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REVIEW

Physical rehabilitation for lung transplant candidates and recipients: An evidence-informed clinical approach

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Abstract

Physical rehabilitation of lung transplant candidates and recipients plays an important in optimizing physical function prior to transplant and facilitating recovery of function post-transplant. As medical and surgical interventions in lung transplantation have evolved over time, there has been a demographic shift of individuals undergoing lung transplantation including older individuals, those with multiple co-morbidites, and candidates with respiratory failure requiring bridging to transplantation. These changes have an impact on the rehabilitation needs of lung transplant candidates and recipients. This review provides a practical approach to rehabilitation based on research and clinical practice at our transplant centre. It focuses on functional assessment and exercise prescription during an uncomplicated and complicated clinical course in the pre-transplant, early and late post-transplant periods. The target audience includes clinicians involved in pre- and post-transplant patient care and rehabilitation researchers.

Key words: Lung transplantation; Rehabilitation; Physical therapy; Exercise training; Physical activity

Core tip: This expert review brings together clinical experience and research evidence on physical rehabilitation for lung transplant candidates and recipients. The evaluation of exercise capacity, muscle function, mobility, activities of daily living and physical activity is discussed. Rehabilitation training guidelines for pre-transplant, acute care, early and late post-transplant phases are provided with special attention to complicated and uncomplicated clinical courses. Special populations such as heart-lung transplant and paediatric lung transplant are also included.

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INTRODUCTION

Lung transplantation is performed for a variety of advanced lung diseases, with primary indications including interstitial lung disease (ILD), chronic obstructive pulmonary disease (COPD), cystic fibrosis (CF) and pulmonary vascular disease[1]. Since the world's first successful single lung transplant in Toronto, Canada[2] physical rehabilitation has played an integral role in preparing individuals for lung transplantation and facilitating their recovery[3,4].

Although pre- and post-transplant rehabilitation is recommended in the majority of lung transplant centers in Canada[5], there are currently no clinical practice guidelines for rehabilitation in lung transplant candidates and recipients. Several narrative reviews have been published on rehabilitation[6,7], however they have focused on guidelines for individuals with a relatively uncomplicated pre- and post-transplant course. As the selection of lung transplant candidates has evolved over time due to surgical and medical advancements, the demographics of transplant candidates has shifted from only the youngest and fittest candidates to adults of older age and those with increased co-morbidities and functional limitations[1]. This shift in demographics may have important implications for rehabilitation approaches and functional expectations pre- and post-transplant. In addition, lung transplant candidates can present with acute respiratory decompensation, and several medical strategies are being used to "bridge" candidates to transplantation using mechanical ventilation and/or Extra Corporeal Life Support (ECLS)[8-11]. These technologies can have a significant impact on the degree of deconditioning that these individuals experience prior to transplant, as their capacity to participate in active rehabilitation is limited. The rehabilitation needs of individuals who have high oxygen requirements, require hospitalization pre-transplant due to respiratory failure, and/or require extensive rehabilitation post-transplant due to a prolonged and complicated clinical course are not well described.

The overall purpose of this review is to provide an evidence-informed clinical approach to rehabilitation based on over 30 years of clinical rehabilitation experience at our center, integrating the research evidence for rehabilitation in lung transplantation. The specific aims of this review are to: (1) provide a practical approach to functional assessment and exercise training pre- and post-lung transplant, including the peri-operative and long-term follow-up periods; (2) describe and contrast exercise training and mobility for lung transplant candidates and recipients with an uncomplicated and complicated clinical course; and (3) discuss rehabilitative approaches for special populations within lung transplantation such as re-transplant, heart-lung transplant and pediatrics.

FUNCTIONAL ASSESSMENT OF LUNG TRANSPLANT CANDIDATES AND RECIPIENTS

The mechanisms of exercise limitation pre- and post-lung transplant are multifactorial, including alterations in lung mechanics and gas exchange, cardiovascular limitations and peripheral muscle dysfunction, and have been described in detail elsewhere[12,13]. In order to evaluate exercise capacity and function in lung transplant candidates and recipients, a combination of aerobic testing, muscle function, mobility testing and assessment of physical activity is utilized. Measures that may be used in clinical practice for physical assessment in the lung transplant population have been summarized in Table 1. The Rehabilitation Measures Database[14] provides information on the psychometric properties, normative data, instrument description and equipment, minimally clinical important difference and considerations for a number of rehabilitation

Table 1 Physical assessment of lung transplant candidates and recipients

Measured construct	Clinical tests	Clinical utility
Exercise capacity	Lab-based test: Cardiopulmonary exercise test on cycle or treadmill Field-based walk tests: 6MWT, ISWT[19,27] Upper extremity endurance capacity: UULEX[28]	Cause of exercise limitation Assess need for oxygen Assess functional capacity Outcome measure pre-post rehab and pre-post transplant Exercise prescription
Muscle function (strength, endurance)	Peripheral muscles: Manual muscle testing or hand held dynamometry Handgrip force 1-repetition maximum Respiratory muscles: MIP/MEP	Assess muscle strength and/or muscle endurance Outcome measure Exercise prescription (1-RM for peripheral muscles, MIP for IMT)
Physical performance and mobility	Gait speed (over 4 m)[110] Sit-stand tests (*e.g.*, 30 s sit to stand; 5 times sit to stand)[111,112] Short Physical Performance Battery[113] Timed Up and Go[114] Balance tests (*e.g.*, Berg balance scale, BESTest)[115,116] FIM[117] Tests specifically for ICU/inpatients: Egress test[118] Various ICU physical function tests[119-121]	Assess mobility, balance and physical function Assess need for gait aid Outcome measure Exercise prescription Discharge planning
Physical activity	Physical Activity questionnaires, *e.g.*, PASE[122]; IPAQ[123]; DASI[124] Pedometers or accelerometers	Assess physical activity Outcome measure Set activity goals (*e.g.*, target daily step count)

CPET: Cardiopulmonary exercise test; 6MWT: Six-minute walk test; ISWT: Incremental shuttle walk test; UULEX: Unsupported upper limb exercise test; MMT: Manual muscle testing; 1RM: One repetition maximum; HGF: Handgrip force; HHD: Hand-held dynamometry; MIP: Maximal inspiratory pressure, MEP: Maximal expiratory pressure; IMT: Inspiratory muscle testing; SPPB: Short physical performance battery; TUG: Timed Up and Go; FIM: Functional independence measure; PASE: Physical activity scale for the elderly; IPAQ: International physical activity questionnaire; DASI: Duke activity status questionnaire.

assessment instruments included in Table 1.

Aerobic exercise capacity

Exercise capacity is a major predictor of waiting list survival pre-transplant across disease categories[15,16], and is also associated with post-transplant health outcomes including days on mechanical ventilation, length of hospital stay and survival[4,17,18]. The six-minute walk test (6MWT)[19] is the most common functional test of exercise capacity for lung transplant candidates and recipients in Canada[5], and is used widely internationally. It is a global marker of health status reflecting severity of disease and level of functional impairment, and has been found to correlate with VO_{2max} in lung transplant candidates[20]. The six-minute walk distance (6MWD) is incorporated into several composite scores that can determine the urgency for lung transplant including the BODE and Lung Allocation Score[21,22]. A 6MWD of less than 400 m or a predicted distance of between 45%-55% is common in lung transplant candidates[4,15,23,24]. The 6MWD improves significantly following transplant reaching 65%-85% predicted, with the largest gains reported in the first three to four months[23-26]. Other field-based walking tests that have been used in chronic lung disease such as the incremental and endurance shuttle walk tests, (ISWT and ESWT) may also be used to quantify exercise capacity in lung transplant candidates and recipients[27].

Upper extremity exercise capacity plays an important role in many basic and instrumental activities of daily living and may provide unique information about upper extremity endurance not reflected in the field-based walking tests. In individuals with COPD, arm exercise capacity has been measured using the Unsupported Upper Limb Exercise Test (UULEX)[28]. A small group of lung transplant candidates with ILD at our center demonstrated reduced arm exercise capacity compared to controls using the UULEX[29], however this test has not been used in routine clinical evaluation.

Muscle function

Peripheral muscle function can be tested through multiple techniques, some of which are more applicable to the clinical setting due to lower costs and fewer requirements for specialized equipment, training and personnel such as manual muscle testing, hand held dynamometry (HHD), handgrip dynamometry and one-repetition maximum (1-RM; Table 1). The quadriceps is the most common muscle tested in the research literature and lung transplant candidates exhibit quadriceps weakness of 49%-86% predicted[30]. An immediate drop in quadriceps strength from pre-transplant to post-transplant at the time of hospital discharge of 15%-32% has been reported with a gradual recovery to pre-transplant levels by three to four months post-transplant[23-26]. Lower extremity muscles (*e.g.*, quadriceps, ankle plantar flexors) show more pronounced weakness than upper extremity muscles (*e.g.*, biceps)[29-31].

Body composition (muscle and fat mass) can be measured as part of a physical or nutritional assessment using bioelectrical impedance analysis, dual X-ray absorptiometry or skinfolds. More specific measures of muscle size (*e.g.*, cross-sectional area and muscle layer thickness) can be obtained from ultrasound, computerized tomography, or magnetic resonance imaging, however these are not typically performed for clinical assessment. Muscle atrophy has been reported in research studies of lung transplant candidates and recipients using several measures such as low fat free mass, reduced muscle volume and cross-sectional area[29,30].

Short tests of physical performance and mobility may be a useful addition to the functional assessment in the pre-transplant phase (Table 1). Lung transplant candidates have shown reduced functional performance on the Short Physical Performance Battery (SPPB) and Timed Up and Go (TUG) compared with controls[29,30]. The SPPB has recently been used as a marker for frailty pre-lung transplant and shown to be a predictor of disability, delisting and waitlist mortality[32].

Physical activity

Level of physical activity can be evaluated using questionnaires, however there is no specifically validated scale for lung transplant candidates or recipients. Commercially available pedometers or accelerometers may also be used to obtain daily step counts and activity level. Measurement of physical activity can be an important adjunct to exercise capacity testing, since it is reduced pre- and post-transplant and can be used for physical activity counseling and setting targets for daily activity.

Low levels of physical activity with a reported mean of 1400-3200 daily steps, reduced time spent in moderate intensity activity, walking and standing, and greater time in sedentary activities has been reported in lung transplant candidates[23,24,33,34]. A research study conducted in our center demonstrated that lung transplant candidates with ILD had increased physical activity levels on days they participated in pulmonary rehabilitation, and the 90 min rehabilitation session accounted for 58% of the total daily steps[33]. Levels of daily physical activity improve following lung transplant however remain below predicted levels in terms of daily steps, walking time and movement intensity compared to healthy controls; and show great variability[23,24,34-37].

