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VIA MEDICA

**GUIDELINES** 

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# Polish Respiratory Society guidelines for the methodology and interpretation of the 6 minute walk test (6MWT)

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#### Purpose

This statement contains cohesive practical guidelines for the indications, contraindications, methodology and interpretation of 6 minute walk test (6MWT). The authors are convinced that these guidelines may also be helpful in the National Health Fund (Narodowy Fundusz Zdrowia) reimbursement issues (procedure No 89.387 — spirometry with 6 minute walk test).

The document has been prepared by the Polish Respiratory Society Task Force recruited from the members of the PRS Respiratory Physiopathology section in the form of a consensus statement.

#### Background

Disability related to progressive functional impairment is one of the most important consequences in chronic conditions, particularly in chronic cardiovascular and respiratory diseases. Exercise intolerance is a widely accepted measure of the degree of disability [1]. Thus, in many diseases, assessment of exercise tolerance is an important element in the evaluation of the patient.

Functional classifications may provide some information about the physical condition of the patient. The New York Heart Association (NYHA) classification is widely used in patients with heart failure [2], for patients with chronic obstructive pulmonary disease the Medical Research Council (MRC) dyspnea scale is recommended. [3]. Nevertheless, this is a subjective evaluation and in the majority of cases, objective measures are more important and have a higher value.

Cardiopulmonary exercise test is a complex test performed on a treadmill or cycle ergometer. Walk tests are a simple alternative method which also allow to assess exercise response [4]. 6 minute walk test is the most commonly used, however there are various test modalities which include different time durations (e.g. 12 minute walk test), fixed distance, step test or shuttle walk test [5].

6MWT is currently widely used to evaluate functional capacity. It may more adequately reflect patient's activity than complex tests as the level of exercise is comparable to that performed on a daily basis [6]. The main advantage of simple exercise tests is that they do not require equipment and may thus be performed in most healthcare centers. However, they provide little information on the cause of limited exercise tolerance. Only when certain evident signs occur may the differentiation be possible, e.g. chest pain may indicate heart disease, while a decrease in oxygen saturation  $(SpO_2)$  strongly suggests a respiratory background.

#### **Indications and limitations**

According to the American Thoracic Society (ATS) the main indication for 6MWT is the assessment of response to medical interventions in patients with mild to moderate chronic respiratory or cardiovascular disease [7].

The most important indications for 6 MWT are presented in Table 1.

The absence of a disease or clinical condition listed above does not indicate that the 6MWT is not the optimal and only exercise test that may be applied in the given situation.

Controversies concerning the role of 6MWT in the qualification for lung resection in patients with lung cancer may serve as an example. Despite optimistic initial observations on the prognostic role of 6MWT in these patients [81], guidelines do not indicate 6MWT as the method of choice in the assessment of exercise capacity and the cardiopulmonary exercise test (CPET) with maximal oxygen uptake (VO<sub>2max</sub>) is preferred [82-87]. However, considering the limited availability of CPET in Poland, 6MWT should be performed as a screening test in such patients. In patients with a significant decrease in the 6 minute walk distance (6MWD), CPET should be performed before the disgualification from surgery for lung cancer. Of note, a 6MWD of 500 m corresponds roughly with a  $VO_{2max}$  of 15 ml/ kg/min [84, 88], a value which is considered the cut-off point for surgery by most experts in the field. [85, 87, 89].

In some situations, 6MWT may be the only exercise test that the patient is able to perform. This may refer to patients with intellectual disability and mental disorders.

#### Contraindications

Table 2 presents the most relevant contraindications for the 6MWT [4, 7, 90].

Majority of the recommendations for the contraindications do not come from randomized clinical trials and have the form of suggestions with special regard to safety issues. Stable coronary heart disease in not a contraindication for 6MWT, however the patient should receive his or her standard treatment prior to the test and short acting nitrates must readily be available [7].

