Understanding the measurement properties of the Incremental Shuttle Walk Test (ISWT) in patients with severe asthma

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Summary at a Glance

The measurement properties of the ISWT are unknown in patients with severe asthma. The study results show ISWT can be used to assess exercise capacity in patients with severe asthma. However, the small increase in distance on repeated testing would need to be considered in non-randomised trials

Abstract

Background

We investigated the repeatability and validity of the Incremental Shuttle Walk Test (ISWT) distance compared to peak oxygen uptake (VO_{2pk}) during maximal incremental cycle ergometer (ICE) and treadmill (ITM) tests in adults with severe asthma.

Methods

Adults with severe asthma, MRC dyspnoea ≥ 2, were recruited from specialists caring for people with severe asthma. All participants performed three ISWTs (familiarisation and two subsequent tests on the same day), an ICE and an ITM in a randomised order, on separate days to intolerance with expiratory gas analysis.

Results

50 patients (32 female, mean [SD], age 54 [13] yrs, FEV_1 1.9 [0.8] L, BMI 32 [6] kg/m^2) completed all five tests. The mean [SD] ISWT distance for each test were 400 [156]m, 418 [142]m, and 438 [157]m (p=0.001). There was a strong correlation between the ISWT distance with VO_{2pk} derived from ITM (r=0.74, p<0.001) and ICE (r=0.75, p<0.001).

Conclusion

There was a small increase in the mean ISWT distance on sequential testing. In clinical practice, the co-efficient of repeatability and heteroscedasticity needs to be considered

when assessing whether a true change has occurred within an individual patient. The ISWT has validity compared to VO_{2pk} on both ICE and ITM, but they are not interchangeable.

Key Words

Cardiopulmonary Exercise Test, Exercise Capacity, Incremental Shuttle Walk Test, Repeatability, Severe Asthma

Short title

ISWT in patients with severe asthma

Introduction

Adults suffering from asthma may adopt a sedentary lifestyle due to fear of exacerbating asthma symptoms with exercise and are at risk of deconditioning (1). Obesity is a prevalent co-morbidity in asthma (2) associated with disease severity, worse asthma control and poor exercise habits (2). Exertional dyspnoea in this group of patients is a complex and multifactorial issue and may have different characteristics among patients with different levels of disease severity (3).

The gold standard assessment of exercise capacity is the measurement of peak oxygen uptake (VO_{2pk}) during a maximal cardiopulmonary exercise test (CPET) with expired gas analysis. These tests are laboratory based requiring specialised equipment and trained operators. The incremental shuttle walk test (ISWT), a simple and inexpensive field test, has been shown to be valid and repeatable in other chronic lung diseases and has been used extensively to assess changes in exercise capacity after an intervention (4-7). However, the ISWT may have a ceiling effect due to the flat nature of the course, walking rather than running, and the changes in gait pattern with the turns at either end of the 10 metre course which may be relevant for some patients with severe asthma who have a high body mass index..

We therefore aimed to assess both the short term repeatability of the ISWT distance and the validity of the ISWT distance by comparing it to the VO_{2pk} derived from maximal incremental treadmill (ITM) and cycle ergometer tests (ICE) in patients with severe asthma.

Methods

Study design

This study was a prospective cross-sectional study approved by the National Research Ethics Service Committee of the East Midlands (ref 127552). The study timetable is shown in Figure 1. After providing written consent, participants performed a familiarisation ISWT and subsequently two further ISWTs (30 minutes apart) within 2 weeks. Participants were randomly assigned to perform either an ITM or ICE test first with one week between visits.

Participants

Participants were recruited from a population of patients attending severe asthma clinics with a multi-disciplinary team, at a tertiary referral centre Glenfield Hospital, Leicester, UK, for at least six months. All underwent thorough diagnostic assessment and an appropriate treatment strategy prior to recruitment. Patients were recruited if they were using high dose therapies at step 4 or 5 of the previous SIGN/British Thoracic Society Guidelines 2014 (8). Exclusion criteria included a diagnosis of a smoking-related COPD, co-existing fixed airflow obstruction (FEV_1/FVC < 70%) with a smoking history of ≥ 10 pack years, and inability to exercise due to significant musculoskeletal or neurological deficit, unstable cardiac disease (myocardial infarction within the last three months, unstable angina, heart failure, or valvular disease). Specific exclusions relating to severe asthma were a severe exacerbation in the preceding month prior to entry to the programme, a hospital admission within the last three months, and/or an admission involving intensive care and intubation within the last year.