GENERAL PRINCIPLES OF EXERCISE TRAINING

Exercise prescription should be individualized, include both aerobic and resistance training, and follow general exercise training principles of specificity, overload and progression[38]. Based on our clinical experience, respiratory and cardiovascular reserve, stability and clinical course of lung disease, muscle strength and muscle endurance can have a significant impact on the frequency, intensity, type and duration of exercise that is prescribed and the rate of progression. Figure 1 outlines general rehabilitation guidelines used at our center during the pre- and post-transplant phases.

Pre-transplant rehabilitation

Pre-transplant exercise training is recommended in Canadian lung transplant centers for a specified duration or during the entire waiting period prior to transplant to optimize fitness and prevent the cycle of inactivity and deconditioning that can occur with advanced lung disease[5]. There are few randomized controlled trials that examine the effect of exercise training pre-transplant[39,40], however retrospective and pre-post studies of exercise training in lung transplant candidates have shown that 6MWD can be maintained or even increased in spite of progressive lung disease[4,41-43]. Predictors of rehabilitation success pre-transplant (*e.g.*, improved 6MWD) have not been identified in lung transplant candidates[43].

Pulmonary rehabilitation guidelines for exercise training can be applied to lung transplant candidates with modifications to account for increased severity of lung disease and multiple underlying disease states[44,45]. If disease progression and functional deterioration occurs during the waiting period, physical function needs to be reassessed on an ongoing basis and exercise prescription modified as needed. Alternative modes of training including high intensity interval training[39] and Nordic pole walking[42] have been described in lung transplant candidates. Inspiratory muscle training has been utilized in chronic lung disease, primarily COPD, to improve inspiratory muscle strength and endurance; however studies have not been specific to lung transplant candidates[46]. Although supervised outpatient pulmonary rehabilitation in a hospital or community setting are common[5], alternative modes of delivery such as tele-rehabilitation may be an important alternative for individuals living far from a transplant center, however pre-transplant tele-rehabilitation has not yet been studied in lung transplant candidates[47].

Guidelines for pre-transplant exercise prescription have been summarized in Table 2 from protocols used in research studies and our current clinical guidelines. Exercise intensity and duration are prescribed and progressed according to exertional oxygen saturation, heart rate and symptoms of dyspnea and leg fatigue using the modified 0-10 Borg scale[48]. A percentage of the 6MWT speed can be used for lung transplant candidates to prescribe walking speed on the treadmill[49].

Special considerations for pre-transplant rehabilitation

Supplemental oxygen for exercise training: As lung transplant candidates often require supplemental oxygen for rest and/or exertion[4], oxygen titration is an important component of exercise training. Guidelines for oxygen supplementation for exercise are not clearly defined[50], so oxygen titration orders, institutional policies and delegation practices may vary between facilities. At our center, all lung transplant candidates have a prescribed oxygen titration range provided by a physician, which is often to maintain an oxygen saturation (% SpO_2) of at least 88% with exercise, however, oxygen prescription may be modified based on patient diagnosis, medical co-morbidities, arterial blood gases, functional capacity and symptoms. Lung transplant candidates are supported with sufficient oxygen to maintain the prescribed oxygen saturation in an attempt to increase aerobic exercise intensity and duration to obtain a greater physiological benefit with training. In our clinical experience, oxygen requirements for exertion may increase during the waiting

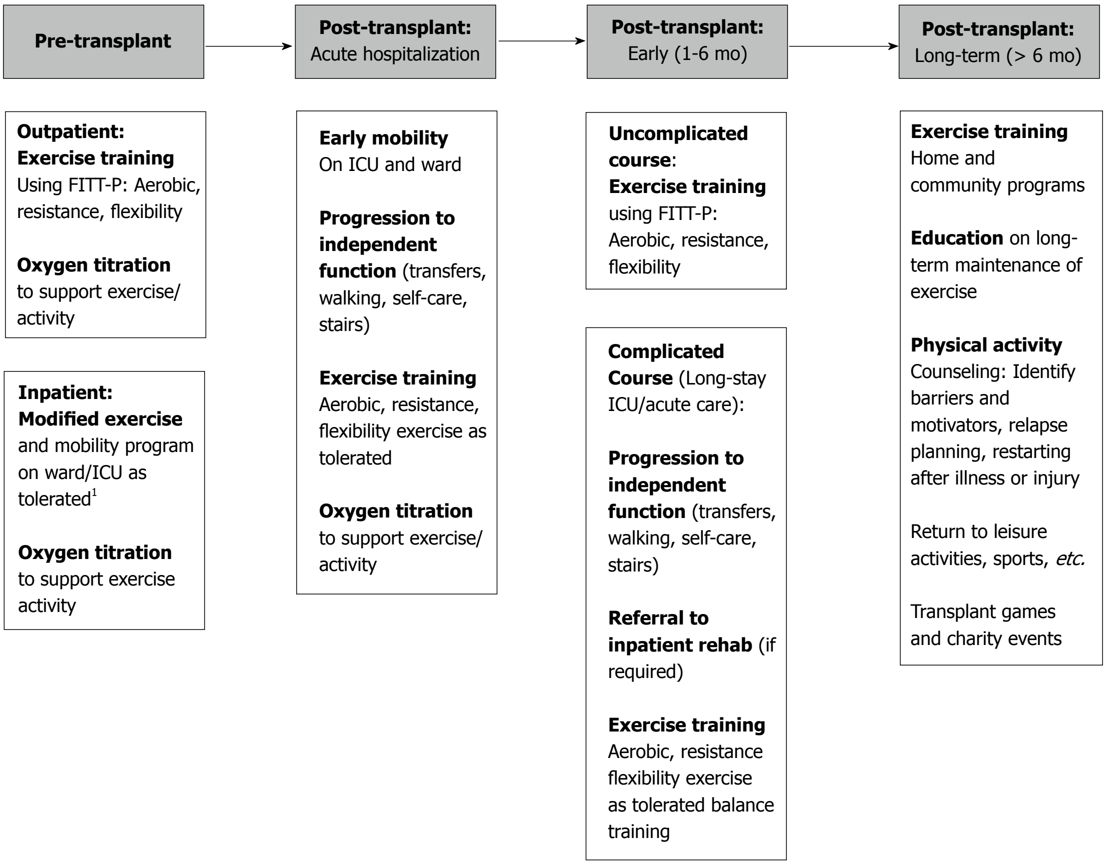

Figure 1 Overview of rehabilitation during the pre- and post-transplant phases. At each phase, monitoring and re-assessment are needed to modify/progress the exercise program. [1]Some hospitalized lung transplant candidates and recipients may require mechanical ventilation and/or extracorporeal life support (ECLS) and can be mobilized on these devices. FITT-P: Frequency, intensity, type, time, progression; ICU: Intensive care unit.

period pre-transplant with some individuals (such as those with ILD) requiring very high levels of oxygen supplementation, high flow oxygen delivery devices and/or non-invasive ventilation. There is a lack of literature on the safety guidelines and hazards of high flow oxygen for exercise training[51], and our clinical practice is to communication closely with the medical team regarding arterial blood gases and/or other medical concerns.

Exercise training in pulmonary hypertension: Historically, individuals with pulmonary arterial hypertension (PH) were excluded from exercise training, however alongside changes in medical management, a number of studies over the past decade have shown efficacy and safety of carefully prescribed exercise in stable, medically optimized individuals with PH[52]. For individuals with moderate to significant primary or secondary PH who are not symptomatic at rest, our clinical practice is to avoid of exertional hypoxemia, symptoms of chest pain, dizziness, pre-syncope, nausea and visual changes during exercise training. We prescribe exercise intensity and duration as guided by lower dyspnea scores (*e.g.*, Borg score 2-3 or slight to moderate). High intensity aerobic and resistance training and Valsalva maneuvers are avoided. Changes in weight, abdominal circumference, lower leg edema and other evidence of worsening right heart failure are monitored with close communication with the medical team, and care is taken to avoid interruption of continual intravenous vasodilators (*e.g.*, prostaglandins).

Infection control: Infection control procedures are essential for preventing spread of certain infections such as methicillin-resistant staphylococcus aureus, mycobacterium abscessus or CF-related infections during group exercise programs. At our center, individuals with CF are physically separated by three meters during group exercise training and individuals with Burkholderia cepacia exercise separately at the end of the day. Guidelines on cleaning equipment, hand-washing, gown and mask use and isolation practices may vary at different institutions.

Team approach to rehabilitation: Education is an important component of rehabilitation, specifically on issues related to safe and effective exercise, exertional oxygen use, home exercise, assistive devices and energy conservation techniques[53]. Psychosocial support to address stress and expectations during the waiting period and concerns regarding surgery is also beneficial[54]. Collaboration with the registered dietitian to ensure that nutritional needs are being met and balancing exercise participation with nutritional needs

Table 2 Guidelines for pre-transplant exercise prescription in stable outpatients

	Aerobic	Resistance	Flexibility
Frequency	2-5 d/wk	2-3 d/wk	3-5 d/wk
Intensity	50%-80% HR reserve Dyspnea > leg fatigue: Moderate to hard (3-5 on modified Borg scale)[48] SpO_2 > 85%-90% Continuous or intermittent training[1]: 60%-80% 6MWT speed for walking[41,49] 60% peak workload for cycling[39,43] or just above anaerobic threshold[40] Interval training[2]: 100%: 0% peak work rate (cycle)[39]	30%-80% 1-RM or use 8-15-RM[125]	
Type	Walking (treadmill, corridor, Nordic poles)[42] Cycling (leg and/or arm ergometer)	Major muscle groups of upper and lower body (quadriceps, hamstrings, plantar flexors, gluteals, biceps, triceps, pectorals, latissimus dorsi) Training modalities: Free weights/dumbbells Elastic bands Pulleys Gym equipment Body weight (stairs, squats, heel raises, wall push-ups)	Major muscle groups of upper and lower body Thoracic cage and chest wall mobility
Time/Training Volume	Continuous: 15-30 min Intermittent: 5-10 min × 2-3 bouts Interval[2]: 30 s exercise: 30 s rest (12-36 min)[39]	1-2 sets × 8-15 reps	Hold up to 10-30 s each, repeat 2-4 times
Progression	Progress time up to 20-30 min continuous Perform regular 6MWTs and adjust speed accordingly for treadmill training; and increase Watts on cycle Higher level patients may tolerate a treadmill incline of 1%-4%	Increase weights based on tolerance; (approximately 0.5 kg or 1 lb. per week, as tolerated)[41] Body weight exercises: Can add hand or ankle weights	Hold stretches to point of tightness/slight discomfort

[1]Intermittent training is regular or irregular intervals of the same low to moderate intensity *vs* interval training, which involves pre-set, alternating, short intervals of high intensity to intervals of rest or lower intensity; [2]There are several different interval training protocols described in chronic lung disease[126]. SpO_2: Oxygen saturation measured by pulse oximetry; HRR: Heart rate reserve; 6MWT: Six-minute walk test; ISWT: Incremental shuttle walk test; HR: Heart rate; BP: Blood pressure; RR: Respiratory rate; ESWT: Endurance shuttle walk test; reps: Repetitions; RM: Repetition maximum.

with close monitoring of weight are performed at our center. Some individuals are required to lose weight pre-transplant and may benefit from nutritional counseling in addition to aerobic exercise training. A palliative care referral for opioid administration may be beneficial to assist with symptom control of dyspnea, cough and other symptoms that may impact on exercise ability and quality of life. A study at our center observed a trend towards increased caloric expenditure during exercise training in 64 lung transplant candidates referred to palliative care post opioid initiation[55].

