Combined arm-leg ergometry in persons with a lower limb amputation



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1

General introduction

A lower limb amputation (LLA) is one of the main patient categories in rehabilitation medicine, with reported incidence rates showing considerable global variation, ranging from 3.6 to 69.4 per 100,000 person-years[1]. The incidence of diabetes mellitus (DM), global average age, ethnic differences and social deprivation all influence the incidence of amputation worldwide. More than 90% of the lower limb amputations in the United States and Western European countries are related to peripheral arterial disease and DM[2,3]. Other causes of amputations are cancer related, trauma related or because of congenital deficiencies[1]. The age-standardized incidence rate of first ever dysvascular LLA in Northern Netherlands in 2012–2013 was 7.7 per 100,000 person-years[4].

Many persons with a LLA due to peripheral arterial disease have had severely limited physical activity for weeks to months, sometimes years, prior to the amputation as a result of gangrene, osteomyelitis, pain or vascular claudication[5-7]. In addition, having a LLA results in a severe decline in physical fitness. This decline is caused by physical inactivity due to bed rest during hospitalization prior to and after the operation, a reduced ability to perform daily activities with a LLA[8] and the prevalence of co-morbidities, especially cardiovascular diseases[9].

> *Mr. X, 62 years old, has undergone a lower limb amputation because of peripheral arterial disease. After surgery he starts with rehabilitation. His main goal of rehabilitation is to walk with a prosthesis because he wants to reintegrate into his work as a teacher and wants to play golf. Before the amputation, he went through a period of inactivity of several months because of pain. Consequently, Mr. X experienced a decline in physical fitness. The physiotherapist involved wants to start an exercise training program to improve physical fitness. He needs to know the level of physical fitness at the start of the rehabilitation and has to make choices with regard to training intensity and duration.*

Lower limb amputation often leads to long-term disability. It has a major impact on almost every aspect of a person's life in the domains of the International Classification of Functioning, Disability and Health (ICF) (Fig. 1). It affects the body functions and structures and level of activities and participation[10,11]. For example, the function and/or structure of the leg is affected by the LLA, resulting in a change in gait and walking ability (activity) and probably in changes in work,

family or sport participation. These different effects are in turn dependent on environmental (physical and social) and personal characteristics. Rehabilitation is one of those environmental factors designed to impact functionality of people with a disability. The main purpose of rehabilitation is to restore function and to regain optimal levels of functioning, participation and quality of life[12].

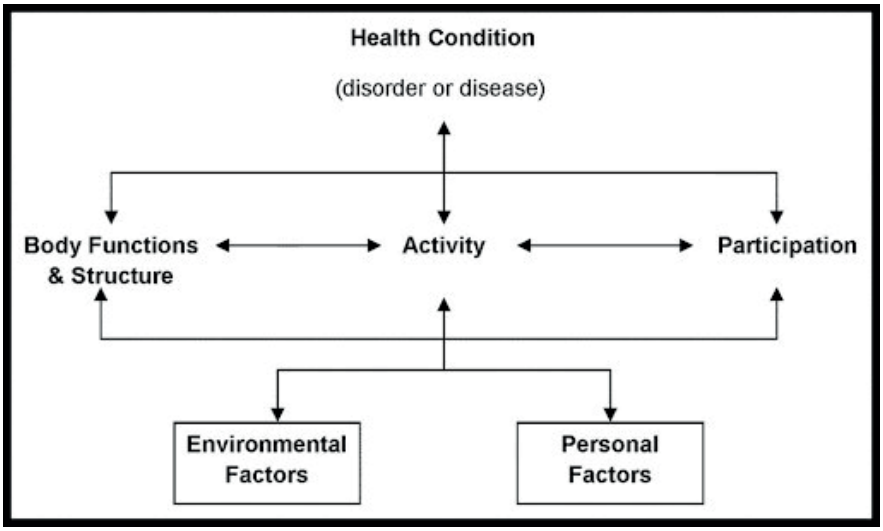

Figure 1. ICF model: International Classification of Functioning, Disability and Health[11].

Energy cost of ambulation after a lower limb amputation

Walking ability after a LLA is multidimensional defined and can be influenced by many different aspects, such as disease characteristics, personal and environmental factors. A relevant personal factor that may seriously impact walking ability is physical fitness. Physical fitness has been defined in several ways, but a generally accepted definition is the ability to carry out daily tasks with vigor and alertness, without undue fatigue, and with ample energy to enjoy leisure-time pursuits and meet unforeseen emergencies[13]. In relation to physical fitness, two other terms are often used; physical activity and exercise. Physical activity is defined as any bodily movement produced by the contraction of skeletal muscles that results in a substantial increase in caloric requirements over resting energy expenditure[13]. Exercise is a type of physical activity

consisting of planned, structured, and repetitive bodily movement done to improve and/or maintain one or more components of physical fitness[13]. Physical fitness is composed of various elements that can be further grouped into health-related components (cardiorespiratory endurance, body composition, muscular strength, muscular endurance and flexibility) and skill-related components (agility, coordination, balance, power, reaction time and speed)[13]. Poor physical fitness influences the progress of rehabilitation in a negative way[14]. In addition, the energy cost of walking with a prosthesis is much higher compared to walking with two healthy legs. Energy cost of walking tends to rise with the level of amputation[15]. Rehabilitation in persons with a LLA is about relearning and training ADL (activities of daily living) and ambulation, preferably to regain walking ability and daily functioning, generally with the help of assistive technology. It requires practice to create controlled, comfortable, efficient and safe ambulation and ADL. Often the physical strain during rehabilitation is insufficient to elicit potential improvements in cardiorespiratory fitness. It is suggested that gait training with a prosthesis should be accompanied by some kind of endurance exercise training to improve the overall cardiorespiratory and muscular parts of physical fitness[6,14]. Individualized training requires individualized goal setting, based on valid, reliable and specific exercise capacity tests. In order to determine individual cardiorespiratory fitness in persons with a LLA, a safe, valid and specific exercise test, testing equipment and testing environment are essential.

Cardiorespiratory fitness and ergometry

The cardiorespiratory fitness or aerobic exercise capacity can reliably be measured in healthy individuals by determining the peak oxygen uptake (VO_2 peak)[16]. The VO_2peak can be directly measured by a peak exercise test or calculated from a submaximal exercise test[17]. Submaximal exercise tests are terminated when a certain percentage of the predicted maximal heart rate is reached. The oxygen uptake during the course of the test is recorded and the data are used to estimate VO_2peak based on a predicted, age and gender corrected, peak heart rate. Especially in persons with a LLA submaximal exercise testing can be unreliable[17]. The peak oxygen uptake cannot be reliably estimated from submaximal oxygen uptake and heart rate data when persons

with a LLA take medication that influences the exercise capacity[18]. ß-Blockers for instance are known to reduce heart rate and systolic blood pressure[19]. In addition, persons with a LLA may have altered blood pressure and heart rate responses to exercise[18]. For these reasons VO_2peak cannot be predicted reliably from the submaximal oxygen uptake and heart rate. Given these conditions, VO_2peak of these persons has to be determined in an actual peak exercise test.

In order to measure the VO_2peak validly and reliably, it is important to apply a reliable testing protocol that involves the largest possible active muscle mass during exercise[16]. When using a large muscle mass during testing, more oxygen is consumed which allows a more reliable estimate of VO_2peak and heart function. This in itself is a challenge in persons with a LLA. Different ergometers were used in the past to evaluate aerobic capacity in persons with a LLA like a motor driven treadmill (only in those with walking ability with a prosthesis), unilateral bicycle ergometer, arm ergometer, rowing ergometer or a combined arm-leg ergometer[20-22]. Exercise testing via arm ergometry can provide useful data to generate a safe upper extremity exercise program[23]. However, arm ergometry is less specific in ambulant LLA, while it excludes functional leg muscle mass and does not stress the cardiovascular and the respiratory system as much as regular leg cycling or treadmill walking exercise. During arm ergometry peak oxygen uptake will be 50 to 70% of peak oxygen uptake during bicycle ergometry[24-26]. For reaching higher levels of VO_2 in persons with a LLA, it is attractive to use both arms and the unaffected leg. The use of a bicycle ergometer with one leg[27] is limited in applicability as persons with a LLA often need help to make the cycling movement with one leg, it is more difficult to maintain balance, and the muscle mass of only one leg is applied. Combined arm-leg ergometers have the advantage that a person applies a large muscle mass, since arms, trunk as well as leg(s) are contributing to peak power production.

A pilot study[28] showed that combined arm-leg ergometry with the Cruiser ergometer (Fig. 2), is appropriate to test the cardiorespiratory fitness in persons with a unilateral LLA. The main advantages of the Cruiser ergometer are that persons with a LLA can safely perform the test in a relatively low sitting position with proper back support and with support for the residual limb, while using one leg, both arms and trunk, without external help (e.g. a therapist). The Cruiser ergometer allows a combined cyclic action of the trunk and arms that push and

pull both handles in an synchronous manner, while the sliding seat is pushed and pulled back and forth by the actions of the leg(s), trunk and arms. Persons with a LLA require the use of a balance-securing leg support for the amputated leg that connects to the frame under the seat.



Figure 2. The Cruiser, a combined arm-leg, ergometer with the special purpose leg support.