Outcome Measures

Incremental Shuttle Walk Test (ISWT)

The modified ISWT is a 16-level test with an incremental acceleration every minute (7). The participant walks around two cones nine metres apart with a shuttle distance of 10 metres (4). Standard encouragement was provided at the start of a new level and if they were unable to maintain the required speed whereby the test was terminated if the correct speed was not achieved by the subsequent 10m shuttle.

Heart rate and oxygen saturation were measured continuously via portable pulse oximetry (Konica Minolta Pulsox-300i, Osaka, Japan). Blood pressure using sphygmomanometry, and perceived breathlessness and exertion using the Borg Scale (9), were recorded before, every two minutes during and immediately at the end of the test. The main limiting symptom was recorded.

Cardiopulmonary exercise tests (CPET)

Cardiopulmonary exercise tests were performed using a metabolic cart (Quark-CPET, COSMED-Rome, Italy) and expired gas analysis was measured breath by breath. Other monitoring was similar to the ISWT with the addition of with real-time cardiac monitoring with 12 lead electrocardiography (Quark C12x, COSMED-Rome, Italy).

Incremental Treadmill Test (ITM)

Participants performed a CPET on a trackmaster treadmill (Full Vision INC-Newton, Kansasa USA). Six minutes of resting measurements were followed by three minutes of slow walking on a flat surface as a warm up before the incremental protocol commenced. The incremental protocol used a simultaneous change in speed and grade every minute to achieve a linear response in VO_2 (10), aiming to elicit a test duration between 8-12 minutes.

The protocol was individualised for each participant by using their fast walking speed and their predicted peak power (11).

The presence and assessment of exercise induced bronchoconstriction (EIB) was assessed during the CPET according to ATS guidelines (12) by measuring FEV_1 before and repeatedly after at 5, 10, 15, 20 and 30 minutes post exercise. EIB severity was defined by the percentage decrease in FEV_1 from baseline : mild $\geq$ 10% to <25%, moderate $\geq$ 25% to <50% and severe if $\geq$ 50% as per ATS guidelines on EIB..

Incremental Cycle Ergometry (ICE)

Participants performed a CPET on an electrically braked cycle ergometer (Lode Corival, Lode B.V., Groningen, The Netherlands). Six minutes of resting measurements were followed by three minutes of unloaded pedalling at 60 revolutions per minute (RPM) before the ramp protocol commenced. The rate of work increase was calculated according to the predicted maximum work rate for each participant, accounting for their height, age and weight (11) with the aim to elicit exhaustion within 8-12 minutes (13).

Statistical Analysis

The normality of the data was assessed using the Kolmogorov-Smirnov test. The difference between parametric data was assessed using repeated measures ANOVA. Friedman's test was used to assess the difference between groups for non-parametric data. For post hoc analysis, Bonferroni adjustment was used to correct for multiple testing. The intra-class correlation coefficients were determined between the three shuttle walk tests. The coefficient of repeatability, and the precision, for the difference between the second and third ISWT distance were calculated using the methods described by Bland and Altman (14). Heteroscedasticity was demonstrated by performing linear regression on the absolute difference between the second and third ISWT distance versus the average ISWT distance (15) Pearson's correlation coefficient was used to assess the validity between the third ISWT distance and the VO_{2pk} derived from both the ITM and ICE. All p values less than 0.05 were considered statistically significant.

Results

61 patients were recruited and 50 patients completed all three visits. Three patients were withdrawn from the study, two due to hospital admission for asthma exacerbation and one due to a new diagnosis of sarcoma. Eight patients dropped out of the study for personal reasons. In total 50 patients completed both ITM and ISWT and 49 patients completed ICE; one patient was not able to perform the CPET on the cycle ergometer due to limited knee extension from previous bilateral knee replacements. The baseline characteristics of the participants (Table 1) were similar between the completers and non-completers except for FEV_1 which was higher for the non-completers.