# Table 1. Indications and potential applications of the 6MWT

#### **Evaluation of functional capacity (single measurement)**

COPD [8] Pulmonary hypertension [9–11] Heart failure [12–15] Cystic fibrosis [16, 17] Interstitial lung diseases [18, 19] Peripheral arterial disease [20] Parkinson's disease [21, 22] Brain injury (e.g. stroke) [23–25] Elderly disabled patients [26–28] Intellectual disability [29, 30] and mental disorders [31, 32] Fibromyalgia [33] Recovery after abdominal surgery [34]

#### Qualification for medical interventions and/or follow-up

Lung resection Lung transplantation [35–38] Lung volume reduction surgery (LVRS) [39, 40] Pulmonary rehabilitation [41–46] Rehabilitation in other conditions [47] COPD [48–51] Pulmonary hypertension [52, 53] Heart failure [14, 54, 55] **Predicting survival** Heart failure [56, 57]

COPD [58-60]

Primary pulmonary hypertension [61-63]

Peripheral arterial disease [64-66]

Chronic liver diseases [67], qualification for liver transplantation [68]

Lung injury in other conditions: Radiation-induced pulmonary toxicity [69]

Evaluation of functional capacity in children [70, 71] Pulmonary hypertension [72] Evaluation of selected metabolic parameters [73] Diabetes mellitus [74] Cerebral palsy [75], neuromuscular diseases [76-79] Qualification for lung transplantation in cystic fibrosis [80]

Literature data indicate that 6MWT is a safe procedure. Despite the large number of tests performed, there are no reports on serious complications, even in patients with heart failure and other diseases [6, 91-93].

#### Table 2. Contraindications for the 6MWT

Absolute	Relative
< 7–10 days from primary angioplasty due to STEMI < 24 h from elective coronary angioplasty	Resting heart rate > 120/min
Acute myocarditis or pericarditis	Systolic blood pressure > 140 mm Hg
Symptomatic arrhythmias	Diastolic blood pressure > 90 mm Hg
Acute deep venous thrombosis, pulmonary embolism, pulmonary infarction	
Acute heart failure	
Acute infectious diseases or other con- ditions which may have relevant impact on the capability of performing the test (e.g. severe anemia, acute renal or liver failure, hypo- or hyperthyroidism etc.)	

## Recommendation

1. The most important absolute contraindication for 6MWT is the period of < 7-10 days from primary coronary angioplasty due to STEMI and < 24 h from elective angioplasty.

#### Methodology

The 6 minute walk test should be performed along a straight and flat corridor with a hard surface and a length of 30 m [7]. This corridor length was applied in the majority of large studies involving 6MWT [55, 56, 92, 94–98], however other lengths have also been used: 20-25 m [13, 14, 57, 99], 45-50 m [100, 101], 90 m [102] and 125 m [103]. The walking distance may be shorter in shorter corridors because of more turns to change direction are needed [7]. A study in patients with COPD demonstrated that the 6MWD was approximately 13 m longer when the test was performed on a 40 m circular course when compared to a straight 30 m corridor [104].

Performing the test on a treadmill is not recommended [7]. A comparative analysis of a 12 minute walk test in a 40 m corridor and on a treadmill showed that the distance walked was longer during the test on the corridor (791  $\pm$  224 m vs. 742  $\pm$  224 m), however the difference did not reach statistical significance [105]. Swerts et al. also noted a longer distance during the 12 minute walk test performed in a corridor than on a treadmill [106]. Other authors confirmed that the distance covered during the test on a corridor is significantly longer than that on a treadmill  $(374.3 \pm 77.7 \text{ m vs. } 323.1 \pm 118.6)$  [107]. Elazzazi et al., however, did not find any difference between the distance walked in the corridor and the treadmill [108]. In all the three mentioned studies a motorized treadmill was used and the treadmill speed could be modified. Janaudis-Ferreira et al. who compared the performance in tests performed in the corridor and on a non-motorized treadmill found that the distance covered in the corridor was 153 m longer [109].

The advantage of the 6MWT on a treadmill is that it can be conducted in small spaces.

### **Required equipment**

6MWT does not have complicated equipment requirements. The following are necessary:

- straight 30 m long corridor with a hard surface. It is recommended that the corridor should be at least 2-3 m wide and seldom travelled. The course should be marked every 2 m
- two colored cones which mark the starting point and the end of the lap
- timer
- sphygmomanometer
- pulse oximeter
- a chair/wheelchair
- a worksheet to note the number of laps or a mechanical lap counter (Appendix 1)
- a big-font reprint of the Borg scale (Appendix 2)
- a set of encouraging instructions (Appendix 3)
- referral form (Appendix 4)
- signed informed consent of the patient (Appendix 5).

