its complexity to demonstrate a treatment effect.[31] The ISWT shares benefits of both the 6MWT and CPET in that it is simple and quick to perform (median time 3.67 minutes) but also has the benefits of an incremental nature to maximum exercise capacity. Despite the test protocol requiring the patient to walk or run at increasing speed, which may be thought challenging for older patients or those with mobility problems, ISWD was able to predict survival in older subjects (age >60) and patients with systemic sclerosis. Additionally, the test uses a 10m corridor rather than the 30m corridor required for the

6MWT, making it easier to perform in the clinical environment. As with the 6MWT, use of %pred distance did not improve the prognostic value of the ISWT.[32]

Changes in autonomic function has been well described in PAH. Previous investigators have shown that autonomic responses to exercise such as peak systolic blood pressure[30] and chronotropic response[29,33] provide prognostic information. Our data confirmed these findings. More recently, in an effort to improve the prognostic ability of the 6MWT, interest has been shown in the use of post-exercise HRR1 as an additional indicator. Minai et al. reported HRR1 to be prognostic of clinical worsening in patients with idiopathic PAH and patients with connective tissue disease-associated PH and to be a stronger predictor of clinical worsening than the 6MWD.[2,3] However, HRR1 was not found to be an independent predictor of mortality.[3] In our study looking at HRR1 after ISWT, we are the first to demonstrate that changes in HRR1 are predictive of survival in treatment-naive Group 1 PAH. As in previous studies,[2,3,34,35] alteration in autonomic control correlated with exercise capacity, and we confirmed that HRR1 is not an independent predictor of mortality. Alterations in autonomic response to exercise may therefore add supplemental information but the need for a valid field exercise reflecting the full range of disease severity is still vital.

In keeping with studies with the 6MWT the use of %change from baseline as an outcome measure was not supported by our data (Supplemental Figure 1). Greatest percentage change in distance, both positive and negative, occurred in patients with low baseline ISWT distance (Supplemental Table 1). If baseline distance is low, even a large percentage improvement may result in a relatively low distance walked at follow-up and survival reflects distance walked at follow-up. In addition, although ΔISWD was a predictor of survival, bivariate Cox proportional hazard analysis demonstrated that absolute ISWD at follow-up was the strongest predictor, and our data support the observation that prognosis depends not on how much the patient has improved but rather on how good their current status is.[36]

The improved sensitivity and specificity of the ISWT at one year compared to baseline emphasises the need for assessment at multiple time-points.[37]

So how could the ISWT be used in clinical practice? Firstly, it performs well as a prognostic tool across the spectrum of PAH. It is able to discriminate patients with high versus low risk of mortality with increasing sensitivity but decreasing specificity with increasing cut-off points. The high sensitivity found at the higher distances allows reassurance to be given to those patients who walk furthest. Secondly, the ISWD is sensitive to change and these changes where they translate into clinically meaningful outcomes tend to be large (Table 3). For an individual patient, even with mild disease, change in ISWD may reflect an altered risk of mortality, and a decline in ISWD should warrant a review of management.

Study limitations

We studied a large cohort of patients with PAH but this was a single centre study and further work to assess the utility of the ISWT in other centres is required. In addition, there was no direct comparison of the ISWT with the 6MWT or cardiopulmonary exercise testing as we wished to explore the potential value of the ISWT to assess disease severity and detect change in PAH before considering a prospective study. The complete data set of baseline ISWT's was used to develop the ISWT Band model. As there was post hoc theorizing the data may have been over-fitted,[38] however, internal validation was carried out which supported the Band model.

Conclusion

In a large study we have shown that in patients with PAH the ISWT correlates with disease severity, is sensitive to treatment effect, predicts outcome and has no ceiling-effect. We propose further work to explore the ISWT as an alternative to the 6MWT in the assessment of disease severity and monitoring of patients with PAH. **Disclosure statement:** None of

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Supplementary data are available in the online version of this article at www.jhltonline.org.

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FIGURE LEDGENDS

Figure 1 – Relationship between baseline Incremental Shuttle Walk Test Band and: CI: cardiac index; PVR: pulmonary vascular resistance, RAP: right atrial pressure; $SmVO_{2:}$ mixed venous oxygen saturation; %WHO Class 1+2: percentage of patients in World Health Organisation functional class I and II (all $p<0.001$). Band 1:10-30 m; Band 2: 40-120 m; Band 3: 130-250 m; Band 4: 260-420 m; Band 5: 430-1020 m.