Repeatability of ISWT

The mean ISWT distance for the three ISWTs were 400 (156) m, 418 (142) m and 438 (157) m, p=0.001 (Table 2) with an intraclass correlation of 0.963, p<0.001. Overall, there was a significant difference between the distance walked for ISWT1 and ISWT3 (mean difference [95% CI] -38 [-68 to -8], p=0.008), and between ISWT2 and ISWT3 distance (mean difference [95% CI] -20 [-34 to -6], p=0.003). The most common reason for terminating the tests on all three occasions was breathlessness (Table 2).

Figure 2 represents the coefficient of repeatability (80m) of the distance walked between the second and third ISWT. However, the variation of the difference between the second and third ISWTs (R^2 = 0.273, p < 0.01) was dependent on the magnitude of the average ISWT distance i.e. the increase in the third ISWT distance was greater in patients with a higher average ISWT distance which is termed heteroscedascity. .

Validity of the ISWT distance

Table 3 shows the peak physiological values for the CPETs derived from the ITM and ICE. Our study population reached more than 80% of their predicted maximum heart rate (82% on ICE and 89% on ITM). 22/50 developed mild to moderate EIB (no participant developed severe EIB).

The ISWT distance showed a strong correlation with VO_{2pk} on ITM (r=0.74, $p < 0.001$) and ICE (r=0.75, $p < 0.001$) (Figure 3).

Discussion

Among patients with severe asthma, a small increase in ISWT distance occurs on repeated testing which is more pronounced in patients with better exercise capacity. We demonstrated that there was a strong correlation between the ISWT distance and VO_{2pk} derived from either an incremental cycle ergometer test or an incremental treadmill test. The ISWT distance has validity as a measure of exercise capacity in patients with severe asthma but is not interchangeable with laboratory exercise testing methods.

The mean ISWT distance is repeatable after a familiarisation test in other pulmonary and cardiac diseases (16). According to our data, patients with severe asthma improve their ISWT distance despite having an initial familiarisation test. The within group difference between the second and the third shuttle walk tests was small (approximately 20 metres). However, in clinical practice to be certain a true change in ISWT distance has occurred within an individual post intervention, a distance of greater than 80m would need to be achieved (i.e more than the co-efficient of repeatability). This is slightly higher than the distance reported for patients with either Chronic Obstructive Pulmonary Disease (COPD) or Chronic Heart Failure (CHF) of 60m (17).

There could be some potential factors contributing to improvement in ISWT distance on repeated testing in patients with severe asthma. By comparing the peak values on the third ISWT, ICE and ITM for heart rate, BP, and perceived breathlessness and exertion (Table 3) we can conclude that patients did not achieve their maximal values and performed sub-maximally on their initial shuttle walk test. As a result the improvement in the shuttle walk test could have been as a result of patients pushing themselves slightly harder at each test. Low self-confidence and fear of exacerbating asthma symptoms among this group of patients could have contributed to the submaximal performance on the shuttle walk tests which slightly improved at each repeated testing (18), perhaps as patients were reassured by how they felt following the initial test. Assessment of maximal exercise capacity via a laboratory based test such as CPET elicited a maximal exercise performance compared to the field based ISWT. Since our study population perceived themselves as being unfit with low confidence to exercise, the reassuring presence of the monitoring devices used in laboratory based testing may have contributed to their better performance on CPETs.

As expected, the mean [SD] ISWT distance was higher in our patients with severe asthma compared to the studies among COPD and CHF patients with moderate to severe disease (302 [133] m and 380 [190] m accordingly)(4,19). However, the average ISWT distance was lower in our study population compared to adults with obstructive sleep apnoea (OSA) with obesity, cystic fibrosis (CF) and the healthy population reported in other studies (580 [207], 754 [362] and 733 [183] respectively)(20-22). The protocol used for ISWT in the OSA and CF studies differed from other studies in that patients were allowed to run as the speed on the ISWT increased. We adhered to the original protocol for performing ISWT as described by Singh et al (4), where ISWT was validated with walking only. This could explain why patients with CF had a slightly higher ISWT distance compared to healthy individuals and may also explain the better performance on ISWT among patients with OSA and CF compared to the patients with severe asthma in our study. Additionally, the lower ISWT distance among our patients could indicate that walking on the flat surface was not enough of a stimulus to provoke a maximal exercise test from them.