The evaluation of oxygen saturation during 6MWT is an important element of the test. A number of studies published recently indicate that there is a relationship between  $\mathrm{SpO}_2$  decrease during the test and the BODE index [110], the degree of airflow limitation [111, 112], mortality risk [111]. Hypoxemia during exercise is very common in patients with chronic respiratory diseases [48]. Two types of SpO<sub>2</sub> variability during the walk test have been documented: a gradual decline with a plateau and return to baseline after the test is completed; a decline at the beginning of the test with subsequent increase during exercise (SpO2 at the end of the test is usually lower than baseline and, at the same time, higher than the lowest value recorded during the test) [48, 113, 114]. To obtain a reliable evaluation of oxygen saturation during 6MWT, a continuous SpO<sub>2</sub> monitoring during the whole test is recommended.

The better quality of recordings form the finger clip than earlobe sensor [115, 116], differences in the measurement accuracy of various devices [117-119] and the potential influence of other factors on the measurements should be considered [120, 121].

For safety reasons, the following should be provided:

- the possibility of immediate contact with the physician responsible for conducting exercise tests or the attending physician of the patient
- access to an oxygen source
- access to a resuscitation kit.

### **Recommendations**

- 2. The 6-minute walk test should be performed in a flat and straight corridor with a hard surface and a length of 30 m.
- 3. Performing the 6MWT on a treadmill is not recommended.
- 4. The walking course should be marked every 2 m.
- 5. Continuous oxygen saturation monitoring during 6MWT is indicated.

# Methodology of the test

#### **Patient preparation:**

- the patient should carefully read and sign the informed consent form
- repeated tests (if indicated) should be performed at the same time of the day
- pre-test warm-up is not recommended
- the patient should refrain from intensive exercise within 2 hours before the test
- loose, comfortable clothing which does not affect mobility should be worn
- comfortable non-slip shoes are necessary. The test should not be performed in slippers, high-heel shoes or barefoot
- the test should be performed after a light meal (depending on the time of the day) and administration of the patient's daily medication
- if necessary, usual walking aid (e.g. cane, walker, corset) should be used during the test

### Recommendations

- 6. The patient should carefully read and sign the informed consent form.
- 7. Repeated tests should be performed at the same time of the day.
- 8. Pre-test warm-up is not recommended.

- 9. The patient should refrain from intensive exercise within 2 hours before the test.
- 10. Loose, comfortable clothing which does not affect mobility should be worn.
- 11. Comfortable non-slip shoes are necessary. The test should not be performed in slippers, high-heel shoes or barefoot.
- 12. The test should be performed after a light meal (depending on the time of the day) and administration of the patient's daily medication.
- 13. If necessary, usual walking aid (e.g. cane, walker, corset) should be used during the test.

# Technical aspects

- 1. The presence of a physician during 6MWT is not mandatory, however it is indicated in high-risk patients
- 2. The patient should rest in a sitting position for 5-10 minutes before the test, near the starting point. During this time:
- patient preparation and potential contraindications for the test should be checked
- arterial blood pressure and heart rate should be measured and recorded
- oxygen saturation should be evaluated
- Borg scale should be used to assess dyspnea (all measurements should be noted on the test worksheet)
- the principles of the test should be explained to the patient. It is recommended that every patient is provided with exactly the same information on the test:

The aim of the test is to walk as far as possible for 6 minutes. You will be asked to walk back and forth along this corridor. The exercise you will perform during these six minutes is intensive, therefore you may feel short of breath or tired. You may slow down or even stop and lean against the wall to rest if necessary, but please resume walking as soon as you can [7].

The patient should then get prepared to start the test:

Are you ready to start? Once you start, the counter will be turned on and you will hear it click with every turn, this will be noted on the worksheet. Remember that you are supposed to walk as fast as possible for 6 minutes, so do not jog or run. You may start, when you are ready.

1. The technician should stand close to the starting point and start the counter the moment the patient starts walking. It is not recommended to walk with the patient.