Gross mechanical efficiency and learning effects

The combined arm-leg movement on the Cruiser ergometer is a different cyclic multi-limb exercise compared with the oftentimes well-trained leg movement on the bicycle ergometer. Most people in the Netherlands are used to cycling. The movement on the Cruiser ergometer is for most people an unknown form of cyclic multi-limb exercise. This implicates that the movement may be subject to natural motor learning, i.e. learning through practice. With natural motor learning in cyclic motor actions, the movement becomes more smooth and efficient, reducing energy cost, while optimizing technique of movement and force production. In learning a (novel) cyclic exercise (e.g. walking, cycling, wheelchair propulsion) the underlying motor learning processes can be

monitored adequately with physiological measures such as energy cost and gross mechanical efficiency (GE) during submaximal exercise intensities[29,30]. Assuming that biological systems inherently seek for optimal motor performance in terms of strain and metabolic costs, novel users of the Cruiser ergometer may be subject to motor learning. They inherently learn to fine-tune the arm trunk and leg movements, force production and muscle activation patterns in timing and co-contraction thus optimizing metabolic costs at a given power output and muscle effort. From that perspective, it is important to understand the physiology of a novel cyclic task, such as Cruiser ergometry, and the motor learning effects in terms of submaximal cardiorespiratory variables, GE and perceived exertion. Submaximal cardiorespiratory variables are heart rate, oxygen input, carbon dioxide output, breathing frequency, ventilation and respiratory exchange rate. The rate of perceived exertion is a psychophysiological outcome that can easily be determined by asking the patient at the end of the exercise test to score their level of exertion on a 10 point Borg scale[31]. The GE is defined as a percentage of external work (work output (W)) performed in relation to the total metabolic production of energy (internal metabolic power produced by the subject) which can be determined during steady state submaximal exercise from the oxygen uptake and respiratory exchange ratio (RER)[32]. Gross mechanical efficiency is indicative of the whole body task efficiency and may help elucidate potential learning or skill requirements. A high efficiency is important in the effective use of limited energy resources in many patient groups and may be helpful in preventing mechanical overuse[33,34]. Gross mechanical efficiency is dependent on the work load, speed, the detailed characteristics of the task (use of arms or legs or both, their rhythm and whether or not the task is simple or complex), the amount of active muscle mass and coordination of the movement, as well as individual training status.

Exercising on the Cruiser is a cyclic exercise, and assumed as a somewhat complex movement, in which arm and leg movement have to act together over time and in repetition. Because of the seemingly complex nature of combined arm-leg movement, it is imaginable to find motor learning effects when the exercise is repeatedly practiced, as is for instance seen in manual wheelchair studies[29,35-37]. For the Cruiser ergometer it has not been tested yet whether or not learning effects are prominent when exercising on it. One-legged Cruiser exercise is expected to be more complicated than two-legged exercise, due to stability issues and a lower muscle mass involved. As such a lower GE and

higher physical strain are expected in one-legged Cruiser exercise compared to two-legged exercise at the same external power output and speed.

Cardiopulmonary exercise testing and exercise prescription

The Cruiser ergometer can potentially be used both as a training as well as an exercise testing device. However, a suitable test protocol for the Cruiser ergometer to measure the peak aerobic capacity in persons with a LLA is up to now not available. Also no publications are available about the optimal practice or training dose for Cruiser ergometry during rehabilitation after a LLA.
Clinical cardiopulmonary exercise testing protocols for leg ergometry are used for evaluation of exercise intolerance and exercise-related symptoms and for measuring the peak aerobic capacity[16]. With these results the optimal individual training dose can be defined. This can be related to a percentage of maximal exercise capacity or maximal heart rate or linked to the concept of the so-called lactate threshold[38]. For instance, the three-phase model of lactic acid accumulation with two ventilatory thresholds can be used for exercise prescription[39]. There are many names for these thresholds. The most commonly used semantics are anaerobic threshold and respiratory compensation point (Wasserman) or first (VT1) and second (VT2) ventilatory threshold[39]. We prefer in this thesis the VT1 and VT2. The level of the ventilatory thresholds is age, exercise modality, and protocol specific[16]. The VT1 and VT2 increase with age when expressed as percentage (%) of VO_2max predicted. Arm exercise results in lower ventilatory thresholds compared to leg exercise and bicycle ergometry results in lower (5-11%) values versus treadmill exercise[16]. The determination of the VT1 and VT2 is also protocol specific, while the best protocol to reach the peak exercise capacity within 10-12 minutes has to be individually chosen. The determination of the VT1 and VT2 is helpful as an indicator of level of fitness, for safe and efficient exercise prescription, and to monitor the effect of physical training[38]. When using the Cruiser ergometer for exercise testing in persons with a LLA, it is important that evaluation of undiagnosed exercise intolerance, exercise-related symptoms and determination of peak aerobic capacity is possible in a feasible, safe, reliable and valid way. In addition, with the results of the exercise test, individual prescription of the optimal training dose during the rehabilitation program after a LLA should be possible.

Aims of the thesis

The general aim of this thesis is to determine whether the Cruiser ergometer is clinically applicable as an instrument for cardiopulmonary exercise testing in persons with a LLA.

In this respect, the sub-aims of this thesis are:

- To compare and understand the physiology of submaximal cyclic exercise on the Cruiser ergometer, regular cycling and treadmill handcycling on cardiorespiratory variables, gross mechanical efficiency (GE) and perceived exertion in healthy persons.
- To study potential motor learning effects during low-intensity submaximal steady state one-legged and two-legged practice on the Cruiser in healthy persons with respect to GE and cardiorespiratory strain.
- To establish the repeatability and validity of peak exercise testing on the Cruiser ergometer in a population of healthy persons.
- To determine the feasibility, safety, and reliability of (sub)maximal exercise testing on the Cruiser ergometer in a study population with a LLA.
- To determine the inter-observer and intra-observer reliability of the first (VT1) and second (VT2) ventilatory thresholds in subjects with a unilateral LLA and healthy subjects during a peak exercise test on the Cruiser ergometer.

Based on the outcomes of this thesis, future work is intended to lead to the development of an elaborated exercise test protocol for persons with a LLA using the Cruiser ergometer. In addition, in future, based on an individual exercise prescription for persons with a LLA , Cruiser ergometer-based training programs will be developed to improve the physical fitness during and after rehabilitation.

Thesis outline

In **chapter 2** the GE, cardiometabolic strain and perceived exertion of low-intensity Cruiser ergometer exercise is described and compared with leg cycling and hand cycling. Ten healthy men and 12 healthy women enrolled in four discontinuous submaximal graded exercise tests on respectively the Cruiser ergometer, a bicycle ergometer, a handbike on a motor driven treadmill and again the Cruiser ergometer.

In **chapter 3** we explored in a low-intensity practice study among healthy individuals whether differences exist in cardiorespiratory variables and GE comparing one-legged and two-legged exercise on the Cruiser ergometer and whether motor learning occurs over time.

In **chapter 4**, the repeatability and validity of peak exercise testing on the Cruiser ergometer was established. Thirty healthy volunteers carried out three incremental exercise tests, once on the bicycle ergometer and twice on the Cruiser ergometer. The repeatability of the Cruiser ergometer peak exercise test was assessed by studying the mean values of the test-retest and the validity by studying the mean values of the bicycle and the two repeated Cruiser ergometer tests.

In **chapter 5** the feasibility, safety, and reliability of (sub)maximal exercise testing on the Cruiser ergometer was established. Seventeen persons with a LLA performed one submaximal exercise test and three maximal exercise tests on the Cruiser ergometer.

In **chapter 6** the inter-observer and intra-observer reliability of determining the ventilatory thresholds in subjects with a LLA and healthy subjects during a peak exercise test on Cruiser ergometer were described. Two observers determined two ventilatory thresholds of the exercise tests performed in the studies described in chapters 4 and 5.

In **chapter 7** the main findings of the previous chapters are recapitulated and discussed. Based on the information deduced from the reported studies, future research recommendations are formulated. Finally, recommendations are provided for a protocol for persons with a LLA for an exercise test on a Cruiser ergometer in rehabilitation practice.