Other factors that could have limited the value of the ISWT as a maximal exercise test in this group of patients include the effects of their elevated BMI on both agility and, hip and knee joints, which may have made the turning points uncomfortable and slower to complete. Whilst patients with OSA had a similar mean BMI (at 33 kg/m^2) to our patients with severe asthma, patients with OSA were allowed to run during the ISWT which may have compensated for the effects of slowing at the turn points.

Patients with severe asthma often have persisting eosinophilic airway inflammation and issues with non-adherence to medication, and as a result may be prone to develop EIB. EIB usually occurs 5-10 minutes after the cessation of modest periods of high intensity exercise and a short period of hyperpnoea and resolves spontaneously within 30-90 minutes (12). After resolution of EIB, patients enter a refractory period for up to 2 to 4 hours and if they engage in another bout of exercise within the refractory period, they may not develop EIB (23). 22/50 patients developed EIB (13 patients mild and 9 patients moderate EIB) after the ITM, which supports the possibility of EIB post the ISWT among some of these participants. This refractory period could potentially account for some of the improvement in the third

ISWT distance that was performed at least 30 minutes after the second ISWT supported by our data as the statistically significant difference occurred after the third ISWT.

There were some limitations of this study including 1) portable expiratory gas analysis was not performed during the ISWT to assess whether there was the same linear increase in oxygen uptake and VO_{2pk} as achieved in the ITM and ICE. However, in clinical practice the outcome measure for ISWT is the distance covered by the participant and the results from our study showed that there was strong correlation between the ISWT distance and VO_{2pk} on both ITM and ICE but the tests are not interchangeable. 2) We cannot exclude the effect of refractory period post EIB on the improvement in the third ISWT distance as we did not perform spirometry after the second and third shuttle walk test. 3) A specific sample size calculation was not performed, from our sample size of 49 participants the precision of the coefficient repeatability was ($\pm$ 20m) so we are 95% confident that the co-efficient of repeatability of the ISWT lies between 60 - 100m (Figure 2). A larger sample size would only refine the estimate within this range which is unlikely to aid further interpretation within an individual in clinical practice. 4) The familiarisation ISWT was performed in the same visit as a cardiopulmonary exercise test which may have led to a submaximal performance if they had not fully recovered after the cardiopulmonary exercise test despite the thirty minutes rest.

In conclusion, there was a small increase in ISWT distance on repeated testing which needs to be considered when used as an outcome measure for non-randomised clinical trials. In clinical practice, the co-efficient of repeatability and the presence of heteroscedasticity need to be considered when assessing whether a true change has occurred from an intervention within an individual patient. The ISWT distance has validity compared to VO_{2pk} both on ITM and ICE, but they are not interchangeable in patients with severe asthma.

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Table 1: Baseline characteristics of participants

Patient characteristics	Completers (n=50)	Non-completers (n=11)
Age (years)	54 (13)	51 (16)
Female, n (%)	33 (66)	5 (45)
MRC*	2 (2-3)	2 (2-3)
BMI (kg/m^2)	32 (6)	34 (8)
FEV_1 (litres)	1.9 (0.8)†	2.3 (0.4)
FEV_1 %	69 (20)	71 (15)
%FEV_1/FVC	68 (11)%	75 (12)%
ICS dose (µg/d)	1586 (326)	1455 (311)
Maintenance Oral Steroid, n (%)	28 (56)	22 (44)
Oral steroid dose (mg)	8 (4)	9 (4)
Atopic, n (%)	34 (68)	8 (73)

Data presented as mean (SD) unless *: median (IQ), percentage or frequency as indicated, n: number, MRC: medical research council dyspnoea score, BMI: body mass index, FEV_1: forced expiratory volume in 1 s, FVC: forced vital capacity, ICS: inhaled corticosteroids
† $p < 0.05$