Considerations for a complicated pre-transplant clinical course: In cases of a prolonged waiting period prior to transplant, we find that exercise intensity and duration may not be progressed if there is significant disease progression, respiratory exacerbations and infections, medical instability and hospital admission for respiratory failure. Maintenance of physical function or slowing the rate of physical deterioration can become important functional goals. Increased dyspnea, decreased function or acute worsening of gas exchange should be investigated as they can indicate underlying infection, respiratory exacerbation or pulmonary embolism. Some lung transplant candidates experience profound respiratory deterioration and need to await lung transplantation on the hospital ward or in the intensive care unit (ICU). Although there is no research evidence on inpatient rehabilitation for lung transplant candidates hospitalized with respiratory deterioration and failure, we provide a modified exercise program based on patient tolerance to help offset functional decline. Corridor ambulation and bedside cycling are encouraged as tolerated, but may not be tolerable by some individuals due to severe gas exchange abnormalities that are not corrected with high levels of supplemental oxygen. Resistance exercises, which do not confer the same degree of exertional desaturation should be continued as tolerated, with a focus on maintaining proximal muscle strength (*e.g.*, shoulder and hip) and lower limb strength in anticipation of early ambulation and return to self-care activities post-transplant[56]. Neuromuscular electrical stimulation (NMES) has been shown to enhance muscle mass and function in individuals with severe COPD and incapacitating dyspnea, and may be a useful adjunct for individuals unable to participate in a traditional outpatient pulmonary rehabilitation program[57].

Selected lung transplant candidates require bridging to transplant due to respiratory failure. Mechanical ventilation and ECLS can be associated with significant deconditioning due to increased sedation time limiting mobility and active participation in rehabilitation, and in some cases, irreversible muscle damage from persistent critical illness polyneuropathy and myopathy[58]. Facilities with an experienced critical care mobility team can mobilize individuals on mechanical ventilation and/or ECLS who are medically stable and cognitively capable[59]; although guidelines for mobility prescription

Table 3 Exercise and mobility for hospitalized lung transplant candidates and recipients

Setting	Interventions/prescription	Considerations for a complicated hospital course
Intensive care unit	Upright positioning AROM for upper extremities Acupuncture for incisional pain Progressive mobility program, consisting of: Bed mobility > dangling > transfer to chair > standing > marching on spot > ambulation with HWW up to 100-200 m with or without MV In sitting or lying: Resistance training using light weights, elastic resistance bands	PROM, A/AROM for those who are sedated/not actively moving Trunk control and sitting balance prior to standing and walking Specialized equipment to facilitate mobility, such as: Standing frames, sit-stand lifts or mechanical lifts, standing and walking slings, portable treadmills, portable ventilators for ambulation in ICU (with appropriate settings to facilitate exercise), manual resuscitation bag with PEEP valve Bedside cycle ergometer or treadmill for aerobic training Video gaming system (*e.g.*, Nintendo Wii™) for balance and strengthening exercises[127]
Step-down unit/ward	AROM upper extremities Progressive mobility program: Up to chair 1-3 ×/day; supervised walking 1 × /day building up to 100 m; progress to 4-5 ×/day for 10-15 min bouts and increase distance > 100 m Stair climbing Resistance training: Up to 5 lbs. (1 set × 10 reps) Education re: Lifting restrictions Postural correction/re-education Oxygen titration: Maintain SpO_2 > 88% on exertion	Transfer training Gait training Gait aids: Progress from HWW > rollator > no gait aids, if able Specialized seating Referral to inpatient rehabilitation for those who are not independent for discharge home

ROM: Range of motion; HWW: High-wheeled walker; MV: Mechanical ventilation; AROM: Active range of motion; PROM: Passive range of motion; A/AROM: Active/assisted range of motion; PEEP: Positive end expiratory pressure.

in critically ill individuals are not clearly defined[60]. A recent systematic review presented evidence that early mobilization and ambulation is safe even in patients awake on veno-venous Extra Corporeal Membrane Oxygenation (ECMO) support[61]. Physiotherapists at our center undergo specialized training in managing ECMO circuits, and with the support of an early mobility team, close communication with the medical team and a positive ICU culture towards the safe mobilization of selectively assessed critically ill patients[62].

Post-transplant rehabilitation

Immediate post-transplant rehabilitation in the ICU: The rehabilitation goals in the early phase post-transplant are to increase general mobility, functional capacity, muscle strength and endurance, and facilitate discharge from hospital. Reduced ICU length of stay has been associated with increased quadriceps muscle strength at hospital discharge in lung transplant recipients[26]. One study identified factors that contribute to an extended hospital stay which included high urgency listing status, bridging to transplant with mechanical ventilation and/or ECLS, diagnosis of pulmonary hypertension, prolonged intubation post-transplant and colonization with multidrug resistant pathogens[63]. The functional consequences of a prolonged ICU stay can be profound and long-term[64].

Physical rehabilitation should begin as early as possible post-operatively and should prioritize upright positioning (*e.g.*, sitting) and mobilization (*e.g.*, out of the bed)[65,66]. Early mobilization in the ICU has not yet been studied specifically in lung transplant patients, but the same treatment approaches reported for other critically ill patients are likely applicable. Table 3 Muscle wasting related to critical illness is early and impactful[67,68], highlighting the need for rapid and effective interventions to protect the muscle from atrophy and weakness. To date, several systematic reviews support safety, feasibility and beneficial impact of early physical therapy and mobilization in mechanically ventilated patients[69-76]. There is evidence that early physical therapy and mobility training can result in improved quality of life[71], physical function[71,72], muscle strength[71,73] and functional outcomes[69]. Further research is needed to determine whether these improvements translate into decreased hospital and ICU length of stay[77,78] and better long-term physical function[60].

Rehabilitation in the ICU should take into consideration pre-transplant function, cardiorespiratory function, muscle strength, range of motion (ROM), balance, cognitive impairments, pain control and medical stability. Early active muscle training and cardiopulmonary conditioning should begin as soon as feasible within the hospital setting (*e.g.*, turning in bed, sitting at the edge of bed, sitting in a chair, standing, and walking). In addition, self-care and activities of daily living should be encouraged as soon as possible[79]. Low levels of exercise (*e.g.*, with elastic therapy bands or unloaded pedaling on the bicycle) with subsequent increases in the duration and workload can be made as the patient progresses[79,80]. In critically ill patients, even passive or active exercise training sessions for 20 min/d using a bedside ergometer is able to increase short-term functional recovery[75].

The emerging literature using NMES has shown that it may be a safe, low cost treatment for early intervention in critically ill patients who may not be able to participate in active exercise[75,81] since it can passively activate the muscles[75,81,82]. However, studies to date have included a general, mixed population of ICU patients and the evidence is not specific to lung transplant recipients. Furthermore, the ability to deliver NMES effectively in the context of underlying ICU acquired myopathy and polyneuropathy[83] has not been substantiated.

Post-transplant rehabilitation in the hospital step-down unit and ward: At our center functional reassessment and exercise are resumed following ICU transfer until discharged home or to inpatient rehabilitation, with oxygen titration orders to maintain oxygen saturation at least 88% on exertion. Most lung transplant recipients at our center are weaned off supplemental oxygen prior to hospital discharge, but a few may still require low flow oxygen for exertion for several weeks to months, especially single lung transplant recipients.

Rehabilitation interventions provided at our center during the hospital stay post-transplant are summarized in Table 3. Medical issues that may be encountered in this early post-transplant phase that can impact exercise include infection, acute rejection, anxiety, depression, post-surgical pain at the thoracotomy tube site and chest wall, arrhythmias, veno-thrombotic events, infections requiring isolation, postural hypotension, skin ulcers and poor wound healing. Side effects of medications include fluid retention, anemia, nausea, tremors, decreased visual acuity, hyperglycemia and hypertension[65], which need to be considered when prescribing exercise so that appropriate modifications should be made.

Outpatient rehabilitation: Structured outpatient rehabilitation within the first three months following lung transplant is available at Canadian transplant centers[5]. Functional goals in the outpatient phase may include ambulation without gait aids, liberation from supplemental oxygen, return to pre-transplant muscle strength and 6MWD of 65%-85% predicted levels[23-26,84]. Large functional gains are reported during this period of rehabilitation in individuals with a relatively uncomplicated post-operative course[23-26]. Lung transplant recipients indicate that exercise training is a valuable part of their post-transplant care and essential to improve physical function[85]. A greater improvement in 6MWD post-transplant is predicted by greater recovery of muscle strength and a lower pre-transplant 6MWD[25,84]. Studies examining exercise training following lung transplantation show significant increases in exercise capacity, muscle strength and bone mineral density[24,86-88] (Table 4).

Considerations for a complicated post-transplant clinical course: There are a multitude of complications that can significantly increase the length of hospital stay and impact rehabilitation including: Major bleeding, infections, prior multi-drug resistant infections and colonization, difficulty weaning with prolonged mechanical ventilation, pre- and post-transplant ECLS, diaphragmatic paralysis, severe agitation, delirium, depression, acute neurological events, critical illness polyneuropathy, hemodynamic instability, primary graft dysfunction and acute renal failure requiring hemodialysis[65,66].