- 2. The supervising technician should not be distracted and click the lap counter in an expressive manner (for encouragement) or note every turn on the worksheet. Every stop and rest should also be noted. The stopwatch should not be turned off for the time of the rest this time is included in the duration of the 6MWT.
- 3. Encouragement of the patient during the test is strongly recommended. An even tone should be used for standard phrases [7]. The motivation should be customized to the patient profile. For example, a 10-year old child and a 75-year old COPD patient with basic education as well as a 40-year old patient with lung fibrosis require a different set of encouragement phrases. Motivation should be used at one-minute intervals and 15 s before the end of the test. An example of encouragement sentences is given below:

# First minute:

You are doing very well. There are 5 minutes left. Second minute:

Your pace is very good. You have 4 more minutes to go.

# Third minute:

You are doing good. Half of this test is done.

# Fourth minute:

Your pace is very good. There are only 2 minutes left .

# Fifth minute:

Keep on walking like this. There is only one minute to go.

# 15 s to the end of the test:

You will be asked to stop in a few moments. When you stop, please wait for me at the point you finished the test.

# If the patient stops during the test:

Please rest, you may lean against the wall, if you need to. Continue walking as soon as you are able.

- 4. After six minutes, the technician should say loudly: *Please stop*. If the patient appears exhausted providing him/her with a chair or wheelchair should be considered.
- 5. Immediately after the end of the test:
- SpO<sub>2</sub>, heart rate and arterial blood pressure should be measured and recorded on the test worksheet
- dyspnea should be reported (Borg scale). If the patient stopped during the test, the reason why he/she needed to rest should also be noted in the study protocol.
- the distance walked should be calculated by adding the distance from the number of laps

(1 lap = 60 m) and number of meters in the final lap. The distance should be rounded to the nearest meter.

 the patient should be congratulated on the effort and offered a rest with a glass of water.

## Recommendations

- 14. The presence of a physician during 6MWT is not mandatory, however it is indicated in high-risk patients.
- 15. The principles of the 6MWT should be explained to the patient. It is recommended that every patient is provided with exactly the same information on the test.
- 16. Before the 6MWT test:
- patient preparation and potential contraindications for the test should be checked
- arterial blood pressure and heart rate should be measured
- oxygen saturation should be evaluated
- Borg scale should be used to assess dyspnea All measurements should be noted on the test worksheet.
- 17. Every stop and rest should also be noted. The stopwatch should not be turned off for the time of the rest — this time is included in the duration of the 6MWT.
- 18. To improve effort, the use of standardized encouragement phrases with an even tone during the test is recommended. Motivation should be customized to the patient profile. Encouragement should be used at one-minute intervals and 15 s before the end of the test.
- 19. Post-walk evaluation should be done immediately after exercise and include:  $SpO_2$ , heart rate and arterial blood pressure
- dyspnea (Borg scale)
- distance walked (calculation with 1 meter accuracy)
- reason for stopping exercise, if the patient stopped during the test

All the above should be recorded in the study protocol.

# Factors influencing 6MWD

Like many other diagnostic test, the result of 6MWT may be influenced by various factors (Table 3).

Methodological factors affecting 6MWD which may be modified include learning effect, the experience of the supervising technician and encouragement intensity during the test.

# Table 3. Factors influencing the distance covered during 6MWT [7]

6MWD reduction
older age [28]
shorter height
elevated body weight
female sex
lack of motivation, depression
shorter corridor (more turns) [122]
inappropriate walking shoes [123]
cognitive disorders
chronic respiratory diseases [124, 125]
chronic vascular diseases [126]
chronic musculoskeletal disorders
6MWD increase
taller height
male sex
strong motivation (encouragement during the test)
experience in the test performance
pre-test administration of medication for disabling disease
supplemental oxygen in patients with exercise induced hypoxemia, $\mbox{HeO}_2$ use [127]

### Learning effect

Despite a substantial number of studies which address the reproducibility of 6MWT, it is still not clear if performing a practice test is necessary. According to literature data a practice test may increase 6MWD by 7-17% [8, 100, 107, 128, 129].

In the opinion of the experts from the ATS, a practice test is not necessary in most clinical settings. Nevertheless, if it is performed, there should be an interval of at least 1 hour between the two tests and the higher 6MWD should be reported [7].