References

1. Moxey PW, Gogalniceanu P, Hinchliffe RJ, Loftus IM, Jones KJ, Thompson MM, et al. Lower extremity amputations--a review of global variability in incidence. Diabet Med 2011;28(10):1144-1153.
2. Dillingham TR, Pezzin LE, MacKenzie EJ. Limb amputation and limb deficiency: epidemiology and recent trends in the United States. South Med J 2002;95(8):875-883.
3. Unwin N. Epidemiology of lower extremity amputation in centres in Europe, North America and East Asia. Br J Surg 2000;87(3):328-337.
4. Fard B, Dijkstra PU, Stewart RE, Geertzen JHB. Incidence rates of dysvascular lower extremity amputation changes in Northern Netherlands: A comparison of three cohorts of 1991-1992, 2003-2004 and 2012-2013. PLoS One 2018;13(9):e0204623.
5. Chin T, Sawamura S, Fujita H, Nakajima S, Ojima I, Oyabu H, et al. The efficacy of the one-leg cycling test for determining the anaerobic threshold (AT) of lower limb amputees. Prosthet Orthot Int 1997;21(2):141-146.
6. Chin T, Sawamura S, Fujita H, Ojima I, Oyabu H, Nagakura Y, et al. %VO2max as an indicator of prosthetic rehabilitation outcome after dysvascular amputation. Prosthet Orthot Int 2002;26(1):44-49.
7. Davidoff GN, Lampman RM, Westbury L, Deron J, Finestone HM, Islam S. Exercise testing and training of persons with dysvascular amputation: safety and efficacy of arm ergometry. Arch Phys Med Rehabil 1992;73(4):334-338.
8. Saltin B, Blomqvist G, Mitchell JH, Johnson RL,Jr, Wildenthal K, Chapman CB. Response to exercise after bed rest and after training. Circulation 1968;38(5 Suppl):VII1-78.
9. Remes L, Isoaho R, Vahlberg T, Hiekkanen H, Korhonen K, Viitanen M, et al. Major lower extremity amputation in elderly patients with peripheral arterial disease: incidence and survival rates. Aging Clin Exp Res 2008;20(5):385-393.
10. Xu J, Kohler F, Dickson H. Systematic review of concepts measured in individuals with lower limb amputation using the International Classification of Functioning, Disability and Health as a reference. Prosthet Orthot Int 2011;35(3):262-268.
11. World Health Organization. The International Classification of Functioning, Disability and Health. Geneva: WHO; 2001.
12. Roepke AM, Williams RM, Turner AP, Henderson AW, Norvell DC, Henson H, et al. A Longitudinal Study of Social Participation After Dysvascular Lower Extremity Amputation. Am J Phys Med Rehabil 2017;96(10):741-747.
13. American College of Sports Medicine. ACSM Guidelines for Exercise Testing. Chapter 1.Benefits and Risks Associated with Physical Activity. ninth edition ed.: Wolter Kluwer / Lippincot Williams & Wilkins; Philadelphia, United States of America 2014.
14. Wezenberg D, Dekker R, van Dijk F, Faber W, van der Woude L, Houdijk H. Cardiorespiratory fitness and physical strain during prosthetic rehabilitation after lower limb amputation. Prosthet Orthot Int 2019;43(4):418-425.
15. van Schaik L, Geertzen JHB, Dijkstra PU, Dekker R. Metabolic costs of activities of daily living in persons with a lower limb amputation: A systematic review and meta-analysis. PLoS One 2019;14(3):e0213256.

16. American Thoracic Society, American College of Chest Physicians. ATS/ACCP Statement on cardiopulmonary exercise testing. Am J Respir Crit Care Med 2003;167(2):211-277.
17. Smith AE, Evans H, Parfitt G, Eston R, Ferrar K. Submaximal Exercise-Based Equations to Predict Maximal Oxygen Uptake in Older Adults: A Systematic Review. Arch Phys Med Rehabil 2016;97(6):1003-1012.
18. Kurdibaylo SF. Cardiorespiratory status and movement capabilities in adults with limb amputation. J Rehabil Res Dev 1994;31(3):222-235.
19. Fletcher GF, Lloyd A, Waling JF, Fletcher BJ. Exercise testing in patients with musculoskeletal handicaps. Arch Phys Med Rehabil 1988;69(2):123-127.
20. van Velzen JM, van Bennekom CA, Polomski W, Slootman JR, van der Woude, L H, Houdijk H. Physical capacity and walking ability after lower limb amputation: a systematic review. Clin Rehabil 2006;20(11):999-1016.
21. van Alste JA, Cruts HE, Huisman K, de Vries J. Exercise testing of leg amputees and the result of prosthetic training. Int Rehabil Med 1985;7(3):93-98.
22. Cruts HE, de Vries J, Zilvold G, Huisman K, van Alste JA, Boom HB. Lower extremity amputees with peripheral vascular disease: graded exercise testing and results of prosthetic training. Arch Phys Med Rehabil 1987;68(1):14-19.
23. Finestone HM, Lampman RM, Davidoff GN, Westbury L, Islam S, Schultz JS. Arm ergometry exercise testing in patients with dysvascular amputations. Arch Phys Med Rehabil 1991;72(1):15-19.
24. Bar-Or O, Zwiren LD. Maximal oxygen consumption test during arm exercise--reliability and validity. J Appl Physiol 1975;38(3):424-426.
25. Vokac Z, Bell H, Bautz-Holter E, Rodahl K. Oxygen uptake/heart rate relationship in leg and arm exercise, sitting and standing. J Appl Physiol 1975;39(1):54-59.
26. Casaburi R, Barstow TJ, Robinson T, Wasserman K. Dynamic and steady-state ventilatory and gas exchange responses to arm exercise. Med Sci Sports Exerc 1992;24(12):1365-1374.
27. Wezenberg D, de Haan A, van der Woude, L H, Houdijk H. Feasibility and validity of a graded one-legged cycle exercise test to determine peak aerobic capacity in older people with a lower-limb amputation. Phys Ther 2012;92(2):329-338.
28. Vestering MM, Schoppen T, Dekker R, Wempe J, Geertzen JH. Development of an exercise testing protocol for patients with a lower limb amputation: results of a pilot study. Int J Rehabil Res 2005;28(3):237-244.
29. Sparrow WA, Newell KM. Energy expenditure and motor performance relationships in humans learning a motor task. Psychophysiology 1994;31(4):338-346.
30. Almasbakk B, Whiting HT, Helgerud J. The efficient learner. Biol Cybern 2001;84(2):75-83.
31. Borg GA. Psychophysical bases of perceived exertion. Med Sci Sports Exerc 1982;14(5):377-381.
32. Powers, S., Howley, E. Exercise Physiology. Theory and Application to Fitness and Performance. sixth edition ed.: McGraw-Hill; 2007.
33. Klute GK, Kallfelz CF, Czerniecki JM. Mechanical properties of prosthetic limbs: adapt-

ing to the patient. J Rehabil Res Dev 2001;38(3):299-307.
34. Jain NB, Higgins LD, Katz JN, Garshick E. Association of shoulder pain with the use of mobility devices in persons with chronic spinal cord injury. PM R 2010;2(10):896-900.
35. De Groot S, Veeger DH, Hollander AP, Van der Woude, L. H. Wheelchair propulsion technique and mechanical efficiency after 3 wk of practice. Med Sci Sports Exerc 2002;34(5):756-766.
36. de Groot S, Veeger HE, Hollander AP, van der Woude, L. H. Adaptations in physiology and propulsion techniques during the initial phase of learning manual wheelchair propulsion. Am J Phys Med Rehabil 2003;82(7):504-510.
37. de Groot S, Veeger HE, Hollander AP, van der Woude, L. H. Short-term adaptations in co-ordination during the initial phase of learning manual wheelchair propulsion. J Electromyogr Kinesiol 2003;13(3):217-228.
38. Mann T, Lamberts RP, Lambert MI. Methods of prescribing relative exercise intensity: physiological and practical considerations. Sports Med 2013;43(7):613-625.
39. Binder RK, Wonisch M, Corra U, Cohen-Solal A, Vanhees L, Saner H, et al. Methodological approach to the first and second lactate threshold in incremental cardiopulmonary exercise testing. Eur J Cardiovasc Prev Rehabil 2008;15(6):726-734.



2

Gross Mechanical Efficiency of the combined arm-leg (Cruiser) ergometer: a comparison to the bicycle ergometer and handbike

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Abstract

The combined arm–leg (Cruiser) ergometer is assumed to be a relevant testing and training instrument in the rehabilitation of patients with a lower limb amputation. The efficiency and submaximal strain have not been established and thus cannot be compared with alternative common modes of exercise. A total of 22 healthy able-bodied men (n=10) and women (n=12) were enrolled in four discontinuous submaximal graded exercise tests. Each test consisted of seven bouts of 3 min exercise ranging from 20 to 45W and was performed on, respectively, the Cruiser ergometer, a bicycle ergometer, a handbike, and again the Cruiser ergometer. Cardiorespiratory parameters were measured and rate of perceived exertion was determined. Gross mechanical efficiency (GE) was determined from power output and submaximal steady-state energy cost. Repeated-measures analysis of variance ($P<0.05$) was used to evaluate the effects of exercise mode, exercise intensity, ad sex. No differences in GE and cardiorespiratory strain were found between both Cruiser tests (GE 45W: men 13.0%, women 15.0%) and the bicycle test (GE 45W: men 13.2%, women 14.6%). GEs of handbiking (45W: men 11.2%, women 12.2%) were lower compared with the Cruiser and bicycle test results, whereas cardiorespiratory strain in handbiking was consistently higher. Apart from a lower rate of perceived exertion at the second Cruiser test, no differences were found between the repeated Cruiser tests. It can be concluded that GE and cardiorespiratory strain in submaximal Cruiser exercise are comparable with leg cycling, the repeatability was good, and no obvious learning effects were observed. The results of this study form a base for further research in patients with a lower limb amputation.

Keywords: ergometry, exercise testing, gross mechanical efficiency, lower limb amputation, physical strain, rehabilitation, submaximal exercise.