An assessment of functional goals can help inform discharge planning and recommendations for inpatient transplant rehabilitation, complex continuing care or homecare services. A retrospective study from our center showed that lung transplant candidates who were older, had a lower pre-transplant 6MWD, were mechanically ventilated prior to transplant and had a longer total length of hospital stay were more likely to be discharged to an inpatient rehabilitation facility *vs* home[89]. Compared to other inpatient rehabilitation patients (*e.g.*, stroke, joint surgery) lung transplant recipients are more likely to require transfer back to acute care for medical management related to complications such as infection, rejection and cardiac events[90,91].

In our clinical practice, individuals who experienced a complicated post-transplant course may require a referral to a multidisciplinary inpatient rehabilitation program to regain basic mobility (*e.g.*, independent transfers, walking, and the ability to engage in activities of daily living such as self care) prior to discharge home. Upon discharge, these individuals are encouraged to enroll in an outpatient pulmonary rehabilitation program, or be prescribed a program that can be done in the community or home setting to work on improving endurance and strength. These individuals often require a mobility aid (*e.g.*, rollator walker or cane) and their 6MWD is well below predicted values, showing a slow improvement over 12 to 18 mo. Specific exercises to target balance and coordination impairments are sometimes needed to be included in the outpatient or home exercise program. Individuals with a complicated post-transplant clinical course may experience persisting myopathies and/or neuropathies, and not all critically ill survivors recover to the same extent as there may be significant differences in recovery of muscle function and rehabilitation potential[58]. This remains an area of active research.

Late/ongoing post-transplant maintenance

The 6MWT is reassessed regularly post-transplant[5], to monitor changes in exercise capacity and exertional oxygen saturation, which may change over time. Although the majority of exercise training programs occur in the first three to four months following transplant, longer-term exercise training may provide additional benefits to exercise capacity and the management of long-term co-morbidities of hypertension, hyperlipidemia and diabetes are prevalent at one, three and five years post-transplant[1,24]. A randomized trial found that lung transplant recipients who underwent rehabilitation in the first three months following transplant had higher physical activity levels, improved fitness and lower 24-h blood pressure one year post-transplant compared to recipients who did not participate in rehabilitation[24]. Daily physical activity has been reported to be significantly reduced one year following transplantation as

Table 4 Guidelines for early post-transplant exercise prescription in stable outpatients

	Aerobic	Resistance	Flexibility
Frequency	3-5 d/wk	2-3 d/wk	3-5 d/wk
Intensity	50%-80% HR reserve or < 85% age-predicted HRmax[4,23] Leg fatigue > dyspnea: Moderate to hard (3-4 on Borg scale) SpO_2 > 88% Continuous training: 75%-100% 6MWT speed for walking[24,25] 50%-80% peak workload for cycling[24,59,128]	60%-80% 1RM[24,26] 10-RM No upper extremity lifting/pulling/pushing > 10 lbs. first 3 month Extra restrictions if sternal instability	Hold stretches to point of tightness/slight discomfort
Type	Walking (treadmill, corridor) Cycling (leg); avoid arm ergometry in first 3 month to allow for incision healing	See pre-transplant Avoid abdominal muscle exercises for first 3 month	Major muscle groups of upper and lower body Thoracic cage and chest wall mobility Postural re-education
Time/Training Volume	Continuous: 20-30 min	1-3 sets × 8-15 reps	Hold up to 10-30 s each, repeat 2-4 times
Progression	Progress time to 30 min, then progress speed on treadmill; increase incline after approximately 6 wk post-transplant (if tolerated) Increase Watts on cycle Walk: Run program for some high level patients (at least 6 wk post-transplant) 30-60 s running bouts interspersed with walking for 20-30 min	Start with sit-stands and when able to perform without arm support progress to squats with hand weights Weekly increase weights based on tolerance; (approximately 0.5 kg or 1 lb. per week, as tolerated) within lifting guidelines (*e.g.*, < 10 lbs. for upper extremities for first 3 month) Body weight exercises: Can add hand or ankle weights (*e.g.*, squats and stair climbing)	Hold stretches to point of tightness/slight discomfort Extra restrictions if sternal instability (*e.g.*, avoid chest expansion stretches)

6MWT: Six-minute walk test; CPET: Cardiopulmonary exercise test; HR: Heart rate; HRR: Heart rate reserve; SpO_2: Oxygen saturation measured by pulse oximetry; RR: Respiratory rate; BP: Blood pressure; ISWT: Incremental shuttle walk test; ESWT: Endurance shuttle walk test.

compared to healthy controls[35]. Physical activity levels varied in long-term recipients and have been found to be inversely associated with body weight[37].

Exercise training in lung transplant recipients in the long-term phase (> 6 mo) has been shown to have beneficial effects on endurance capacity and muscle strength[87,88,92]. Long-term adherence to exercise may be greater if individuals participate or resume activities they enjoy. Thinking beyond a traditional gym protocol and exploring individuals' interests, access and resources can be helpful when counseling individuals about increasing and maintaining physical activity in their home community. National and World Transplant Games[93,94] and charity events are excellent opportunities for setting fitness and performance goals and staying active while raising awareness of lung disease and transplantation. As an example of the benefits of this training, lung and heart-lung transplant recipients (> 6 mo post-transplant) who participated in ten weeks of upper extremity training through Dragon boat racing showed improved aerobic and anaerobic fitness[95].

Inexpensive pedometers, activity watches, fitness monitors and smart phone applications can be used to track daily steps and activity levels, and set targets to increase physical activity. Additional activities such as yoga, Tai Chi, dance and seasonal activities such as swimming, paddling, outdoor cycling, hiking, skating and snowshoeing can be done in a social setting with family and friends. A gradual introduction to new activities should be emphasized, and we counsel transplant recipients to avoid activities with an increased theoretical risk of injury such as contact sports, skydiving, bungee jumping and scuba diving. Episodic medical issues such as illness, infection or injury can interrupt an exercise regimen, so physical activity counseling on how to modify and resume exercise after an episode of illness is important and can be addressed at reassessment.

SPECIAL POPULATIONS

Heart-lung, multi-organ and re-transplantation

At our center individuals who have undergone heart-lung transplantation, multi-organ transplantation (*e.g.*, lung-liver) and re-transplantation participate in a similar pre-and post-transplant rehabilitation program as lung transplant candidates and recipients. Individuals awaiting a heart-lung transplantation may have congenital heart disease with cardiac shunts that can lead to right heart shunting and severe hypoxemia that may not be responsive to supplemental oxygen[96]. This may necessitate lower training intensity[97] (*e.g.*, using heart rate and/or Borg dyspnea and fatigue scores) and lower oxygen saturation guidelines for exercise training. Following heart-lung transplantation, a longer warm-up and cool down is recommended to allow for the slower changes in heart rate due to disrupted cardiac innervation[98]. The modified Borg scale is used to guide exercise training instead of heart rate. There is a lack of information on exercise training for individuals listed for re-transplant[99], but based on clinical experience at our center, individuals often have a lower functional capacity compared to listing for their first transplant.

Pediatrics

Children (from birth to 18 years of age) are typically followed in specialized pediatric healthcare centers. Clinical assessment of the pediatric lung transplant candidate should include posture, ROM, muscle strength and gross motor function appropriately for the age of the child. The 6MWT has been shown to be a valid measure in children[100] and is utilized by a majority of pediatric centers in North America[101]. There are published normative values for 6MWD across various ages[102], however interpretation of the 6MWT data is sometimes difficult to differentiate from growth and development of the child, so it should be used as part of a thorough clinical assessment to identify issues amenable to rehabilitation. While pre-transplant physical functioning and its relationship to post-transplant outcomes has not been studied extensively, one study in pediatric patients found a correlation between 6MWD and short term transplant outcomes including length of ICU stay, days of mechanical ventilation and time until discharge[18].

Pre-transplant rehabilitation: There are no studies examining the impact of exercise training in pediatric lung transplant candidates, however clinical experience indicates that it can be of significant benefit for these children and helps to prevent deterioration in function. Due to the limitations of available programs for children, families must often commute to the transplant center. However, older teens may be referred to adult pulmonary rehabilitation programs with support from pediatric specialists. Children may also have exacerbations of their underlying condition requiring hospitalization and modification of their exercise programs. Exercise prescription with slow progression can be approached similarly as for adults including both aerobic and resistance training[103,104]. Strength training is unlikely to increase muscle bulk for pre-pubertal children, but can improve function. Exercise training for younger children should include activities encouraging gross motor skill development, such as integration of physical education activities and incorporate growth and developmental factors of the child's maturing system. Physical therapists should also encourage regular school attendance, participation in physical education curriculums (within medical restrictions) with appropriate modifications to help ensure adequate levels of physical activity. Collaboration with school professionals, teachers, and physical education instructors may be needed to ensure safe follow through of these recommendations.

Post-transplant rehabilitation: Exercise capacity and general fitness improves for children following lung transplant but remains reduced compared to age-predicted values[104-106]. Opportunities and access to rehabilitation post-transplant are often limited. A study examining the impact of an early semi-individualized physiotherapy prescribed exercise program early (within the first three months) after hospital discharge found similar improvements in 6MWD, strength and flexibility in children who attended the hospital three times a week compared to children who performed the exercise at home with parents[105], suggesting that home-based training may be a way to bridge the gap in accessibility. A study at our center with children who were attending the World Transplant Games showed the positive effects of home-based training, which included general exercise programs and event-specific, skill-based training done independently for three months prior to the Games. The children showed short term benefits in levels of physical activity and each subject demonstrated an increase in at least one parameter of fitness on the Fitness-GRAM®[106]. Taken together, these studies suggest that home-based intervention or exercise prescription can be of benefit for these children when provided with appropriate education regarding safe exercise. The transition of adolescents and young adults to adult care is an increasingly important area of focus since this has been recognized as a vulnerable time for adolescent transplant recipients[107]. Research on strategies to optimize successful transition highlights the importance of an inter-professional approach with involvement from both the pediatric and adult care centers.

CONCLUSION AND FUTURE DIRECTIONS

Medical and surgical advances continue to improve the availability of lung transplantation[108]. Exercise training provides an essential role in optimizing functional capacity and fitness pre-transplant, as well as improving outcomes and quality of life post-transplant. Physiotherapists and clinical exercise specialists working with lung transplant candidates and recipients require expertise in general exercise training principles and specialized knowledge of pre- and post-transplant complications, oxygen titration, side effects of medications and a sound understanding of how to modify exercise programs during episodic illnesses/ exacerbations and/or change in lung function pre- and post-transplant. Although studies have been conducted on exercise training in lung transplantation, there is a need for larger studies examining long-term outcomes[109]. Individuals with a complicated pre- and post-transplant course pose a particular challenge for clinicians, and further research on rehabilitation for this population is needed. The development of standardized physical function measures that can help predict post-transplant outcomes, and the investigation of alternative modes of exercise training are also warranted.