Table 2: Results of the Incremental Shuttle Walk Test

	ISWT 1	ISWT 2	ISWT 3	P value
Distance (m)	400 (156)	418 (142)	438 (157)	‡¥
BORG breathlessness scale*				
Before	0.5 (0-1)	0 (0-0.5)	0.5 (0-0.5)	†‡
After	3(3-4)	3 (2-4)	3 (3-5)	‡
BORG perceived exertion scale*				
pre-test	6 (6-7)	6 (6-7)	6 (6-7)	‡
post-test	13 (11-15)	13 (11-14)	13 (12-15)	‡
Heart Rate				
Pre-test	88 (13)	82 (11)	82 (13)	†¥
Post-test	123 (21)	120 (18)	124 (18)	‡
Systolic blood pressure				
Pre-test	128 (15)	128 (16)	131 (17)	N/A
Post-test	144 (22)	146 (21)	141 (21)	N/A
Diastolic blood pressure				
Pre-test (mmHg)	86 (11)	82 (10)	85 (11)	†¥
Post-test (mmHg)	87 (19)	88(14)	88 (14)	N/A
Oxygen saturation (SpO_2)				
Pre-test	95 (2)%	96 (2)%	96 (2)%	†‡
Post-test	93 (3)%	93 (3)%	93 (3)%	N/A
Limiting Symptom				
SOB (n)	20	20	24	N/A
leg fatigue (n)	11	12	9	N/A
SOB and leg fatigue (n)	2	5	8	N/A
General fatigue (n)	14	12	8	N/A
Others (n)	3	1	1	N/A

Data presented as mean (SD) unless *: median (IQ), ISWT: Incremental Shuttle Walk Test, SpO_2: oxygen saturation, SOB: shortness of breath

† $p < 0.05$ between ISWT1 and 2

‡ $p <0.05$ between ISWT2 and 3

¥ $p< 0.05$ between ISWT 1 and

Table 3: Comparison between the results of the cardiopulmonary exercise tests and the incremental shuttle walk test

	ITM	ICE	ISWT	P Value
VO_{2pk} (ml/min)	1969 (586)	1528 (500)	N/A	†
VO_{2pk} (ml/min/kg)	23 (6)	18 (5)	N/A	†
VCO_{2pk} (ml/min)	1974 (721)	1606 (563)	N/A	†
Peak RR (breath/min)	37 (8)	33 (8)	N/A	†
Peak HR (beat/min)	145 (19)	137 (21)	124 (18)	†‡¥
%Predicted HR	89 (10)	82 (10)	75 (11)	†‡¥
VE_{max}(l/min)	64 (23)	53 (21)	N/A	†
%MVV (l/min)	94 (25)	80 (22)	N/A	†
RER at VO_{2pk}	1.0 (0.1)	1.03 (0.1)	N/A	†
Systolic BP (mmHg)	155 (23)	154 (26)	141 (21)	‡¥
Diastolic BP (mmHg)	83 (15)	80 (14)	88 (14)	¥
SpO_2	97 (3)%	98 (2)%	93 (3)%	†‡¥
BORG breathlessness*	5 (4-8)	5 (4-7)	3 (3-5)	‡¥
Perceived exertion*	15 (13-17)	17 (15-19)	13 (12-15)	†‡¥

Data presented as mean (SD) unless *: median (IQ), ITM: maximal incremental treadmill test, ICE: maximal incremental cycle ergometer test, ISWT: incremental shuttle walk test, VO_{2pk}: peak oxygen uptake, VO_2: oxygen uptake, VCO_{2pk} : peak carbon dioxide output, RR: respiratory rate, HR: heart rate, VE_{max}: maximum minute ventilation, %MVV: percent maximum voluntary ventilation, RER: respiratory exchange ratio, BP: blood pressure, SpO_2:, oxygen saturation, N/A: not applicable.

† $p < 0.05$ between ITM and ICE
‡ $p < 0.05$ between ITM and ISWT
¥ $p < 0.05$ between ICE and ISWT

Figure1: Study Design

ITM: maximal incremental treadmill test, ICE: maximal incremental cycle ergometer test, ISWT: incremental shuttle walk test.

Figure 2: Repeatability of Incremental Shuttle Walk Test among patients with severe asthma.

The Solid line represents the mean difference between ISWT 3 and ISWT 2, the dashed lines represent the repeatability coefficient, the dotted lines represent the precision of the coefficient of repeatability, ISWT: Incremental Shuttle Walk Test

Figure 3: A comparison between VO_{2pk} measured on ITM (A) and ICE (B) with the ISWT distance

The solid line represents the best line of fit with dashed lines representing 95% CI. VO_2: oxygen uptake, ITM: maximal incremental treadmill test, ICE: maximal incremental cycle ergometer test, ISWT: incremental shuttle walk test