### Recommendations

- 20. Practice tests are not necessary in patients who achieve normal 6 MWD values in the first test.
- 21. Practice tests should be considered in:
- patients who have a relatively short 6MWD, which does not correspond with their general condition.
- patients in whom the result of 6MWT may have significant practical implications, e.g. qualification for transplantation, lung resection, modification of medical interventions

- elderly patients with impairment of motor coordination in whom simple maneuvers (turns) may by problematic
- clinical study participants.
- 22. There is no evidence for the usefulness of more than 2 practice tests
- practice tests and 6MWT should be performed within a period no longer than 7 days
- when performed the same day, an interval of at least one hour should be kept between subsequent tests
- the longest recorded distance should be considered as the result of the 6MWD.

# **Technician experience**

The laboratory staff should be trained by the person responsible for exercise tests; training in basic life support is also strongly recommended. Quality control should be performed every 6 months. Quality control is mandatory as it may affect the results of 6MWD. In a study which involved 4 centers and more than 2000 elderly patients, the differences in the methodology of the test (including the application of encouragement) in two centers resulted in a 7% shorter distance [92].

# Recommendations

- 23. The laboratory staff should be trained by the person responsible for exercise tests.
- 24. Technician training in basic life support is also strongly recommended.
- 25. Quality control should be performed by the person responsible for exercise tests every 6 months.

# Encouragement

The use of encouragement as described in the methodology section is recommended. As previously mentioned, encouragement can improve the walking distance by approximately 30 m. [130]. ATS experts, however, do not recommend encouraging patients to walk as fast as possible, as applied by some authors [100]. Such a motivation may lead to a higher walking speed, earlier termination of exercise and excessive stress for the cardiorespiratory system. [7].

# **Oxygen supplementation**

When the patient requires oxygen supplementation and repeated tests are necessary, the use of the same source and oxygen flow during the walk test is recommended. The mode of oxygen therapy and oxygen flow should be recorded in the study protocol. Disregarding oxygen supplementation during 6MWT leads to misinterpretation of its result.

# Interpretation

6MWT is performed as a single test to assess the functional status of the patient or it may be repeated to evaluate the impact of medical intervention (change in treatment regimen, rehabilitation, oxygen supplementation) on the patient's exercise performance.

The final result of the test should comprise the following information:

- Basic patient data:
  - name
  - age
  - height, weight
- Indication for 6MWT
- Data on methodology of the test
  - corridor length
  - for tests performed on a treadmill: speed, acceleration mode
  - for test performed with oxygen supplementation: oxygen source and oxygen flow
- Walk distance
  - absolute value and percent of predicted value; information on the author and source of the reference value should also be provided
  - information on the number of stops/time of rest during the test if applicable
- Heart rate
  - at rest
  - at peak exercise (6 min.)
  - Blood pressure
  - at rest
  - at peak exercise (6 min.)
  - Blood oxygen saturation
  - at rest
  - lowest recorded value
  - at peak exercise (6 min.)
  - desaturation (the difference between SpO<sub>2</sub> at rest and SpO<sub>2</sub> at peak exercise)
- Dyspnea according to the Borg scale
  at rest
  - at peak exercise (6 min.)
- Comments of the supervising technician

# Recommendations

26. The final result of the test should comprise information on the basic data of the patient, indications for 6MWT, methodology, distance walked and results of the following measurements (at rest and at peak exercise, i.e. after 6 min.): heart rate, blood pressure, blood oxygen saturation and dyspnea.

#### **Reference values**

No uniform reference values for 6MWD have been established to date. Table 4 presents the most relevant publications on reference values for 6MWD.

The choice of the source of the 6MWD reference equations is the decision of the exercise laboratory team; the reference population should correspond to the study population.

#### Recommendation

27. The choice of the source of the 6MWD reference equations is the decision of the exercise laboratory team; the reference population should correspond to the study population

# Single measurement interpretation — assessment of functional status

Both absolute and percent of predicted values of 6MWD should be considered during the interpretation of the result of 6MWT. Despite a number of factors modifying 6MWD, the absolute value of the distance walked provides useful information. In patients with COPD, 6MWD is used to calculate the BODE index, which defines prognosis in this disease. The cut-off values for 6 MWD applied for the stratification of functional impairment severity are 350 m, 250 m and 150 m [60]. In patients with COPD, absolute 6MWD is an important predictor for mortality, with the lowest risk for patients who achieve a distance longer than 400 m [58]. Earlier studies on patients qualified for lung resection, reported cut-off values of 300 m [81] and 450-500 m [83, 89] for predicting postoperative complications.