REFERENCES

1 **Yusen RD**, Edwards LB, Kucheryavaya AY, Benden C, Dipchand AI, Goldfarb SB, Levvey BJ, Lund LH, Meiser B, Rossano JW, Stehlik J. The Registry of the International Society for Heart and Lung Transplantation: Thirty-second Official Adult Lung and Heart-Lung Transplantation Report--2015; Focus Theme: Early Graft Failure. *J Heart Lung Transplant* 2015; **34**: 1264-1277 [PMID: 26454740 DOI: 10.1016/jhealun.2015.08.014]

2 Unilateral lung transplantation for pulmonary fibrosis. Toronto Lung Transplant Group. *N Engl J Med* 1986; **314**: 1140-1145 [PMID:

3515192 DOI: 10.1056/NEJM198605013141802]
3 **Craven JL**, Bright J, Dear CL. Psychiatric, psychosocial, and rehabilitative aspects of lung transplantation. *Clin Chest Med* 1990; **11**: 247-257 [PMID: 2189660]
4 **Li M**, Mathur S, Chowdhury NA, Helm D, Singer LG. Pulmonary rehabilitation in lung transplant candidates. *J Heart Lung Transplant* 2013; **32**: 626-632 [PMID: 23701852 DOI: 10.1016/j.healun.2013.04.002]
5 **Trojetto T**, Elliott RJ, Rashid S, Wong S, Dlugosz K, Helm D, Wickerson L, Brooks D. Availability, characteristics, and barriers of rehabilitation programs in organ transplant populations across Canada. *Clin Transplant* 2011; **25**: E571-E578 [PMID: 21955056 DOI: 10.1111/j.1399-0012.2011.10501.x]
6 **Mathur S**, Hornblower E, Levy RD. Exercise training before and after lung transplantation. *Phys Sportsmed* 2009; **37**: 78-87 [PMID: 20048531 DOI: 10.3810/psm.2009.10.1732]
7 **Langer D**. Rehabilitation in Patients before and after Lung Transplantation. *Respiration* 2015; **89**: 353-362 [PMID: 25924770 DOI: 10.1159/000430451]
8 **Gottlieb J**, Warnecke G, Hadem J, Dierich M, Wiesner O, Fühner T, Strueber M, Haverich A, Welte T. Outcome of critically ill lung transplant candidates on invasive respiratory support. *Intensive Care Med* 2012; **38**: 968-975 [PMID: 22527069 DOI: 10.1007/s00134-012-2551-y]
9 **Vermeijden JW**, Zijlstra JG, Erasmus ME, van der Bij W, Verschuuren EA. Lung transplantation for ventilator-dependent respiratory failure. *J Heart Lung Transplant* 2009; **28**: 347-351 [PMID: 19332261 DOI: 10.1016/j.healun.2009.01.012]
10 **Cypel M**, Keshavjee S. Extracorporeal life support as a bridge to lung transplantation. *Clin Chest Med* 2011; **32**: 245-251 [PMID: 21511087 DOI: 10.1016/j.ccm.2011.02.005]
11 **Fuehner T**, Kuehn C, Hadem J, Wiesner O, Gottlieb J, Tudorache I, Olsson KM, Greer M, Sommer W, Welte T, Haverich A, Hoeper MM, Warnecke G. Extracorporeal membrane oxygenation in awake patients as bridge to lung transplantation. *Am J Respir Crit Care Med* 2012; **185**: 763-768 [PMID: 22268135 DOI: 10.1164/rccm.201109-1599OC]
12 **Mathur S**, Reid WD, Levy RD. Exercise limitation in recipients of lung transplants. *Phys Ther* 2004; **84**: 1178-1187 [PMID: 15563258]
13 **Williams TJ**, McKenna MJ. Exercise limitation following transplantation. *Compr Physiol* 2012; **2**: 1937-1979 [PMID: 23723030 DOI: 10.1002/cphy.c110021]
14 **Rehabilitation Measures Database**. The Rehabilitation Clinician's Place to Find the Best Instruments to Screen Patients and Monitor Their Progress. Available from: URL: http: //www.rehabmeasures.org
15 **Martinu T**, Babyak MA, O'Connell CF, Carney RM, Trulock EP, Davis RD, Blumenthal JA, Palmer SM. Baseline 6-min walk distance predicts survival in lung transplant candidates. *Am J Transplant* 2008; **8**: 1498-1505 [PMID: 18510641 DOI: 10.1111/j.1600-6143.2008.02264.x]
16 **Lederer DJ**, Arcasoy SM, Wilt JS, D'Ovidio F, Sonett JR, Kawut SM. Six-minute-walk distance predicts waiting list survival in idiopathic pulmonary fibrosis. *Am J Respir Crit Care Med* 2006; **174**: 659-664 [PMID: 16778159 DOI: 10.1164/rccm.200604-520OC]
17 **Armstrong HF**, Garber CE, Bartels MN. Exercise testing parameters associated with post lung transplant mortality. *Respir Physiol Neurobiol* 2012; **181**: 118-122 [PMID: 22503816 DOI: 10.1016/j.resp.2012.02.003]
18 **Yimlamai D**, Freiberger DA, Gould A, Zhou J, Boyer D. Pretransplant six-minute walk test predicts peri- and post-operative outcomes after pediatric lung transplantation. *Pediatr Transplant* 2013; **17**: 34-40 [PMID: 23067306 DOI: 10.1111/petr.12010]
19 **ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories**. ATS statement: guidelines for the six-minute walk test. *Am J Respir Crit Care Med* 2002; **166**: 111-117 [PMID: 12091180 DOI: 10.1164/ajrccm.166.1.at1102]
20 **Cahalin L**, Pappagianopoulos P, Prevost S, Wain J, Ginns L. The relationship of the 6-min walk test to maximal oxygen consumption in transplant candidates with end-stage lung disease. *Chest* 1995; **108**: 452-459 [PMID: 7634883 DOI: 10.1378/chest.108.2.452]
21 **Celli BR**, Cote CG, Marin JM, Casanova C, Montes de Oca M, Mendez RA, Pinto Plata V, Cabral HJ. The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. *N Engl J Med* 2004; **350**: 1005-1012 [PMID: 14999112 DOI: 10.1056/NEJMoa021322]
22 **Egan TM**, Murray S, Bustami RT, Shearon TH, McCullough KP, Edwards LB, Coke MA, Garrity ER, Sweet SC, Heiney DA, Grover FL. Development of the new lung allocation system in the United States. *Am J Transplant* 2006; **6**: 1212-1227 [PMID: 16613597 DOI: 10.1111/j.1600-6143.2006.01276.x]
23 **Wickerson L**, Mathur S, Singer LG, Brooks D. Physical activity levels early after lung transplantation. *Phys Ther* 2015; **95**: 517-525 [PMID: 25504488 DOI: 10.2522/ptj.20140173]
24 **Langer D**, Burtin C, Schepers L, Ivanova A, Verleden G, Decramer M, Troosters T, Gosselink R. Exercise training after lung transplantation improves participation in daily activity: a randomized controlled trial. *Am J Transplant* 2012; **12**: 1584-1592 [PMID: 22390625 DOI: 10.1111/j.1600-6143.2012.04000.x]
25 **Walsh JR**, Chambers DC, Davis RJ, Morris NR, Seale HE, Yerkovich ST, Hopkins PM. Impaired exercise capacity after lung transplantation is related to delayed recovery of muscle strength. *Clin Transplant* 2013; **27**: E504-E511 [PMID: 23815281 DOI: 10.1111/ctr.12163]
26 **Maury G**, Langer D, Verleden G, Dupont L, Gosselink R, Decramer M, Troosters T. Skeletal muscle force and functional exercise tolerance before and after lung transplantation: a cohort study. *Am J Transplant* 2008; **8**: 1275-1281 [PMID: 18444941 DOI: 10.1111/j.1600-6143.2008.02209.x]
27 **Holland AE**, Spruit MA, Troosters T, Puhan MA, Pepin V, Saey D, McCormack MC, Carlin BW, Sciurba FC, Pitta F, Wanger J, MacIntyre N, Kaminsky DA, Culver BH, Revill SM, Hernandes NA, Andrianopoulos V, Camillo CA, Mitchell KE, Lee AL, Hill CJ, Singh SJ. An official European Respiratory Society/American Thoracic Society technical standard: field walking tests in chronic respiratory disease. *Eur Respir J* 2014; **44**: 1428-1446 [PMID: 25359355 DOI: 10.1183/09031936.00150314]
28 **Janaudis-Ferreira T**, Beauchamp MK, Goldstein RS, Brooks D. How should we measure arm exercise capacity in patients with COPD? A systematic review. *Chest* 2012; **141**: 111-120 [PMID: 21659430 DOI: 10.1378/chest.11-0475]
29 **Mendes P**, Wickerson L, Helm D, Janaudis-Ferreira T, Brooks D, Singer LG, Mathur S. Skeletal muscle atrophy in advanced interstitial lung disease. *Respirology* 2015; **20**: 953-959 [PMID: 26081374 DOI: 10.111/resp.12571]
30 **Rozenberg D**, Wickerson L, Singer LG, Mathur S. Sarcopenia in lung transplantation: a systematic review. *J Heart Lung Transplant* 2014; **33**: 1203-1212 [PMID: 25044057 DOI: 10.1016/j.healun.2014.06.003]
31 **Kelm DJ**, Bonnes SL, Jensen MD, Eiken PW, Hathcock MA, Kremers WK, Kennedy CC. Pre-transplant wasting (as measured by muscle index) is a novel prognostic indicator in lung transplantation. *Clin Transplant* 2016; **30**: 247-255 [PMID: 26701203 DOI: 10.111/ctr.12683]
32 **Singer JP**, Diamond JM, Gries CJ, McDonnough J, Blanc PD, Shah R, Dean MY, Hersh B, Wolters PJ, Tokman S, Arcasoy SM, Ramphal K, Greenland JR, Smith N, Heffernan P, Shah L, Shrestha P, Golden JA, Blumenthal NP, Huang D, Sonett J, Hays S, Oyster M, Katz PP, Robbins H, Brown M, Leard LE, Kukreja J, Bacchetta M, Bush E, D'Ovidio F, Rushefski M, Raza K, Christie JD, Lederer DJ. Frailty Phenotypes, Disability, and Outcomes in Adult Candidates for Lung Transplantation. *Am J Respir Crit Care Med* 2015;**192**: 1325-1334 [PMID: 26258797 DOI: 10.1164/rccm.201506-1150OC]
33 **Wickerson L**, Mathur S, Helm D, Singer L, Brooks D. Physical activity profile of lung transplant candidates with interstitial lung disease. *J Cardiopulm Rehabil Prev* 1975; **33**: 106-112 [PMID: 23403914 DOI: 10.1097/HCR.06013e318283993]
34 **Langer D**, Cebrià i Iranzo MA, Burtin C, Verleden SE, Vanau-