Introduction

Patients with a lower limb amputation (LLA) experience a decline in physical fitness and higher relative and absolute energy costs during walking[1]. Evidence from Chin et al.[2] suggests that when prosthetic rehabilitation only covers walking with prosthesis, maximal aerobic capacity of patients with a LLA does not improve to the level of able-bodied persons. Therefore, training in prosthetic walking should be accompanied by some forms of endurance exercise training. Before commencing training, an appropriate maximal exercise test is required to determine individual work capacity[3]. At present, different types of ergometers and modes of exercise are available for exercise testing and training in rehabilitation: treadmill walking, wheeling and handbiking, bicycle ergometry, arm-ergometry and combined arm-leg ergometry. Treadmill walking and bicycle ergometry cannot be used in patients with a lower limb amputation without prosthesis or without assistance and are therefore not useful for training and testing in the early phase of rehabilitation when the patient does not have prosthesis yet. When using arm-ergometry for training or exercise testing, the considerably lower muscle mass of the upper body is involved and the VO_2 peak will be lower compared to leg exercise tests. The Cruiser ergometer (Enraf-Nonius[4] , Fig.1) might provide the ideal alternative, as it combines cyclic arm and leg exercise in the sitting posture. In the early stage, the residual limb can be securely positioned on a special support for the stump, whereas in a later stage the prosthetic leg can be actively involved. The main advantage of the Cruiser ergometer is the safe and comfortable exercise of a large muscle mass in early rehabilitation. Furthermore, the Cruiser ergometer has been shown a reliable and valid instrument to measure the peak oxygen uptake in healthy individuals during an incremental exercise test[5]. In a previous pilot study Vestering et al.[6] also concluded that peak exercise on the Cruiser ergometer led to a higher load on the cardiovascular and respiratory system compared to arm-ergometry in patients with a LLA.



Figure 1: The Cruiser ergometer, a combined arm-leg ergometer.

Apart from its suitability as a testing device, it is currently not known whether the Cruiser ergometer is a suitable training device for patients with a LLA. The exercise on the Cruiser ergometer seems a somewhat complex combined cyclic action of legs and arms that may require a learning period and may initially be slightly less efficient compared to the more common cycling mode. Therefore, before using the Cruiser ergometer as training device, it is important to know the submaximal physical strain, perceived exertion (RPE) and Gross Mechanical Efficiency (GE) of the Cruiser ergometer in comparison to common exercise cyclic exercise modes, as well as its repeatability[7,8].

Exercise on the Cruiser ergometer combines elements of cyclic upper and lower body exercise, such as handbiking, wheeling, rowing and cycling. The optimal values of GE of these exercise forms in literature are in the range of 10-20%, for example, handbiking 6-13%, wheeling 10%, rowing 17-19% and cycling 20% [9,10,11,12] and have been found to be dependent on work load, speed, task, amount of active muscle mass, coordination of the movement and temperature[3,13,14]. We expect to find a GE for the Cruiser ergometer in a similar range[15]. GE is an important measure, because it can be used to evaluate training as well as motor learning effects. Because of the complexity of a combined arm-leg movement, it is imaginable to find small learning effects when the exercise is repeated[16,17.]. When using the Cruiser ergometer as a testing and training instrument it is important to know whether there is a motor learning effect in the movement on the Cruiser ergometer.

Submaximal strain and GE are expected to be different between men and women. It is known that resting oxygen consumption is greater in men than in woman but also that absolute oxygen consumption on the bicycle ergometer is higher in men than in woman[18]. Therefore both men and woman participated in this study.

In the current study, the main goal was to determine the GE, submaximal cardio-respiratory strain and subjective strain in healthy able-bodied men and women during standardized submaximal Cruiser exercise in comparison to exercise on a bicycle ergometer and handbike. In addition the repeatability and motor learning aspects of Cruiser exercise were evaluated.

Methods

Participants

A total of 22 healthy participants (10 men and 12 women) were enrolled in the present study (Table 1). Exclusion criteria for participating in this study were as follows: age less than 18 years, a body mass index of more than 30, neuro-musculoskeletal disorders or complaints that could have affected the test, evidence or serious suspicion of cardiovascular diseases, stress or exercise related pain in the chest, pulmonary diseases, viral or bacterial infection for less than 10 days and use of medication for cardiopulmonary diseases[3]. The inclusion and exclusion was screened using the Physical Activity Readiness Questionnaire (PARQ)[19,20]. All participants signed an Informed Consent and all tests were conducted in accordance with the Declaration of Helsinki. The local Ethics Board of the Center for Human Movement Sciences (UMCG) approved the current experiment.

Procedure and design

All participants performed four discontinuous submaximal steady state exercise tests on four separate days. The four tests were conducted at the same time of the day for each individual, with intervals of approximately one week between subsequent tests. All participants were asked to refrain from stimulants (caffeine, drugs, cigarettes, etc.), exercise and alcohol for at least 12 hours before testing. Each person was asked to have a light breakfast/lunch at least two hours before

the exercise test, and normal hydration was requested. Before testing personal characteristics were determined (Table 1).

Table 1 Personal characteristics (mean and SD)

	Age (y)	Body height (m)	Body mass (kg)
Men (n=10)	24.0 (1.8)	1.86 (0.07)	79.0 (10.5)
Women (n=12)	22.1 (2.4)	1.72 (0.06)	65.8 (10.2)

All tests started with three minutes sitting on the Cruiser ergometer, bicycle ergometer or handbike in order to obtain a baseline. Each exercise test consisted of seven (20W, 25W, 30W, 35W, 40W, 45W and again 20W) three minutes submaximal exercise bouts. The different cardio-respiratory measures: oxygen consumption (VO_2 (ml/ min)), carbon dioxide output (VCO_2 (ml/min)), breathing frequency (BF (breaths/min)), maximal ventilation (VE (l/min)), respiratory exchange rate (RER) and heart rate (HR (beats/minute)) were measured during the last 30 seconds of each of the 7 submaximal exercise bouts. Between each two bouts, the participant had a 30 seconds rest period in which the rate of perceived exertion (RPE) was determined on a ten points Borg scale[21]. In each new exercise bout the external work load was increased from zero to the desired work load, within ~5s.

The four exercise tests were conducted on the Cruiser ergometer (Fig 1), bicycle ergometer, the handbike exercise test on a motor driven treadmill and again the Cruiser test in the same sequence for all participants. The second submaximal exercise test on the Cruiser ergometer served to determine its repeatability as well as potential motor learning effects over time.

Instruments & exercise modes

Cruiser ergometer

The Cruiser ergometer[4] (Fig 1; Enraf Nonius, Delft, the Netherlands, 2011) is a combined arm-leg ergometer equipped with a comfortable seat. The feet are placed against a non-moving yet adjustable footrest. The footrest is used to push off; this makes the seat move backwards. The participant moves the seat forward again by pulling the handlebars with the arms. In this way, the arms and legs are used simultaneously to provide power output to the ergometer. The

resisting load of the ergometer was gradually increased manually. The ergometer was set to operate at the constant power between 35 and 60 revolutions per minute (rpm). Participants were instructed to exercise at 50 rpm. The footrest was adjusted to the individual body height and was fixed for the two Cruiser tests. The accuracy of the Cruiser ergometer for the power output is ± 10 % and for speed ±2 rpm[4].

Bicycle ergometer

The incremental submaximal bicycle exercise test was conducted on an electronically braked bicycle ergometer (Lode Excalibur, Ergo-line, Groningen, The Netherlands). The participants were instructed to cycle at 50rpm. Saddle and steer position were individually adjusted.

Handbike

The incremental submaximal handbike exercise test was conducted on a motor driven treadmill (1.25m x 3.00m, Enraf Nonius, Delft, The Netherlands). The attach-unit handbike (mass 25kg; front wheel diameter: 20.9 inch; tire pressure: 8 bar, 800 kPA) consisted of a hand rim wheelchair (Double Performance, RGK Wheelchair Inc., Staffordshire, UK) and Tracker Challenger, a synchronous arm crank unit (Alois Praschberger, Niederndorf, Austria). The gear was held constant during the entire handbike exercise test so that a rpm of 50 was reached at a treadmill belt speed of 5 km/h (=1.39 m/s). During the exercise test the required load was determined using a Powertap (Powertap SL; CycleOps, Saris Cycling Group inc., Fitchburg, Wisconsin, US; sample frequency: 0.2Hz; reliability: ±1.5% between 0 and 1999 W) in the hub of the front wheel and by the use of a pulley system.

The pulley system (Fig. 2) was used to increase the workload during the exercise test on the handbike, on the basis of the individual powertap readings[22]. The load could be gradually increased by adding mass to the pulley system according to the following formula: PO = (m x g) x v. For instance to increase the load (PO) with 5 W at a velocity of v = 1.39 m/s a mass of m = 0.367 kg was added.