Figure 2 - Kaplan-Meier survival analysis stratified according to baseline Incremental Shuttle Walk Test distance achieved at A) Baseline; B) 1 year

Figure 3 - Kaplan-Meier survival analysis stratified according to baseline Incremental Shuttle Walk Test distance in pulmonary arterial hypertension (PAH) subgroups: A) idiopathic PAH; B) PAH associated with systemic sclerosis C) PAH associated with congenital heart disease; D) in PAH patients >60 years old.

Figure 4 - Kaplan-Meier survival analysis stratified according to: a) highest heart rate; b) change in heart rate c) heart rate recovery at 1 minute; d) highest systolic blood pressure (SBP); e) change in SBP; f) SBP 3 minute ratio

ABBREVIATIONS:

6MWT	Six minute walking test
6MWD	Six minute walking test distance
HR	Heart rate
HRR1	Heart rate recovery at 1 minute
ISWT	Incremental shuttle walking test
ISWD	Incremental shuttle walking test distance
ISWD%pred	Percentage predicted incremental shuttle walking test distance
KM	Kaplan-Meier
PAH	Pulmonary arterial hypertension
PVR	Pulmonary vascular resistance
RHC	Right heart catheterisation
RAP	Right atrial pressure
SBP	Systolic blood pressure

Table 1. Baseline characteristics

	Overall (n=418)	Idiopathic-PAH (n=133)	PAH-SSc (n=120)	PAH-CHD# (n=119)	PAH-CTD-nonSSc (n=24)	Other (n=22)
Female n (%)	307(73)	87(65)	105(88)	83(70)	19(79)	12(55)
Age years	55±17	54±17	66±9	46±18	55±18	52±14
WHO FC I+II / III+IV (%)	22/78	15/85	21/79	34/64	8/92	14/86
mRAP mmHg *	8.0(7.0)	10.0(8.0)	8.0(6.0)		7.0(7.0)	9.0(6.0)
mPAP mmHg	48±13	53±13	43±12		44±12	46±11
CI L/min/m^2 *	2.7±0.9	2.2(1.0)	2.8(1,7)		3.0(1.2)	3.3(1.1)
PVR Wood Unit *	8.7(7.5)	10.5(7.3)	7.0(7.4)		6.7(4.2)	6.3(4.1)
$SmVO_2$ (%)	63±9	61±9	65±8		64±10	65±10
FEV1 %pred	79±20	87±16	84±16	67±20	75±15	69±20
FVC %pred	90±22	97±19	98±17	76±24	87±17	81±18
FEV1/FVC (%)	73±10	75±9	71±10	74±12	73±12	70±11
Tlco %pred	55±23	53±20	41±10	75±25	46±12	57±12
ISWT Distance m *	140(210)	140(230)	130(180)	190(160)	115(145)	190(238)
ISWT time minutes *	3.7(3.2)	3.5(3.8)	3.5(2.9)	4.3(2.5)	3.1(2.5)	4.3(3.7)

Presented as mean±SD for parametric data and * median (interquartile range) for nonparametric data. SSc: systemic sclerosis; CHD: congenital heart disease; PAH-CTD-nonSSc: pulmonary arterial hypertension in association with connective tissue disease excluding systemic sclerosis: Other: includes other forms of PAH including portal-pulmonary PAH and HIV associated PAH; WHO FC: World Health Organization functional class; mRAP: mean right atrial pressure; mPAP: mean pulmonary artery pressure; CI: cardiac index; PVR: pulmonary vascular resistance; SmVO2: mixed venous oxygen saturation; FEV1: forced expiratory volume in 1 second; % pred: % predicted; FVC: forced vital capacity; TL,CO: transfer factor of the lung for carbon monoxide; ISWT: Incremental Shuttle Walk Test; # right heart catheterisation not routinely performed in patients with PAH associated with congenital heart disease.