denaerde BM, Troosters T, Decramer M, Verleden GM, Gosselink R. Determinants of physical activity in daily life in candidates for lung transplantation. *Respir Med* 2012; **106**: 747-754 [PMID: 22305265 DOI: 10.1016/j.rmed.2012.01.003]
35 **Langer D**, Gosselink R, Pitta F, Burtin C, Verleden G, Dupont L, Decramer M, Troosters T. Physical activity in daily life 1 year after lung transplantation. *J Heart Lung Transplant* 2009; **28**: 572-578 [PMID: 19481017 DOI: 10.1016/j.healun.2009.03.007]
36 **Bossenbroek L**, ten Hacken NH, van der Bij W, Verschuuren EA, Koëter GH, de Greef MH. Cross-sectional assessment of daily physical activity in chronic obstructive pulmonary disease lung transplant patients. *J Heart Lung Transplant* 2009; **28**: 149-155 [PMID: 19201340 DOI: 10.1016/j.healun.2008.11.905]
37 **Bossenbroek L**, den Ouden ME, de Greef MH, Douma WR, Ten Hacken NH, van der Bij W. Determinants of overweight and obesity in lung transplant recipients. *Respiration* 2011; **82**: 28-35 [PMID: 21212650 DOI: 10.1159/000322833]
38 American College of Sports Medicine guidelines for exercise testing and prescription 9th Ed. Philadelphia, PA: Lippincott, Williams and Wilkens, 2013
39 **Gloeckl R**, Halle M, Kenn K. Interval versus continuous training in lung transplant candidates: a randomized trial. *J Heart Lung Transplant* 2012; **31**: 934-941 [PMID: 22884381 DOI: 10.1016/j.healun.2012.06.004]
40 **Manzetti JD**, Hoffman LA, Sereika SM, Sciurba FC, Griffith BP. Exercise, education, and quality of life in lung transplant candidates. *J Heart Lung Transplant* 1994; **13**: 297-305 [PMID: 8031815]
41 **Florian J**, Rubin A, Mattiello R, Fontoura FF, Camargo Jde J, Teixeira PJ. Impact of pulmonary rehabilitation on quality of life and functional capacity in patients on waiting lists for lung transplantation. *J Bras Pneumol* 2013; **39**: 349-356 [PMID: 23857680 DOI: 10.1590/S1806-37132013000300012]
42 **Jastrzebski D**, Ochman M, Ziora D, Labus L, Kowalski K, Wyrwol J, Lutogniewska W, Maksymiak M, Ksiazek B, Magner A, Bartoszewicz A, Kubicki P, Hydzik G, Zebrowska A, Kozielski J. Pulmonary rehabilitation in patients referred for lung transplantation. *Adv Exp Med Biol* 2013; **755**: 19-25 [PMID: 22826045 DOI: 10.1007/978-94-007-4545-9_3]
43 **Kenn K**, Gloeckl R, Soennichsen A, Sczepanski B, Winterkamp S, Boensch M, Welte T. Predictors of success for pulmonary rehabilitation in patients awaiting lung transplantation. *Transplantation* 2015; **99**: 1072-1077 [PMID: 25393161 DOI: 10.1097/TP.0000000000000472]
44 **Spruit MA**, Singh SJ, Garvey C, ZuWallack R, Nici L, Rochester C, Hill K, Holland AE, Lareau SC, Man WD, Pitta F, Sewell L, Raskin J, Bourbeau J, Crouch R, Franssen FM, Casaburi R, Vercoulen JH, Vogiatzis I, Gosselink R, Clini EM, Effing TW, Maltais F, van der Palen J, Troosters T, Janssen DJ, Collins E, Garcia-Aymerich J, Brooks D, Fahy BF, Puhan MA, Hoogendoorn M, Garrod R, Schols AM, Carlin B, Benzo R, Meek P, Morgan M, Rutten-van Mölken MP, Ries AL, Make B, Goldstein RS, Dowson CA, Brozek JL, Donner CF, Wouters EF. An official American Thoracic Society/European Respiratory Society statement: key concepts and advances in pulmonary rehabilitation. *Am J Respir Crit Care Med* 2013; **188**: e13-e64 [PMID: 24127811 DOI: 10.1164/rrcm.201309-1634ST]
45 **Holland AE**, Wadell K, Spruit MA. How to adapt the pulmonary rehabilitation programme to patients with chronic respiratory disease other than COPD. *Eur Respir Rev* 2013; **22**: 577-586 [PMID: 24293474 DOI: 10.1071/AH13067]
46 **Geddes EL**, Reid WD, Crowe J, O'Brien K, Brooks D. Inspiratory muscle training in adults with chronic obstructive pulmonary disease: a systematic review. *Respir Med* 2005; **99**: 1440-1458 [PMID: 15894478 DOI: 10.1016/j.med.2005.03.006]
47 **Lee AL**, Goldstein RS. Chapter 19. The Role of Telemedicine in COPD. In Controversies in COPD. (editor: John Hurst). *European Respiratory Monograph* 2015; **69**: 1-28
48 **Borg GA**. Psychophysical bases of perceived exertion. *Med Sci Sports Exerc* 1982; **14**: 377-381 [PMID: 7154893]
49 **Caramete A**, Longmuir C, McQuade K, Shaver L, Wickerson L, Helm D, Mathur S. Exercise prescription using the six-minute walk test in individuals awaiting lung transplantation. *Cardiopulm Phys Ther J* 2014; **25**: 106-112
50 **Duong M**, Bertin K, Henry R, Singh D, Timmins N, Brooks D, Mathur S, Ellerton C. Developing a physiotherapy-specific preliminary clinical decision-making tool for oxygen titration: a modified delphi study. *Physiother Can* 2014; **66**: 286-295 [PMID: 25125782 DOI: 10.3138/ptc.2013-42]
51 **Kenn K**, Gloeckl R, Behr J. Pulmonary rehabilitation in patients with idiopathic pulmonary fibrosis--a review. *Respiration* 2013; **86**: 89-99 [PMID: 23942353 DOI: 10.1159/000354112]
52 **Pandey A**, Garg S, Khunger M, Garg S, Kumbhani DJ, Chin KM, Berry JD. Efficacy and Safety of Exercise Training in Chronic Pulmonary Hypertension: Systematic Review and Meta-Analysis. *Circ Heart Fail* 2015; **8**: 1032-1043 [PMID: 26185169 DOI: 10.1161/CIRHEARTFAILURE.115.002130]
53 **Rochester CL**, Fairburn C, Crouch RH. Pulmonary rehabilitation for respiratory disorders other than chronic obstructive pulmonary disease. *Clin Chest Med* 2014; **35**: 369-389 [PMID: 24874132 DOI: 10.1016/j.ccm.2014.02.016]
54 **Crouch RH**, Schein RL. Integrating psychosocial services for lung volume reduction and lung transplantation patients into a pulmonary rehabilitation program. *J Cardiopulm Rehabil* 1997; **17**: 16-18 [PMID: 9041066]
55 **Colman R**, Singer LG, Barua R, Downar J. Outcomes of lung transplant candidates referred for co-management by palliative care: A retrospective case series. *Palliat Med* 2015; **29**: 429-435 [PMID: 25634636 DOI: 10.1177/0269216314566839]
56 **Herridge MS**, Chu LM, Matte A, Tomlinson G, Chan L, Thomas C, Friedrich JO, Mehta S, Lamontagne F, Levasseur M, Ferguson ND, Adhikari NK, Rudkowski JC, Meggison H, Skrobik Y, Flannery J, Bayley M, Batt J, Dos Santos C, Abbey SE, Tan A, Lo V, Mathur S, Parotto M, Morris D, Flockhart L, Fan E, Lee CM, Wilcox ME, Ayas N, Choong K, Fowler R, Scales DC, Sinuff T, Cuthbertson BH, Rose L, Robles P, Burns S, Cypel M, Singer L, Chaparro C, Chow CW, Keshavjee S, Brochard L, Hebert P, Slutsky AS, Marshall JC, Cook D, Cameron JI; RECOVER Program Investigators (Phase 1: towards RECOVER) and the Canadian Critical Care Trials Group. The RECOVER Program: Disability Risk Groups & amp; One Year Outcome after ≥ 7 Days of Mechanical Ventilation. *Am J Respir Crit Care Med* 2016: Epub ahead of print [PMID: 26974173 DOI: 10.1164/rccm.201512-2343OC]
57 **Maddocks M**, Nolan CM, Man WD, Polkey MI, Hart N, Gao W, Rafferty GF, Moxham J, Higginson IJ. Neuromuscular electrical stimulation to improve exercise capacity in patients with severe COPD: a randomised double-blind, placebo-controlled trial. *Lancet Respir Med* 2016; **4**: 27-36 [PMID: 26701362 DOI: 10.1016/S2213-2600(15)00503-2]
58 **Dos Santos C**, Hussain SN, Mathur S, Picard M, Herridge M, Correa J, Bain A, Guo Y, Advani A, Advani S, Tomlinson G, Katzberg H, Streutker CJ, Cameron JI, Schols A, Gosker H, Batt J; MEND ICU Group, the RECOVER Program Investigators and the Canadian Critical care Translational Biology Group. Mechanisms of Chronic Muscle Wasting and Dysfunction After an Intensive Care Unit Stay: A Pilot Study. *Am J Respir Crit Care Med* 2016: Epub ahead of print [PMID: 27058306 DOI: 10.1164/rccm.201512-2344OC]
59 **Turner DA**, Cheifetz IM, Rehder KJ, Williford WL, Bonadonna D, Banuelos SJ, Peterson-Carmichael S, Lin SS, Davis RD, Zaas D. Active rehabilitation and physical therapy during extracorporeal membrane oxygenation while awaiting lung transplantation: a practical approach. *Crit Care Med* 2011; **39**: 2593-2598 [PMID: 21765353 DOI: 10.1097/ccm0b013e3182282bbe]
60 **Moss M**, Nordon-Craft A, Malone D, Van Pelt D, Frankel SK, Warner ML, Kriekels W, McNulty M, Fairclough DL, Schenkman M. A Randomized Trial of an Intensive Physical Therapy Program for Patients with Acute Respiratory Failure. *Am J Respir Crit Care Med* 2016; **193**: 1101-1110 [PMID: 26651376]
61 **Polastri M**, Loforte A, Dell'Amore A, Nava S. Physiotherapy for Patients on Awake Extracorporeal Membrane Oxygenation: A Systematic Review. *Physiother Res Int* 2015 Aug 14; Epub ahead of print [PMID: 26274362 DOI: 10.1002/pri.1644]