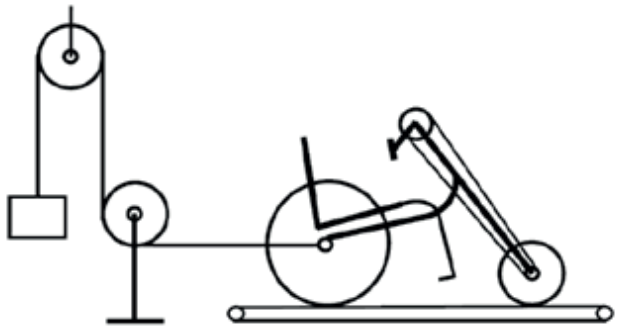

Figure 2: Pulley system used for regulation of power output level during the handbike exercise test on the motor-driven treadmill

Outcome variables

The Oxycon Delta (Jaeger, Bunnik, The Netherlands) was set to measure breath-by-breath the cardio-respiratory parameters (VO_2, VCO_2, BF, VE and RER). The gas analyzer was calibrated for volume every session with a 3-l-syringe (Jaeger). Room air and a standard gas mixture of 18% O_2 and 5.0% CO_2 were used to calibrate the sensors. Heart rate was measured by a Polar heart rate monitor (Polar Transmitter Chest Strap, type T34, Polar Electro Nederland bv, Almere, The Netherlands). The metabolic power (P_{met}) was calculated using: P_{met}(W)=VO2 [(4.940RER+16040)/60][23]. The measured mechanical power output (P_O) divided by the calculated P_{met} defined GE (%).

Statistical analysis

A repeated-measures analysis of varince ($P<0.05$) was performed for each outcome measure to determine main effects between exercise modes (the Cruiser ergometer, bicycle ergometer and handbike). Exercise intensity (power output) was a within-participant factor, sex a between-participant factor.

A repeated-measures analysis of variance ($P< 0.05$) was also carried out on all outcomes for the Cruiser ergometer pretests and post-tests. Pretests and post-tests and exercise intensity were the within-participant factors and sex was again the between-participant factor. The differences in the RPE Borg-scores were assessed by the Wilcoxon signed rank test. A Bonferroni correction was applied in the posthoc testing to control for α inflation.

Results

All 22 participants successfully concluded the study. RER was well below 1.0 in most tests, with the exception of the handbike test, where in the higher workloads for the female participants RER was slightly above 1.0. For those instances, energy cost and efficiencies were calculated using an RER value of 1.0.

Three different exercise modes

No differences in GE or cardio-respiratory strain (apart from BF $P<0.025$) were found between both Cruiser tests (mean GE: 13.0 and 15.0% for men and women at 45 W) and the bicycle test (mean GE: 13.2 and 14.6% for men and women at 45 W) (Fig. 3a-d). GE's of the handbike test (mean:11.2 and 12.2% for men and women at 45 W) were significantly lower and cardio-respiratory strain was significantly higher compared to the Cruiser and bicycle tests. As expected, the GE increased throughout the test as external work was increased for all exercise modes (Fig. 3a). Similar main effects of power output were evidently found for the cardio-respiratory outcomes. Considering the RPE at 45W, all participants found the handbike test (RPE of ~3.0) significantly more exerting than the bicycle and Cruiser tests (both RPE of ~2.0).

Cruiser test-retest

When comparing the GE and cardio-respiratory outcomes [apart from a single difference for RER at 20 W (P= 0,041)] (Fig 3a) of the first and second Cruiser test, no differences were found (range $0.151 > P < 0.888$). Remarkably, RPE scores were lower for the second Cruiser test compared to the first test ($P < 0.001$ for all output levels).

Sex

For men and women some small differences in GE can be noted (Fig. 3a). On all four modes and levels of power output, women were more efficient than men ($P=0.003$) and VO_2 scores were significantly higher in men ($P=0.005$, Fig. 3c). However, HR (Fig. 3b) and BF (Fig. 3d) of men were lower than that of women. In the resting phase before starting the exercise test VO_2 was lower for women than for men for all modes. The VO_2 scores in this relative rest condition before the start of the second Cruiser test was 393.0±72.9 ml/min for men and 327.8±90.9 ml/min for women (Fig 4).

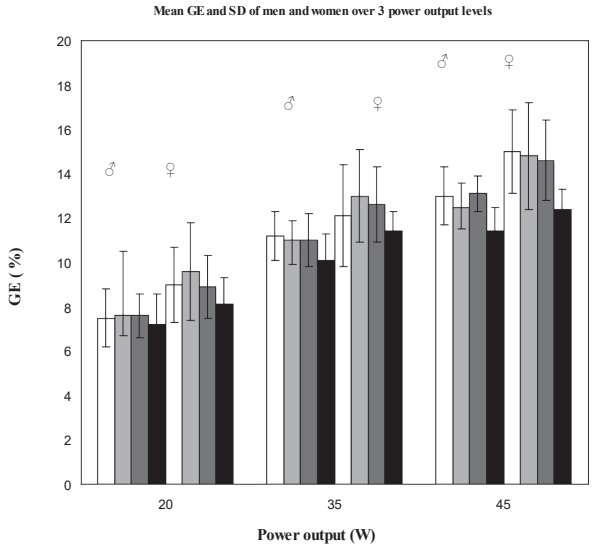

Figure 3a

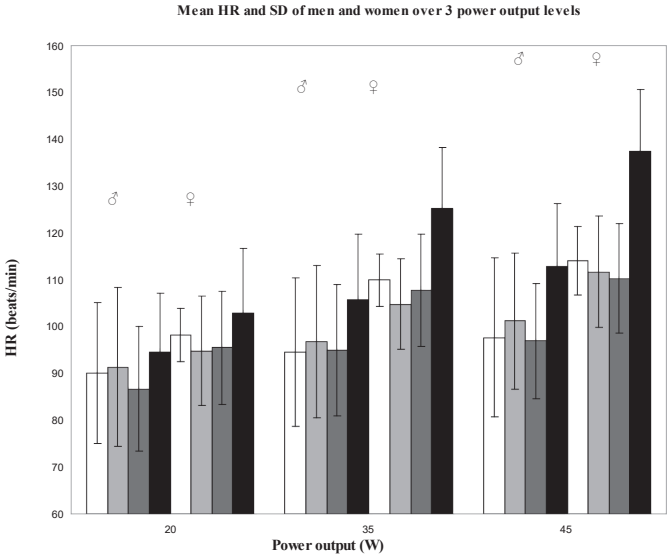

Figure 3b

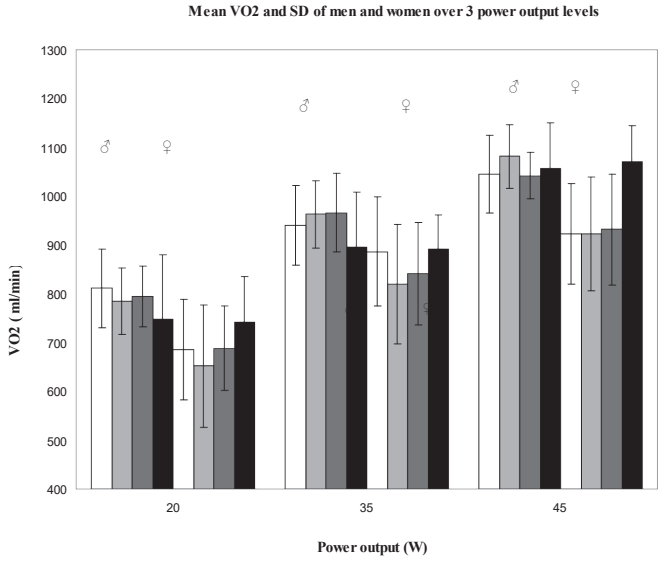

Figure 3c

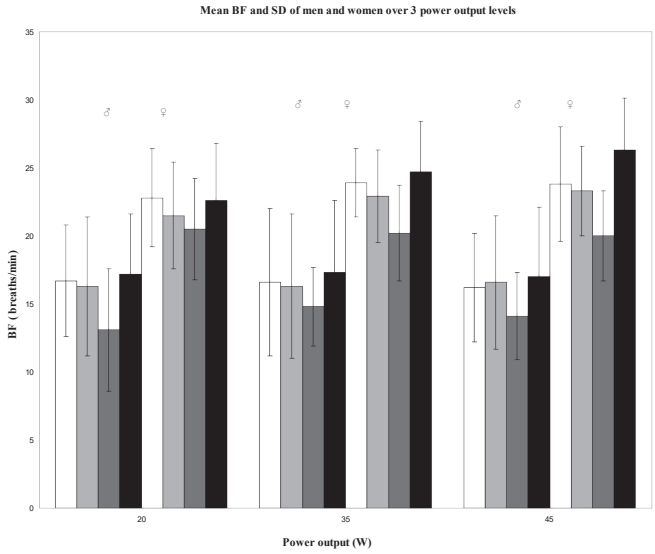

Figure 3d

Figure 3a-d: Representation of Gross mechanical efficiency (GE; a), Heart rate (HR; b), Oxygen uptake (VO_2 ; c) and Breathing freuency (BF; d) (mean ± SD) for men (n= 10; ♂) and women (n= 12; ♀) over 3 different output levels (20, 35 and 45 W) and the three different exercise modes Cruiser pre-test (white) and post-test (light grey), Bicycle test (dark grey) and Handbike test (black). All values were determined during the last 30 seconds of every 3 min submaximal exercise bout