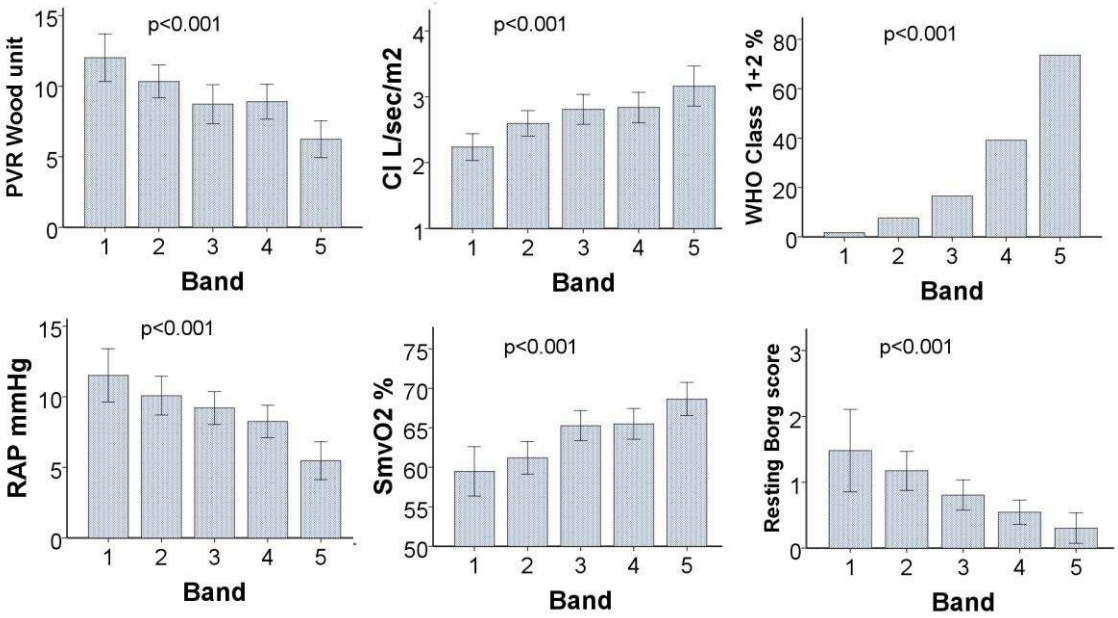
Table 2. Analysis of ISWD versus 1-, 2- and 3-year survival

ISWD cut-off	Sensitivity	Specificity	PPV	NPV
One year survival				
>30m	34	88	27	91
>120m	70	61	19	94
>250m	92	33	15	97
>420m	100	10	12	100
Two year survival				
>30m	28	90	40	83
>120m	65	64	31	88
>250m	89	36	26	93
>420m	100	11	22	100
Three year survival				
>30m	27	92	62	72
>120m	65	69	51	80
>250m	93	23	37	88
>420m	98	11	35	92

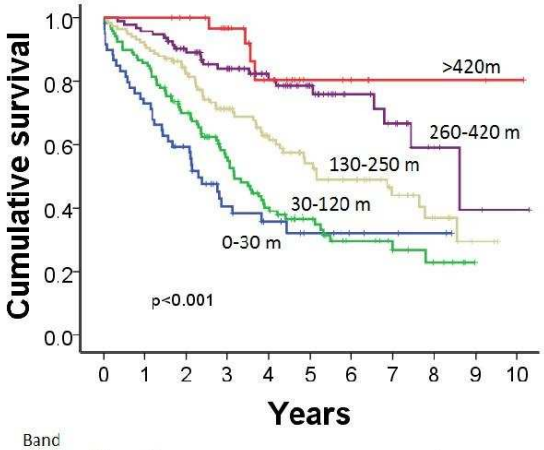
Table 3. Change in Incremental Shuttle Walk distance at 1 year

		n	%	Mean	Median
All	Improve >40m	68	32	111	90
	Stable -20 to +40m	74	35	8	0
	Decline > -20m	68	32	-82	-65
	Overall	210		12	0
Band 1	Improve >40m	9	41	156	120
	Stable -20 to +40m	11	50	21	20
	Decline > -20m	2	9	-30	-30
	Overall	22		71	40
Band 2	Improve >40m	18	32	101	90
	Stable -20 to +40m	22	38	10	10
	Decline > -20m	17	30	-49	-40
	Overall	57		21	10
Band 3	Improve >40m	17	28	99	90
	Stable -20 to +40m	20	33	4	40
	Decline > -20m	24	39	-71	-65
	Overall	61		1	-10
Band 4	Improve >40m	21	37	104	100
	Stable -20 to +40m	16	29	5	0
	Decline > -20m	19	34	-116	-100
	Overall	56		1	0
Band 5	Improve >40m	3	21	147	110
	Stable -20 to +40m	5	35	-2	0
	Decline > -20m	6	4.	-125	-150
	Overall	14		-23	-15

Band 1:10-30m, equivalent to 0.50 m/s; Band 2: 40-120m, equivalent to 0.67-0.84 m/s; Band 3: 130-250m, equivalent to 1.01-1.18 m/s; Band 4: 260-420m, equivalent to 1.35-1.52m/s; Band 5: 430-1020m, equivalent to 1.69-2.37 m/s.