62 **Hodgson CL**, Stiller K, Needham DM, Tipping CJ, Harrold M, Baldwin CE, Bradley S, Berney S, Caruana LR, Elliott D, Green M, Haines K, Higgins AM, Kaukonen KM, Leditschke IA, Nickels MR, Paratz J, Patman S, Skinner EH, Young PJ, Zanni JM, Denehy L, Webb SA. Expert consensus and recommendations on safety criteria for active mobilization of mechanically ventilated critically ill adults. *Crit Care* 2014; **18**: 658 [PMID: 25475522 DOI: 10.1186/s13054=-014-0658-y]

63 **Dierich M**, Tecklenburg A, Fuehner T, Tegtbur U, Welte T, Haverich A, Warnecke G, Gottlieb J. The influence of clinical course after lung transplantation on rehabilitation success. *Transpl Int* 2013; **26**: 322-330 [PMID: 23294442 DOI: 10.1111/tri.12048]

64 **Herridge MS**. Legacy of intensive care unit-acquired weakness. *Crit Care Med* 2009; **37**: S457-S461 [PMID: 20046135 DOI: 10.1097/ccm.0b013e3181b6f35c]

65 **Schuurmans MM**, Benden C, Inci I. Practical approach to early postoperative management of lung transplant recipients. *Swiss Med Wkly* 2013; **143**: w13773 [PMID: 23572438 DOI: 10.4414/smw.2013.13773]

66 **Leal S**, Sacanell J, Riera J, Masclans JR, Rello J. Early postoperative management of lung transplantation. *Minerva Anestesiol* 2014; **80**: 1234-1245 [PMID: 24518214]

67 **Kress JP**, Hall JB. ICU-acquired weakness and recovery from critical illness. *N Engl J Med* 2014; **371**: 287-288 [PMID: 25014703 DOI: 10.1056/NEJMc1406274]

68 **Puthucheary ZA**, Rawal J, McPhail M, Connolly B, Ratnayake G, Chan P, Hopkinson NS, Phadke R, Dew T, Sidhu PS, Velloso C, Seymour J, Agley CC, Selby A, Limb M, Edwards LM, Smith K, Rowlerson A, Rennie MJ, Moxham J, Harridge SD, Hart N, Montgomery HE. Acute skeletal muscle wasting in critical illness. *JAMA* 2013; **310**: 1591-1600 [PMID: 24108501 DOI: 10.1001/jama.2013.278481]

69 **Adler J**, Malone D. Early mobilization in the intensive care unit: a systematic review. *Cardiopulm Phys Ther J* 2012; **23**: 5-13 [PMID: 22807649]

70 **Laurent H**, Aubreton S, Richard R, Gorce Y, Caron E, Vallat A, Davin AM, Constantin JM, Coudeyre E. Systematic review of early exercise in intensive care: A qualitative approach. *Anaesth Crit Care Pain Med* 2016; **35**: 133-149 [PMID: 26655865 DOI: 10.1016/j.accpm.2015.06.014]

71 **Kayambu G**, Boots R, Paratz J. Physical therapy for the critically ill in the ICU: a systematic review and meta-analysis. *Crit Care Med* 2013; **41**: 1543-1554 [PMID: 23528802 DOI: 10.1097/ccm.0b013e31827ca637]

72 **Calvo-Ayala E**, Khan BA, Farber MO, Ely EW, Boustani MA. Interventions to improve the physical function of ICU survivors: a systematic review. *Chest* 2013; **144**: 1469-1480 [PMID: 23949645 DOI: 10.1378/chest.13-0779]

73 **Li Z**, Peng X, Zhu B, Zhang Y, Xi X. Active mobilization for mechanically ventilated patients: a systematic review. *Arch Phys Med Rehabil* 2013; **94**: 551-561 [PMID: 23127305 DOI: 10.1016/j.apmr.2012.10.023]

74 **Castro-Avila AC**, Serón P, Fan E, Gaete M, Mickan S. Effect of Early Rehabilitation during Intensive Care Unit Stay on Functional Status: Systematic Review and Meta-Analysis. *PLoS One* 2015; **10**: e0130722 [PMID: 26132803 DOI: 10.1371/journal.pone.0130722]

75 **Hermans G**, De Jonghe B, Bruyninckx F, Van den Berghe G. Interventions for preventing critical illness polyneuropathy and critical illness myopathy. *Cochrane Database Syst Rev* 2014; **(1)**: CD006832 [PMID: 24477672 DOI: 10.1002/14651858.CD006832]

76 **Hunter A**, Johnson L, Coustasse A. Reduction of intensive care unit length of stay: the case of early mobilization. *Health Care Manag* (Frederick) 2014; **33**: 128-135 [PMID: 24776831 DOI: 10.1097/HCM.0000000000000006]

77 **Morris PE**, Berry MJ, Files DC, Thompson JC, Hauser J, Flores L, Dhar S, Chmelo E, Lovato J, Case LD, Bakhru RN, Sarwal A, Parry SM, Campbell P, Mote A, Winkelman C, Hite RD, Nicklas B, Chatterjee A, Young MP. Standardized Rehabilitation and Hospital Length of Stay Among Patients With Acute Respiratory Failure: A Randomized Clinical Trial. *JAMA* 2016; **315**: 2694-2702 [PMID: 27367766 DOI: 10.1001/jama.2016.7201]

78 **Schweickert WD**, Pohlman MC, Pohlman AS, Nigos C, Pawlik AJ, Esbrook CL, Spears L, Miller M, Franczyk M, Deprizio D, Schmidt GA, Bowman A, Barr R, McCallister KE, Hall JB, Kress JP. Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. *Lancet* 2009; **373**: 1874-1882 [PMID: 19446324 DOI: 10.1016/S0140-6736(09)60658-9]

79 **Carlin BW**, Lega M, Veynovich B. Management of the patient undergoing lung transplantation: an intensive care perspective. *Crit Care Nurs Q* 2009; **32**: 49-57 [PMID: 19077810 DOI: 10.1097/01.CNQ.0000343128.81576.dd]

80 **Burtin C**, Clerckx B, Robbeets C, Ferdinande P, Langer D, Troosters T, Hermans G, Decramer M, Gosselink R. Early exercise in critically ill patients enhances short-term functional recovery. *Crit Care Med* 2009; **37**: 2499-2505 [PMID: 19623052 DOI: 10.1097/CCM.0b013e3181a38937]

81 **Maffiuletti NA**, Roig M, Karatzanos E, Nanas S. Neuromuscular electrical stimulation for preventing skeletal-muscle weakness and wasting in critically ill patients: a systematic review. *BMC Med* 2013; **11**: 137 [PMID: 23701811 DOI: 10.1186/1741-7015-11-137]

82 **Wageck B**, Nunes GS, Silva FL, Damasceno MC, de Noronha M. Application and effects of neuromuscular electrical stimulation in critically ill patients: systematic review. *Med Intensiva* 2014; **38**: 444-454 [PMID: 25060511 DOI: 10.1016/j.medin.2013.12.003]

83 **Batt J**, dos Santos CC, Cameron JI, Herridge MS. Intensive care unit-acquired weakness: clinical phenotypes and molecular mechanisms. *Am J Respir Crit Care Med* 2013; **187**: 238-246 [PMID: 23204256 DOI: 10.1164/rccm.201205-0954SO]

84 **van Adrichem EJ**, Reinsma GD, van den Berg S, van der Bij W, Erasmus ME, Krijnen WP, Dijkstra PU, van der Schans CP. Predicting 6-minute walking distance in recipients of lung transplantation: longitudinal study of 108 patients. *Phys Ther* 2015; **95**: 720-729 [PMID: 25524871 DOI: 10.2522/ptj.20140001]

85 **Fuller LM**, Button B, Tarrant B, Battistuzzo CR, Braithwaite M, Snell G, Holland AE. Patients' expectations and experiences of rehabilitation following lung transplantation. *Clin Transplant* 2014; **28**: 252-258 [PMID: 24372876 DOI: 10.1111/ctr.12306]

86 **Wickerson L**, Mathur S, Brooks D. Exercise training after lung transplantation: a systematic review. *J Heart Lung Transplant* 2010; **29**: 497-503 [PMID: 20133160 DOI: 10.1016/j.healun.2009.12.008]

87 **Ihle F**, Neurohr C, Huppmann P, Zimmermann G, Leuchte H, Baumgartner R, Kenn K, Sczepanski B, Hatz R, Czerner S, Frey L, Ueberfuhr P, Bittmann I, Behr J. Effect of inpatient rehabilitation on quality of life and exercise capacity in long-term lung transplant survivors: a prospective, randomized study. *J Heart Lung Transplant* 2011; **30**: 912-919 [PMID: 21489819 DOI: 10.1016/j.healun,2011.02.006]

88 **Vivodtzev I**, Pison C, Guerrero K, Mezin P, Maclet E, Borel JC, Chaffanjon P, Hacini R, Chavanon O, Blin D, Wuyam B. Benefits of home-based endurance training in lung transplant recipients. *Respir Physiol Neurobiol* 2011; **177**: 189-198 [PMID: 21333761 DOI: 10.1016/j.resp.2011.02.005]

89 **Tang M**, Mawji N, Chung S, Brijlal R, Lim Sze How JK, Wickerson L, Rozenberg D, Singer LG, Mathur S, Janaudis-Ferreira T. Factors affecting discharge destination following lung transplantation. *Clin Transplant* 2015; **29**: 581-587 [PMID: 25918985 DOI: 10.1111/ctr.12556]

90 **Bowman M**, Faux S. Outcomes of an inpatient rehabilitation program following complicated cardio-pulmonary transplantation. *Int J Phys Med Rehabil* 2013: **1**: 1-6 [DOI: 10.4172/2329-9096.1000152]

91 **Patcai JT**, Disotto-Monastero MP, Gomez M, Adcock LE. Inpatient rehabilitation outcomes in solid organ transplantation: results of a unique partnership between the rehabilitation hospital and the multi-organ transplant unit in an acute hospital. *Open J Ther Rehab* 2013; **1**: 52-61 [DOI: 10.4236/ojtr.2013.12009]

92 **Stiebellehner L**, Quittan M, End A, Wieselthaler G, Klepetko W, Haber P, Burghuber OC. Aerobic endurance training program improves exercise performance in lung transplant recipients. *Chest*