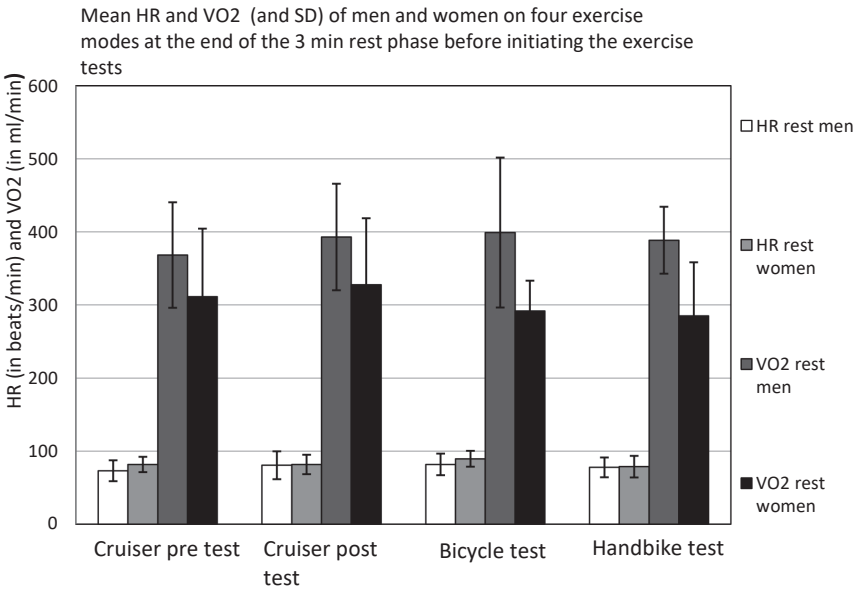

Figure 4: Representation of heart rate (HR) and Oxygen uptake (VO_2) for males(n=10) and females (n=12) at the end of the resting phase and prior to the start of submaximal exercise test in each of the three different modes. All values were determined during the last 30 seconds of the resting phase

Discussion

This study shows that under the current experimental conditions and in the able-bodied participants, cardio-respiratory strain and GE during Cruiser ergometry are similar to exercising on a bicycle ergometer at the same range of power outputs (20-45 W). Handbiking at these power outputs is, however less efficient and more straining than Cruiser and bicycle ergometry. The repeatability of Cruiser ergometry was good and no learning effects were observed, other than a lower RPE on the second test. Finally, distinct differences in GE were observed between men and women in GE and cardio-respiratory strain at this range of submaximal power outputs.

Three different exercise modes; differences and relevance

The intermittent combination of leg and arm exercise generates a similar GE and strain with the Cruiser ergometer as the continued alternating movement of the legs in cycling. The movement on the Cruiser ergometer seems more complex than that for Dutch people well trained in cycling movement. However, both arms and legs, and thereby more muscle mass, can be used during Cruiser exercise. This is a beneficial characteristic of the Cruiser ergometer, in addition to its safe and sitting form of exercise, which can also be performed with one leg. Exercise with the upper body only (handbike) produces a higher strain and lower efficiency[9]. The present study underlined these findings, and as expected, Cruiser ergometry was more efficient than handcycling. An efficiency comparable to that of cycling was shown.

To initiate and continue moving on the Cruiser ergometer the extensor muscles of the upper legs are used to push the participant (and Cruiser seat) backwards. This is beneficial with an amputation because the extensor muscles represent a huge percentage of the active muscle tissue in the upper leg. Ogata and Yano[24] have shown that if the leg muscles are more active during the exercise, the movement is more efficient. In the study of Simmelink et et al.[5], the maximal work load on the Cruiser ergometer was about 200W for healthy individuals. In the current study, seven bouts of 3 min exercise between 20 and 45W were performed by all the participants. This mild exercise level was chosen because patients with a LLA experience a decline in physical fitness because of inactivity and comorbidity. Especially in the period just after the amputation, low intensity

exercise is necessary to prevent further deconditioning and start reconditioning. The Cruiser ergometer seems to be a suitable training instrument in this early period of rehabilitation.

The exercise intensity of cycling in this study is relatively low compared with most cycling studies focusing on solely cycling performance. In the literature, it can be found that GE improves at higher work rates[25], which explains why the values for GE in the present study (~14% at 45 W; ~8% at 20 W) are relatively low compared with the values presented in the literature (up to 20% at higher exercise intensities more relevant to cycling). The relative proportion of energy required for basal metabolism is relatively higher at the lower exercising intensities, leading to a lower GE[25]. Ambient temperature might be another important factor influencing GE[13]. However, the present study was carried out in a climate-controlled laboratory keeping exercise conditions the same throughout all testing; thus, we do not expect that this would have affected our results.

Cruiser ergometer: repeatability and motor learning

Motor learning is often a crucial element in rehabilitation. Novice motor tasks (i.e. wheelchair propulsion and prosthetic walking) often require an extensive motor learning process. In previous research in healthy individuals, significant motor learning effects in wheelchair propulsion emerged after training, expressed in GE and parameters for the propulsion technique[26,27,28]. Although it was expected that exercising on the Cruiser ergometer is a fairly complex and unusual movement, no differences were found between the two Cruiser tests on the seven different power output levels for efficiency and most of the cardiorespiratory outcomes (except for a single RER value and the RPE), indicating that motor learning at these power output levels is short and not a dominant process. Indeed, the Cruiser ergometer seems to be a repeatable instrument at submaximal exercise levels in the healthy population and lower range of power output. The RPE results, initially being higher during Cruiser ergometry, suggest that with a brief practice (seven bouts of exercise of the pretest), exercising on the Cruiser ergometer becomes easier (indicated with the lower RPEs on the post-test). This must be taken into consideration when using the Cruiser ergometer as a testing instrument in patients who have not used the Cruiser ergometer before. To finally evaluate any potential motor learning elements in Cruiser ergometry, it is advised to replicate the work of De Groot et al.[26] and Vegter et al.[28] and systematically monitor the effects of low-intensity practice on the Cruiser ergometer.

Sex

In this study, it was found that women were seemingly more efficient on the Cruiser ergometer, bicycle ergometer, and handbike compared with men at these submaximal absolute power output levels (Fig. 3a). Men showed a higher VO_2 compared with women (Figs. 3c and 4). Also, the VO_2 scores in rest for the second Cruiser test were higher for men, 393.0 ± 72.9 ml/min, compared with women, 327.8 ± 90.9 ml/min (Fig. 4). In agreement with these findings, Toth et al.[18] found that resting oxygen consumption was greater ($P < 0.01$) in men (233 ± 23 ml/min) than in women (190 ± 21 ml/min). The VO_2 resting scores in our study are somewhat higher than those in the study of Toth et al.[18] because these values were obtained just before the start of exercise and therefore the participants in our study were not completely relaxing. Yet, the results from Fig. 4 are indicative for a higher resting metabolism in men. Absolute oxygen consumption in the study of Toth et al.[18] was higher in men at 10 ($P <0.05$), 20 ($P < 0.01$), and 30 min ($P < 0.01$) of exercise on a bicycle ergometer. The lower GE in men in the current study at the current levels of power output may therefore be explained by their higher resting metabolism. In addition, another aspect may be that the absolute power output levels in the submaximal tests are relatively higher for the female participants than for the male participants as men can reach higher peak power outputs compared with women[29,30,31].

Recommendations for future research

In this study, only healthy, relatively young, able-bodied individuals participated because they were able to perform the exercise test on these three different ergometers. These results provide a reference base to compare with future results in patients with a LLA of various fitness levels or other rehabilitation populations. Now, future studies can aim to collect data from LLA patients. Before extensively starting to train and test patients with a LLA on the Cruiser ergometer, it is advised that a group of healthy older individuals should be tested, more or less of similar age and physical fitness to patients with an LLA and in the one-leg and two-leg mode. For the current study population we did not need ECG and blood pressure monitoring for the submaximal exercise. To maintain safety throughout training and testing in older vascular amputees, ECG and blood pressure monitoring must be added as variables to the training and testing protocol.

When the participants exercised on the Cruiser ergometer with two arms and two legs, GE was the same as GE on the bicycle ergometer. Further research is necessary to explore whether this will be the same in patients with a unilateral LLA when exercising on the Cruiser ergometer with one leg and two arms. When the GE of exercising on the Cruiser with two arms and one leg is known, protocols for the Cruiser ergometer as a training instrument used by patients with an LLA can be formulated.

Conclusion

In the present study, it was shown that GE and physical strain in submaximal exercise on the Cruiser ergometer were comparable with cycling exercise. The repeatability of Cruiser ergometry was good and no learning effects were observed, other than a lower RPE on the second test. The advantage for patients with an LLA of the Cruiser ergometer is the safe and comfortable exercise that is possible without prosthesis with one leg and two arms. This is the first study in which GE of the Cruiser ergometer has been described. Further research is necessary to describe training and testing protocols for the Cruiser ergometer in patients with a LLA. The results from this study in a nondisabled population represent a suitable reference base for patients with a LLA.