In patients with Eisenmenger's syndrome, 6MWD < 350 m is related with a three-fold increase in mortality risk [133].

Another study showed that a 6MWD < 250 m in patients with pulmonary hypertension (idio-

#### Table 4. Reference equations for the 6 minute walk distance.

	Author	No of patients	Age (yrs)	Corridor length (m)	Formula — men	Formula — women	r² of statisti- cal model
1	Enright [97]	290 (117 M, 173 F)	40-80	30	6MWD (m) = (7.57 × he- ight) – (5.02 × age) – (1,76 × body weight) – 309a	$\begin{array}{l} \text{6MWD (m)} = (2.11 \times \text{he-}\\ \text{ight)} \\ - (2.29 \times \text{body weight)} \\ - (5.78 \times \text{age}) + 667^{\text{b}} \end{array}$	F — 0.38 M — 0.42
2	Troosters [100]	51 (29 M, 21 F)	50-85	50	$\begin{array}{l} \text{6MWD (m)} = 218 + (5.14 \times \\ \text{height} - 5.32 \\ \times \text{ age}) - (1.80 \times \text{body we} \\ \text{ight} + 51.31)\text{c} \end{array}$	$\begin{array}{l} \text{6MWD (m)} = 218 + (5.14 \times \\ \text{height} - 5.32 \times \text{age}) - (1.80 \\ \times \text{ body weight})^\circ \end{array}$	0.66
3	Camarri [101]	70 (33 M, 37 F)	55-75	45	6MWD (m) = 216.9 + (4.12 x height) - (1.75 × age) - (1.15 × body weight)	$\begin{array}{l} \text{6MWD (m)} = 216.9 + (4.12 \\ \times \text{ height}) - (1.75 \times \text{ age}) - \\ (1.15 \times \text{ body weight}) - 34.04 \end{array}$	0.36
4	Gibbons [131]	79 (41 M, 38 F)	20-80	20	6MWD (m) = 868.8 - (age × 2.99)	$6MWD (m) = 868.8 - (age \times 2.99) - 7.47$	0.41
5	Enright [92]	2117 (853 M, 1264 K)	≥ 68	30	$\begin{array}{l} \text{6MWD (m)} = 493 + (2.2 \\ \times \text{ height}) - (0.93 \times \text{ body} \\ \text{weight}) - (5.3 \times \text{age}) + 17 \end{array}$	$6MWD (m) = 493 + (2.2 \times height) - (0.93 \times body weight) - (5.3 \times age)^{d}$	0.2
6	Chetta [98]	102 (48 M, 54 F)	20-50	30	$\begin{array}{l} \text{6MWD (m)} = 518.53 \ + \\ \text{(1.25} \times \text{height)} - \text{(2.816} \times \\ \text{age)} \end{array}$	6MWD (m) = 518.53 + (1.25 × height) – (2.816 × age) – 39.07	0.42
7	Casanova [93]	444 (238 M, 206 F)	40-80	30	$\begin{array}{l} \text{6MWD (m)} = 361 - (\text{age} \times 4) \\ + (\text{height} \times 2) + (\text{HR}_{\text{max}}\text{HR}_{\text{MAX}} \times 3) \\ - (\text{body weight} \times 1.5) \end{array}$	$\begin{array}{l} \text{6MWD (m)} = 361 - (\text{age} \times 4) \\ + (\text{height} \times 2) + (\text{HR}_{\text{maxk}}\text{HR}_{\text{MAX}} \times 3) - (\text{body weight} \times 1.5) \\ - 30 \end{array}$	0.38
8	Geiger [99]	456 (208 M, 248 F)	3-18	20	$6MWD (m) = 196.72 + (39.81 \times age) - (1.36 \times age ^ 2) + (13.28 \times height)$	6MWD (m) = 188.61 + (51.50×age) – (1.86×age ^ 2) + (86.10×height)	M — 0.49 F — 0.50
9	Prusak [132]	545 (261 M, 284 F)	7-18	the test was performed in a $20 \times 30$ m sports hall	6MWD (m) = 374.9 + (2.22×age) + (3.53×he- ight) - (1.71×body weight)	6MWD (m) = 419.8 + (14.99×age) + (2.56×he- ight) - (3.03×body weight)	M — 0.54 F — 0.48