1998; **113**: 906-912 [PMID: 9554624 DOI: 10.1378/chest.113.4.906]
93 **Canadian Transplant Games**. Check out the promotional video and theme song for the 2016 Canadian Transplant Games. Available from: URL: http: //organ-donation-works.org/english/events/canadian-transplant-games
94 **World Transplant Games Federation**. Available from: URL: http://www.wtgf.org
95 **Warburton DE**, Sheel AW, Hodges AN, Stewart IB, Yoshida EM, Levy RD, McKenzie DC. Effects of upper extremity exercise training on peak aerobic and anaerobic fitness in patients after transplantation. *Am J Cardiol* 2004; **93**: 939-943 [PMID: 15050506 DOI: 10.1016/j.amjcard.2003.12.030]
96 **Kaemmerer H**, Mebus S, Schulze-Neick I, Eicken A, Trindade PT, Hager A, Oechslin E, Niwa K, Lang I, Hess J. The adult patient with eisenmenger syndrome: a medical update after dana point part I: epidemiology, clinical aspects and diagnostic options. *Curr Cardiol Rev* 2010; **6**: 343-355 [PMID: 22043211 DOI: 10.2174/157340310793566154]
97 **Westhoff-Bleck M**, Treptau J, Loffler F, Widder J. Exercise training in adults with complex congenital heart disease. *Ann Sports Med Res* 2015; **2**: 1037-1040
98 **Levy RD**, Ernst P, Levine SM, Shennib H, Anzueto A, Bryan CL, Calhoon JH, Trinkle JK, Jenkinson SG, Gibbons WJ. Exercise performance after lung transplantation. *J Heart Lung Transplant* 1993; **12**: 27-33 [PMID: 8443197]
99 **Warnecke G**, Haverich A. Lung re-transplantation: review. *Curr Opin Organ Transplant* 2012; **17**: 485-489 [PMID: 22907540 DOI: 10.1097/MOT.0b013e328357d8ba]
100 **Gulmans VA**, van Veldhoven NH, de Meer K, Helders PJ. The six-minute walking test in children with cystic fibrosis: reliability and validity. *Pediatr Pulmonol* 1996; **22**: 85-89 [PMID: 8875580]
101 **Radtke T**, Faro A, Wong J, Boehler A, Benden C. Exercise testing in pediatric lung transplant candidates with cystic fibrosis. *Pediatr Transplant* 2011; **15**: 294-299 [PMID: 21244591 DOI: 10.111/j.1399-3046.2010.01471.x]
102 **Hassan J**, van der Net J, Helders PJ, Prakken BJ, Takken T. Six-minute walk test in children with chronic conditions. *Br J Sports Med* 2010; **44**: 270-274 [PMID: 18487250 DOI: 10.1136/bjsm.2008.048512]
103 **Janssen I**, Leblanc AG. Systematic review of the health benefits of physical activity and fitness in school-aged children and youth. *Int J Behav Nutr Phys Act* 2010; **7**: 40 [PMID: 20459784 DOI: 10.1186/1479-5868-7-40]
104 **Nixon PA**, Fricker FJ, Noyes BE, Webber SA, Orenstein DM, Armitage JM. Exercise testing in pediatric heart, heart-lung, and lung transplant recipients. *Chest* 1995; **107**: 1328-1335 [PMID: 7750327]
105 **Deliva RD**, Hassall A, Manlhiot C, Solomon M, McCrindle BW, Dipchand AI. Effects of an acute, outpatient physiotherapy exercise program following pediatric heart or lung transplantation. *Pediatr Transplant* 2012; **16**: 879-886 [PMID: 23050737 DOI: 10.1111/petr.12003]
106 **Deliva RD**, Patterson C, So S, Pellow V, Miske S, McLister C, Manlhiot C, Pollock-BarZiv S, Drabble A, Dipchand AI. The World Transplant Games: an incentive to improve physical fitness and habitual activity in pediatric solid organ transplant recipients. *Pediatr Transplant* 2014; **18**: 889-895 [PMID: 25307141 DOI: 10.1111/petr.12370]
107 **Gold A**, Martin K, Breckbill K, Avitzur Y, Kaufman M. Transition to adult care in pediatric solid-organ transplant: development of a practice guideline. *Prog Transplant* 2015; **25**: 131-138 [PMID: 26107273 DOI: 10.7.82/pit2015833]
108 **Reeb J**, Keshavjee S, Cypel M. Expanding the lung donor pool: advancements and emerging pathways. *Curr Opin Organ Transplant* 2015; **20**: 498-505 [PMID: 26262464 DOI: 10.1097/MOT.0000000000000233]
109 **Mathur S**, Janaudis-Ferreira T, Wickerson L, Singer LG, Patcai J, Rozenberg D, Blydt-Hansen T, Hartmann EL, Haykowsky M, Helm D, High K, Howes N, Kamath BM, Lands L, Marzolini S, Sonnenday C. Meeting report: consensus recommendations for a research agenda in exercise in solid organ transplantation. *Am J Transplant* 2014; **14**: 2235-2245 [PMID: 25135579 DOI: 10.1111/ajt.12874]
110 **Peel NM**, Kuys SS, Klein K. Gait speed as a measure in geriatric assessment in clinical settings: a systematic review. *J Gerontol A Biol Sci Med Sci* 2013; **68**: 39-46 [PMID: 22923430 DOI: 10.1093/Gerona/gls174]
111 **Jones CJ**, Rikli RE, Beam WC. A 30-s chair-stand test as a measure of lower body strength in community-residing older adults. *Res Q Exerc Sport* 1999; **70**: 113-119 [PMID: 10380242 DOI: 10.1080/02701367.1999.10608028]
112 **Buatois S**, Miljkovic D, Manckoundia P, Gueguen R, Miget P, Vançon G, Perrin P, Benetos A. Five times sit to stand test is a predictor of recurrent falls in healthy community-living subjects aged 65 and older. *J Am Geriatr Soc* 2008; **56**: 1575-1577 [PMID: 18808608 DOI: 10.1111/j.1532-5415.2008.01777.x]
113 **Guralnik JM**, Simonsick EM, Ferrucci L, Glynn RJ, Berkman LF, Blazer DG, Scherr PA, Wallace RB. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. *J Gerontol* 1994; **49**: M85-M94 [PMID: 8126356 DOI: 10.1093/geronj/49.2.M85]
114 **Podsiadlo D**, Richardson S. The timed "Up & amp; Go": a test of basic functional mobility for frail elderly persons. *J Am Geriatr Soc* 1991; **39**: 142-148 [PMID: 1991946 DOI: 10.1111/j.1532-5415.1991.tb016.x]
115 **Berg K**, Wood-Dauphine S, Williams JI. Measuring balance in the elderly: preliminary development of an instrument. *Physio Can* 1989; **41**: 304-311 [DOI: 10.3138/ptc.41.6.304]
116 **Horak FB**, Wrisley DM, Frank J. The Balance Evaluation Systems Test (BESTest) to differentiate balance deficits. *Phys Ther* 2009; **89**: 484-498 [PMID: 19329772 DOI: 10.2522/ptj.20080071]
117 **Keith RA**, Granger CV, Hamilton BB, Sherwin FS. The functional independence measure: a new tool for rehabilitation. *Adv Clin Rehabil* 1987; **1**: 6-18 [PMID: 3503663]
118 **Dionne M**. Introducing the Egress Test. *Advance Healthcare Network for Physical Therapy and Rehabilitation Medicine* 2004; **15**: 39
119 **Hodgson C**, Needham D, Haines K, Bailey M, Ward A, Harrold M, Young P, Zanni J, Buhr H, Higgins A, Presneill J, Berney S. Feasibility and inter-rater reliability of the ICU Mobility Scale. *Heart Lung* 2014; **43**: 19-24 [PMID: 24373338 DOI: 10.1016/j.hrtlng.2013.11.003]
120 **Thrush A**, Rozek M, Dekerlegand JL. The clinical utility of the functional status score for the intensive care unit (FSS-ICU) at a long-term acute care hospital: a prospective cohort study. *Phys Ther* 2012; **92**: 1536-1545 [PMID: 22956427 DOI: 10.2522/ptj.20110412]
121 **Denehy L**, de Morton NA, Skinner EH, Edbrooke L, Haines K, Warrillow S, Berney S. A physical function test for use in the intensive care unit: validity, responsiveness, and predictive utility of the physical function ICU test (scored). *Phys Ther* 2013; **93**: 1636-1645 [PMID: 23886842 DOI: 10.2522/ptj.20120310]
122 **Washburn RA**, Smith KW, Jette AM, Janney CA. The Physical Activity Scale for the Elderly (PASE): development and evaluation. *J Clin Epidemiol* 1993; **46**: 153-162 [PMID: 8437031 DOI: 10.1016/0895-4356(93)90053-4]
123 **Booth M**. Assessment of physical activity: an international perspective. *Res Q Exerc Sport* 2000; **71** Suppl 2: 114-120 [PMID: 25680021 DOI: 10.1080/02701367.2000.11082794]
124 **Hlatky MA**, Boineau RE, Higginbotham MB, Lee KL, Mark DB, Califf RM, Cobb FR, Pryor DB. A brief self-administered questionnaire to determine functional capacity (the Duke Activity Status Index). *Am J Cardiol* 1989; **64**: 651-654 [PMID: 2782256 DOI: 10.1016/0002-9149(89)90496-7]
125 **American College of Sports Medicine**. American College of Sports Medicine position stand. Progression models in resistance training for healthy adults. *Med Sci Sports Exerc* 2009; **41**: 687-708 [PMID: 19204579 DOI: 10.1249/MSS.0b013e3181915670]
126 **Beauchamp MK**, Nonoyama M, Goldstein RS, Hill K, Dolmage TE, Mathur S, Brooks D. Interval versus continuous training in individuals with chronic obstructive pulmonary disease - a systematic review. *Thorax* 2010; **65**: 157-164

127 **Kho ME**, Damluji A, Zanni JM, Needham DM. Feasibility and observed safety of interactive video games for physical rehabilitation in the intensive care unit: a case series. *J Crit Care* 2012; **27**: 219.e1-219.e6 [PMID: 21944880 DOI: 10.1016/j.jcrc.2011.08.017]

128 **Gloeckl R**, Heinzelmann I, Seeberg S, Damisch T, Hitzl W, Kenn K. Effects of complementary whole-body vibration training in patients after lung transplantation: A randomized, controlled trial. *J Heart Lung Transplant* 2015; **34**: 1455-1461 [PMID: 26279196]

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