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References

1. Van Velzen JM, van Bennekom CA, Polomski W, Slootman JR, van der Woude LH, Houdijk H. Physical capacity and walking ability after lower limb amputation: a systematic review. Clin Rehabil 2006; 20:999–1016.
2. Chin T, Sawamura S, Fujita H, Ojima I, Oyabu H, Nagakura Y, et al. % VO_2max as an indicator of prosthetic rehabilitation outcome after dysvascular amputation. Prosthet Orthot Int 2002; 26:44–49.
3. Fletcher GF, Balady GJ, Amsterdam EA, Chaitman B, Eckel R, Fleg J, et al. (2001). Exercise standards for testing and training: a statement for healthcare professionals from the American Heart Association. Circulation 2001; 104:1694–1740.
4. Enraf-Nonius, Delft, The Netherlands: Operating Instructions Cruiser 2011. Available at: http://www.enrafnonius.nl/index.php?option = com_doc man&task =search_result& Itemid = 61 (No longer available).
5. Simmelink EK, Wempe JB, Geertzen JH, Dekker R Repeatability and validity of the combined arm–leg (Cruiser) ergometer. Int J Rehabil Res 2009; 32:324–330.
6. Vestering MM, Schoppen T, Dekker R, Wempe J, Geertzen JH (2005). Development of an exercise testing protocol for patients with a lower limb amputation: results of a pilot study. Int J Rehabil Res 2005**;**28:237–244.
7. Klute GK, Kallfelz CF, Czerniecki JM. Mechanical properties of prosthetic limbs: adapting to the patient. J Rehabil Res Dev 2001; 38:299–307.
8. Jain NB, Higgins LD, Katz JN, Garshick E. Association of shoulder pain with the use of mobility devices in persons with chronic spinal cord injury. PMR 2010;2:896–900.
9. Van Ingen Schenau GJ, van Woensel WW, Boots PJ, Snackers RW, de Groot G. Determination and interpretation of mechanical power in human movement: application to ergometer cycling. Eur J Appl Physiol Occup Physiol 1990;61:11-19.
10. Hopker J, Jobson S, Carter H, Passfield L. Cycling efficiency in trained male and female competitive cyclists. J Sports Sci Med 2010;9:332–337.
11. Hopker J, Myers S, Jobson SA, Bruce W, Passfield L. Validity and reliability of the Wattbike cycle ergometer. Int J Sports Med 2010;31:731–736.
12. Hettinga FJ, de Groot S, van Dijk F, Kerkhof F, Woldring F, van der Woude L . Physical strain of handcycling: an evaluation using training guidelines for a healthy lifestyle as defined by the American College of Sports Medicine. J Spinal Cord Med 2013; 36:376–382.
13. Hettinga FJ, de Koning JJ, de Vrijer A,Wüst RC, Daanen HA, Foster C. The effect of ambient temperature on gross-efficiency in cycling. Eur J Appl Physiol 2007;101:465–471.
14. Powers S, Howley E . Exercise physiology. Theory and application to fitness and performance. 6th ed. New York: McGraw-Hill 2007.
15. Astrand P, Rodahl K. Textbook of work physiology, physiological bases of exercise. 3rd ed. New York: McGraw-Hill 1986.

16. Almåsbakk B, Whiting HT, Helgerud J. The efficient learner. Biol Cybern 2001; 84:75–83.
17. De Groot S, Veeger DH, Hollander AP, van der Woude LH. Wheelchair propulsion technique and mechanical efficiency after 3 wk of practice. Med Sci Sports Exerc 2002; 34:756–766.
18. Toth MJ, Gardner AW, Arciero PJ, Calles-Escandon J, Poehlman ET (1998). Gender differences in fat oxidation and sympathetic nervous system activity at rest and during submaximal exercise in older individuals. Clin Sci (Lond*)* 1998; 95:59–66.
19. Chisholm DMM, Collis ML, Kulak LL, Davenport W, Gruber N. Physical activity readiness. Br Col Med J 1975;17:375–378.
20. Cardinal BJ, Esters J, Cardinal MK. Evaluation of the revised physical activity readiness questionnaire in older adults. Med Sci Sports Exerc 1996;28:468–472.
21. Borg GA. Psychophysical bases of perceived exertion. Med Sci Sports Exerc 1982; 14:377–381.
22. Arnet U, van Drongelen S, Veeger DH, van der Woude LH. Are the force characteristics of synchronous handcycling affected by speed and the method to improve power? Med Eng Phys 2012;34:78–84.
23. Garby L, Astrup A. The relationship between the respiratory quotient and the energy equivalent of oxygen during simultaneous glucose and lipid oxidation and lipogenesis. Acta Physiol Scand 1987;129:443–444.
24. Ogata H, Yano T. Kinetics of oxygen uptake during arm cranking with the legs inactive or exercising at moderate intensities. Eur J Appl Physiol 2005; 94 (1–2):17–24
25. Moseley L, Jeukendrup AE. The reliability of cycling efficiency. Med Sci Sports Exerc 2001;33:621–627.
26. De Groot S, Veeger HE, Hollander AP, van der Woude LH. Adaptations in physiology and propulsion techniques during the initial phase of learning manual wheelchair propulsion. Am J Phys Med Rehabil 2003; 82:504–510.
27. De Groot S, Veeger HE, Hollander AP, van der Woude LH. Short-term adaptations in co-ordination during the initial phase of learning manual wheelchair propulsion. J Electromyogr Kinesiol 2003;13:217–228.
28. Vegter RJ, Lamoth CJ, de Groot S, Veeger DH, van der Woude LH. Interindividual differences in the initial 80 min of motor learning of handrim wheelchair propulsion. PLoS One 2014; 9:e89729.
29. Andersen LB. A maximal cycle exercise protocol to predict maximal oxygen uptake. Scand J Med Sci Sports 1995;5:143–146.
30. Cook DB, O'Connor PJ, Oliver SE, Lee Y. Sex differences in naturally occurring leg muscle pain and exertion during maximal cycle ergometry. Int J Neurosci 1998; 95 (3–4):183–202.
31. Billaut F, Giacomoni M, Falgairette G (2003). Maximal intermittent cycling exercise: effects of recovery duration and gender. J Appl Physiol (1985) 2003; 95:1632–1637.



3

One-day low-intensity combined arm-leg (Cruiser) ergometer exercise intervention: cardiorespiratory strain and gross mechanical efficiency in one and two-legged exercise

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Abstract

This study aims to research whether there is a difference in cardiorespiratory variables and gross mechanical efficiency (GE) in healthy individuals during low-intensity one-legged and two-legged exercise on the combined arm–leg (Cruiser) ergometer and whether motor learning occurs. The outcome of this study will support the use of the Cruiser ergometer in future as a testing and training instrument in the rehabilitation of patients with a lower limb amputation. Twenty-eight healthy men participated in this randomized controlled trial. One group (n=14) used one leg and both arms during the exercise and the other group (n=14) used both legs and both arms. All participants performed a 1-day low-intensity exercise protocol. This included a standardized pretest and post-test of three bouts of 4 min exercise at 40W and an exercise intervention of seven bouts of 2×4 min exercise at 40W. The one-legged and two-legged group differed significantly in the heart rate and GE between the pretest and post-test. At the post-test, the one-legged group showed motor learning. GE improved significantly in both groups over the duration of the three exercise bouts of the pretest, but it did not improve during the post-test. There are differences in cardiorespiratory variables and GE between one-legged and two-legged exercise on the Cruiser ergometer. When using this ergometer in the rehabilitation of patients with a lower limb amputation, it is important to consider these differences and the occurrence of motor learning.

Keywords: amputation, ergometry, exercise test, rehabilitation

Introduction

Patients with a lower limb amputation (LLA) experience problems in maintaining their physical fitness due to inactivity, comorbidities and immobility after surgery[1]. To prevent deconditioning, it is important for these patients to start exercising prior to or as soon as possible after surgery in a safe, comfortable, and efficient manner. A suitable and effective training program should include a form of aerobic exercise[2,3]. In addition, at present, a valid and reliable exercise testing modality to measure the physical fitness of patients with a LLA before they commence training is not available.

The Cruiser ergometer[4] (Enraf-Nonius) is a multi-limb exercise modality that can be used in the rehabilitation training of LLA patients. It is a reliable and valid instrument for measuring the peak oxygen consumption in healthy individuals during an incremental exercise test[5] as well as a suitable modality for submaximal exercise testing[6]. In a pilot study[7], the Cruiser ergometer seemed suitable to measure the physical capacity of patients with a unilateral LLA.

An advantage of the Cruiser ergometer over the often used one-legged cycle ergometer[8,9] is that the Cruiser ergometer can be used early on in the rehabilitation when the patient has not yet been fitted with the prosthesis. Also, assistance of a physiotherapist is not required when using the Cruiser ergometer in this phase. Furthermore, because both the residual limb and the upper extremities are used during exercise on the Cruiser ergometer, more muscle mass is assumed to be involved compared with one-legged cycle ergometry. This may impact cardiorespiratory strain and efficiency during submaximal exercise as well as the maximal cardiorespiratory capacity and oxygen consumption (VO_2 max) as mentioned in earlier research[10,6].

The combined arm-leg movement on the Cruiser ergometer is a different cyclic multi-limb exercise compared with the leg movement on the cycle ergometer. This implicates that the combined arm-leg ergometer may be subject to motor learning, that is, learning through practice. Motor learning effects in cyclic exercise are among others expressed in (increased) gross efficiency and (reduced) metabolic costs of that exercise at submaximal intensities[11,12,13].

Consequently, it is important to understand the physiology of this cyclic exercise and the motor learning effects in terms of submaximal cardiorespiratory variables (oxygen consumption [VO_2 (l/min)], carbon dioxide output [VCO_2

(l/min)], breathing frequency [BF (breaths/min)], maximal ventilation [VE (l/min)], respiratory exchange rate (RER), and heartrate [HR (beats/min)]), gross mechanical efficiency (GE), and physical strain in one-legged and two-legged exercise. Outcomes of one-legged Cruiser exercise may also be influenced by the use of the dominant or the nondominant leg[14].