HRmax%HRMAX — heart rate at peak exercise at the end of 6MWT (HRmax) expressed as percent of predicted maximal heart rate (HRMAX) calculated as follows HRMAX = 220-age

<sup>a</sup>to calculate lower limit of normal (LLN) subtract 153 from obtained value

<sup>b</sup>to calculate lower limit of normal (LLN) subtract 139 from obtained value

<sup>c</sup>residual standard deviation (RSD) = 56 m

<sup>d</sup>to calculate lower limit of normal (LLN) subtract 100 from obtained value

pathic and related with interstitial lung disease) is associated with a 50% mortality risk within 2 years [62]. In patients with idiopathic pulmonary hypertension, the 6MWD cut-off value which predicts survival was established at 332 m [61]. According to experts from the American College of Cardiology, an increase in 6MWD to  $\geq$  380–440 m should be one of the goals of treatment in idiopathic pulmonary hypertension [11].

In patients with heart failure, 6MWD < 300 m is associated with a significantly higher mortality compared to patients with 6MWD > 300 m (10% vs. 3%) [56]. Significant differences in mortality risk were also observed in patients with 6MWD < 300 m, 300-450 m and > 450 m [134].

A decrease in 6MWD is also a significant prognostic factor in idiopathic pulmonary fibrosis (IPF). Lederer et al. showed that in patients with IPF, a 6MWD < 207 m (considering the influence a number of other factors) is related with a four-fold higher mortality [63]. Another study showed that the cut-off value for 6MWD which defines functional impairment and has a significant impact on mortality risk in patients with IPF is 350 m [135].

Despite of a number of reference equations proposed by various authors, no algorithm for the interpretation 6MWD expressed as percent of predicted value has been established to date. Troosters et al. propose that a 6MWD below 82% of predicted value should be treated as abnormal [100]. The lower limit of normal for 6MWD may be calculated from equation 1[97] or 5 [92] presented in Table 4.

Equation 2 [100] may be applied for the calculation of residual standard deviation with the use of the following formula.

SR=(actual value-predicted value)/RSD

### Changes in blood oxygen saturation

Desaturation during 6MWT may indicate gas exchange impairment during exercise [136, 137]. A decrease of  $\text{SpO}_2$  by  $\geq 4\%$  or  $\text{SpO}_2 < 88\%$  or 90% during exercise is considered clinically significant [4, 138, 139].

# Interpretation — minimal important difference

Although numerous studies addressed the impact of medical interventions on 6MWT, it is still not clear if the changes in 6MWD should be expressed as an absolute value, relative difference or as the difference in percent of predicted value. It seems that presenting the difference as an absolute value is optimal, as it enables comparative analysis with other studies which may use different reference equations.

The evaluation of the potential effect of medical interventions is strictly related to the so called *minimal important difference* — MID or *minimally clinically important difference* — MICD which is used to describe the minimal significant change in 6MWD which is associated with improvement/ deterioration of functional performance reported by the patients.

Many authors apply the MID cut-off value of 54 m (95% CI 37-71 m) proposed by Riedelmeier et al. who analyzed a group of 112 patients with COPD [140]. In other studies, the MID ranged between 26 and 80 m [141-143]. In the ECLIP-SE study, a > 30 m decrease in 6MWD within 12 months was associated with a higher mortality risk (hazard ratio 1.93) [96].

In elderly patients with heart failure, the reported MID was 24-48 m, depending on the self-reported change in functional performance (slight improvement — significant deterioration)[144].

In patients with pulmonary hypertension, an MID of 33 m was established with a range of 25-39 m depending on the reference equation applied [145]. The MID for patients with idiopathic pulmonary hypertension is 24-45m, and a decrease of > 50 m in 6MWD within 24 weeks is a negative prognostic factor and is related with an at least four-fold higher mortality risk [146].

### **Impact of interventions on 6MWD**

One of the first reports on 6 MWT showed that supplemental oxygen (2 L/min and 4 L/min) improved 6MWD by 51 m and 75 m, respectively, however when portable oxygen was applied, the improvement was irrelevant [147]. Leach et al. demonstrated that the use of portable liquid oxygen with FiO<sub>2</sub> 0.28, 0.4 and 0.53 resulted in an increase in 6MWD by 19.2%, 34.5% and 36.3% when compared to the test performed with the use of an oxygen cylinder of a similar weight as the device with liquid oxygen. Moreover, the degree of desaturation as well as dyspnea were lower [129].