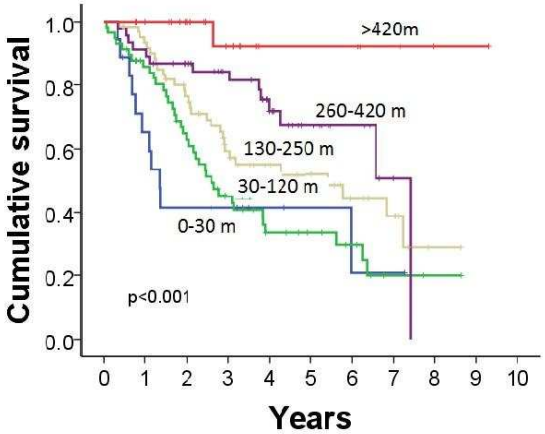


A)



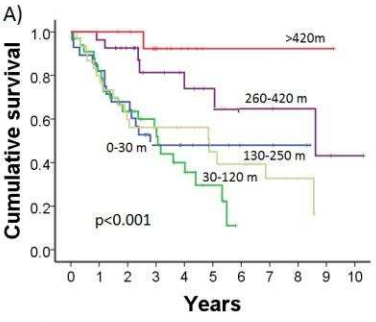
Band										
1	58	42	31	17	12	7	4	3	2	0
2	118	101	76	51	34	23	13	8	5	0
3	115	105	86	62	47	33	27	17	9	2
4	93	89	76	62	44	31	18	13	6	2
5	34	34	34	24	15	6	4	2	2	2
All	418	371	305	216	150	100	66	45	24	6

B)



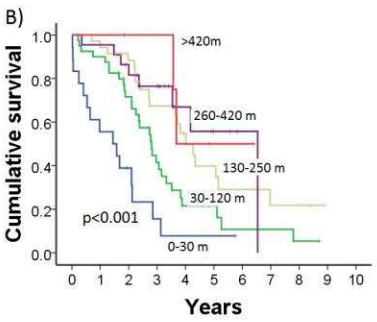
Band										
1	18	11	7	6	3	2	1	1	0	0
2	58	45	32	21	13	10	7	2	1	0
3	63	56	43	29	19	16	10	7	1	0
4	46	42	36	29	19	11	6	1	0	0
5	25	25	25	11	5	5	5	3	1	1
All	210	179	143	96	59	44	29	14	3	1

A)



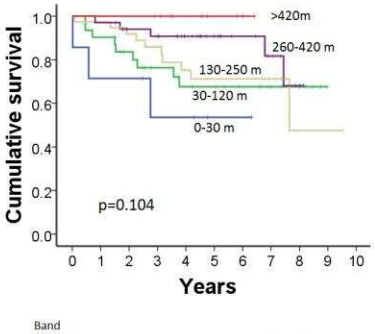
Band									
1	28	23	18	11	7	5	3	3	2	0
2	33	27	20	14	9	4	0	0	0	0
3	30	24	17	15	12	8	7	5	4	0
4	27	26	21	21	11	8	4	4	3	2
5	15	15	15	9	4	1	1	1	1	1
All	133	115	91	70	43	26	15	13	10	3

B)



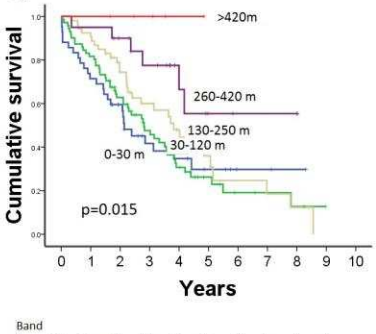
Band									
1	18	10	5	2	1	1	0	0	0	0
2	40	36	26	13	6	4	2	2	1	0
3	35	33	28	16	11	8	5	3	3	0
4	22	21	18	13	6	3	1	0	0	0
5	5	5	5	2	1	1	0	0	0	0
All	120	105	82	46	25	17	9	5	4	0

C)



Band									
1	7	5	5	3	3	1	1	0	0	0
2	31	28	23	18	15	13	11	7	4	0
3	38	37	32	26	20	18	12	7	1	1
4	34	33	29	28	21	15	11	8	3	0
5	9	9	9	8	5	5	3	1	0	0
All	119	112	99	83	64	47	38	23	8	1

D)



Band									
1	42	30	21	12	9	5	2	2	1	0
2	71	58	40	26	16	8	4	3	2	0
3	53	48	33	21	14	7	4	3	2	0
4	20	19	16	12	6	3	2	2	2	0
5	5	5	5	4	3	2	1	0	0	0
All	191	160	114	74	47	24	13	10	7	0