Pulmonary rehabilitation is reported to increase 6MWD by 40-48 m [124, 148].

Lung volume reduction surgery increases the 6MWD by approximately 55 m [149].

Rehabilitation also improves exercise performance in patients with cardiovascular diseases; a 6MWD increase of approximately 60 m may be observed [150].

#### Recommendations

- 28. A significant decrease in 6MWD is defined as a decline < 82% of predicted value or below the lower limit of normal.
- 29. A decrease of  $\text{SpO}_2 \ge 4\%$  (as compared to  $\text{SpO}_2$  at rest) or below 88% (or 90%) is considered clinically significant.
- 30. Disease specific minimal important difference (MID) should be considered in the analysis of the impact of medical interventions on 6MWD.

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# **Appendix 1**

Study protocol 6 minute walk test 30 meter corridor

Name	ID	Date	
Age	Body weight (kg)	Height (cm)	Protocol No
Indication			
Start time:			
Comments:			

	start	end
HR		
RR		
Sp0 <sub>2</sub>		
Dyspnea		
Distance		

Laps

Stops: 1 — duration s, reason:

2 — duration s, reason:

3 — duration s, reason:

4 — duration s, reason:

5 — duration s, reason:

# Appendix 2

Referral for the 6 minute walk test and patient consent form **REFERRAL FOR THE 6 MINUTE WALK TEST** 

Institution:
Indication for 6MWT:
Concomitant diseases:
1. None
2. Concomitant diseases which may influence the course of the test (musculoskeletal disorders in particular)

I DECLARE NO CONTRAINDICATIONS FOR THE 6 MINUTE WALK TEST.

Date and signature of the referring physician Attention: Information for the patient and the consent form are on the reverse page

### INFORMATION for the patient

The aim of the study is to walk the longest distance possible during 6 minutes. You will be walking along the corridor between two marked points. During the test you may slow down or stop if necessary but you should continue walking as soon as you can, so that the distance walked in 6 minutes will be as long as possible. The technician will inform you about the time from the start of the test and about the time left to the end. Directly before and immediately after the test your blood pressure, heart rate and oxygen saturation with a finger sensor will be measured. You will also be asked to evaluate your dyspnea in a 10-point scale.

The distance walked in 6 minutes expressed in meters is the result of the test.

## PATIENT CONSENT FORM

I, .....

have read and understood the above information on the test, had the opportunity to ask additional questions, understood and accepted the given answers. I agree to perform the test and give my consent for storing my personal data.

# Appendix 3

### **INFORMATION FOR THE PATIENT**

The aim of the test is to walk as far as possible for 6 minutes. You will be asked to walk back and forth along this corridor. The exercise you will perform during these six minutes is intensive, therefore you may feel short of breath or tired. You may slow down or even stop and lean against the wall to rest if necessary, but please resume walking as soon as you can.

Are you ready to start? Once you start, the counter will be turned on and you will hear it click with every turn, this will be noted on the worksheet. Remember that you are supposed to walk as fast as possible for 6 minutes, so do not jog or run.

You may start, when you are ready.

#### Appendix 4

#### Encouragement

- only the standardized encouragement phrases presented below should be used
- an even tone during motivation is recommended
- the technician should not talk to the patient or to the potential observers during the test

#### First minute:

You are doing very well. There are 5 minutes left.

#### Second minute:

Your pace is very good. You have 4 more minutes to go.

#### Third minute:

You are doing good. Half of this test is done.

### Fourth minute:

Your pace is very good. There are only 2 minutes left .

#### Fifth minute:

Keep on walking like this. There is only one minute to go.

#### **15 s to the end of the test:**

You will be asked to stop in a few moments. When you stop, please wait for me at the point you finished the test.

If the patient stops during the test:

Please rest, you may lean against the wall, if you need to. Continue walking as soon as you are able to.

### Appendix 5

#### Borg dyspnea scale

- 0 nothing at all
- 1. very, very slight
- 2. very slight
- 3. slight
- 4. moderate
- 5. somewhat severe
- 6. severe
- 7. very severe
- 8.
- 9. very, very severe
- 10. maximal