The aims of this study are as follows: (a) to determine whether there is a difference in cardiorespiratory variables and GE in healthy individuals during exercise on the Cruiser ergometer with two arms and one leg and with two arms and two legs; (b) to determine whether effects of adaptation and motor learning are found after a 1-day low-intensity exercise protocol and whether these effects are different for one-legged versus two-legged exercise; (c) and to determine whether the use of the dominant or the nondominant leg results in a difference in motor learning. It is hypothesized that cardiorespiratory strain will be higher and the GE will be lower in one-legged exercise compared with two-legged exercise on the Cruiser ergometer, especially when the nondominant leg is used. Also, it is expected that cardiorespiratory strain will decrease and GE will increase after the completion of the protocol.

Methods

In this study, 28 healthy male subjects between 18 and 30 years of age were included (Table 1). Exclusion criteria were a BMI greater than 30 kg/m^2 and/or a history of cardiovascular diseases; joint disorders; infections; complaints of the shoulder, back, arm or leg; lung diseases and balance disorders. Participants were screened for the exclusion criteria using the Physical Activity Readiness Questionnaire (PARQ)[15]. All participants signed an informed consent form according to the guidelines of the Declaration of Helsinki. The study was approved by the Ethics Committee of the Center for Human Movement Sciences, University Medical Center Groningen, University of Groningen (registration nr: ECB 22052012).

Research protocol

All subjects performed a 1-day low-intensity exercise protocol that included

a standardized pretest and posttest and an exercise intervention. Using a randomized controlled design, the participants were assigned to one of the two groups in order of attendance (*n*=14). One group was instructed to use only one leg and both arms (one-legged group), whereas the other group was asked to use both legs and both arms (two-legged group). This group was further divided into two groups of seven subjects who randomly used either their dominant or non-dominant leg during the exercises. All participants were asked to refrain from stimulants (e.g., caffeine, tobacco) and alcohol for at least 12 h before each test.

On the basis of previous studies[6,1213,16], both the pretest and the post-test consisted of three bouts of 4 min submaximal exercise at 40W and at 50 rpm (Fig. 1), while the Cruiser was set in the 'constant power' mode. Resting heart rate and resting oxygen consumption (VO_2 rest) were monitored while the subjects sat quietly for 3 min on the ergometer before starting the pretest (Table 1). The cardiorespiratory variables, as mentioned in the introduction, were measured during the last minute of each of the three exercise bouts of the pretest and post-test. The GE was afterwards calculated for the three exercise bouts of the pretest and post-test. The perceived exertion was measured during the 2 min rest period between the three bouts of the pretest and the post-test by the local perceived discomfort scale[17]and the rates of perceived exertion (RPE) on a 10-point Borg scale[18]. The intervention consisted of seven exercise sessions of 10 min (2×4 min, with 2 min rest in between) at 40W and at 50 rpm with a 20 min rest in between the sessions (Fig. 1). The 20 min rest interval was chosen on the basis of earlier research[16] and was chosen for practical reasons as the intervention was performed in 1 day.

Table 1: Personal characteristics and physiological values in rest before the start of the pre-test (mean, SD and p-values)

	One leg / both arms (n = 14)	Both legs / both arms (n = 14)	p-values
Age (y)	22.5 ± 2.2	22.4 ± 1.9	0.856
Body height (m)	1.88 ± 0.09	1.85 ± 0.07	0.508
Body mass (kg)	81.1 ± 10.0	83.7 ± 8.4	0.456
BMI (%)	23.1 ± 2.3	24.4 ± 2.3	0.148
VO_2	0.45 ± 0.31	0.35 ± 0.09	0.279
VE	9.7 ± 1.6	9.8 ± 0.6	0.938
BF	12.5 ± 4.9	13.6 ± 4.3	0.528
HR	74.6 ± 9.6	72.9 ± 8.6	0.638
RER	0.82 ± 0.07	0.79 ± 0.06	0.295

Abbreviations: BMI = Body Mass Index; VO_2 = Aerobic capacity; VE = Ventilation; BF=Breathing frequency; HR = Heart rate; RER = Respiratory Exchange Ratio.

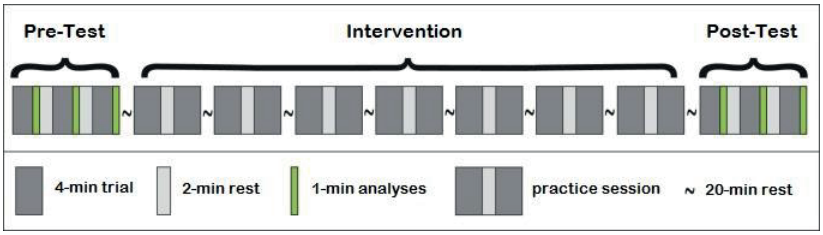

Figure 1. Setup of the 1-day experiment



Figure 2. The Cruiser ergometer (Enraf-Nonius, Delft)

Instruments

The Cruiser ergometer[4] (Enraf-Nonius, 2011) is a combined arm and leg ergometer (Fig. 2). The participant sits on a comfortable seat (low seat height) and places his or her (lifted) feet or foot against a nonmoving, adjustable footrest in front. Participants in the one-legged exercise group placed their inactive leg on a special support connected to the seat. When a patient with an LLA uses the Cruiser ergometer without wearing a prosthesis, the residual limb can be positioned securely on another support especially made for patients with an LLA. When the patient wears a prosthesis, the prosthetic leg can be involved actively in the exercise. The footrest is used to push the sliding seat backwards and the patient can move the seat forwards again by pulling the two-lever arm. In this cyclic process, the sound leg, trunk, and arms are used to provide power output into the ergometer, and thus the patient exercises (an)aerobically. The

ergometer was set to operate at a constant power between 35 and 60 rpm. Participants were instructed to maintain 50 rpm. The accuracy of the Cruiser ergometer is ±10% for power output and ± 2 rpm for speed[4].

The cardiorespiratory variables (VO_2, VCO_2, BF, VE, and RER) were measured with the Metamax II (Cortex Biophysik GmbH, Leipzig, Germany)[19]. HR was measured using a Polar chest band. Metabolicpower (P_{met}) was calculated using Eq. (1).

(1) $$P_{met}(w) = VO_2[\frac{(4.940\ RER+16040)}{60}]$$

GE (%) was derived from the ratio between the mechanical power output (P_o) and the metabolic power (P_{met}), as shown in Eq 2[20].

(2) $$GE\ (\%) = \frac{P_o}{P_{met}} \cdot\ 100\%$$

Statistics

All statistical analyses were carried out using IBM SPSS statistics 20.0 software; USA. Independent-sample *t*-tests were used to compare the baseline values of group characteristics. A mixed factorial analysis of variance was used to detect significant effects for both groups (one-legged vs. two-legged), test moment (pretest and post-test), and exercise bout (1–3) and to determine the interaction effects between group, time point, and exercise bout. Also, to detect differences in the one-legged group between the dominant versus the nondominant group, a mixed factorial analysis of variance was used. A post-hoc Bonferroni correction was applied to all tests to control for α inflation. The statistical significance level was set at *P* value less than 0.05.

Results

All 28 participants completed the study successfully. No significant differences were found in personal characteristics and physiological values (recorded during the rest period) between both groups (Table 1).

One versus two legs

The one-legged and two-legged group differed significantly regarding GE and HR between the pretest and post-test (P=0.031 and P=0.034) (Table 2). At the posttest, the one-legged exercise group had improved significantly in all variables compared with the pretest [GE (P <0.001),VO_2 (P < 0.001), VE (P <0.001), BF (P =0.033), HR (P= 0.002), RER (P < 0.001), and RPE (P = 0.004)] (Table 2). The two-legged exercise group had improved significantly in VE (P <0.001), BF (P< 0.004), RER (P= 0.016), HR (P <0.01), and RPE (P= 0.003), while showing borderline nonsignificant changes in GE (P= 0.143) and VO_2 (P = 0.072). However, no significant interaction effects between both groups and tests were found, indicating no major differences in improvement between both exercise groups after the intervention (Table 2).

Motor learning

GE of the one-legged group increased significantly (P=0.001) from 9.2% at the pretest to 10.9% at the posttest, whereas the two-legged group showed a nonsignificant (P=0.143) increase, with pretest values of 10.8% and posttest values of 12.2%. VO_2 of the one-legged group decreased significantly (P<0.01) from a pretest value of 1.29 l/min to a post-test value of 1.12 l/min. The VO_2 of the two-legged group decreased from 1.16 to 1.03 l/min,but this was a nonsignificant decrease (P=0.072). HR decreased significantly between the pretest and post-test in both the one-legged and the two-legged group, as did VE and BF. Thus, the one-legged group showed more motor learning effects than the two-legged group. Both groups improved significantly in GE during the three exercise bouts of the pretest (Fig. 3). However, during the post-test, no significant improvements in GE were observed in the duration of the exercise bouts of the posttest (Fig. 3 and Table 2).

Dominant versus non-dominant leg

Participants in the one-legged exercise group (*n*=14) were further divided into two groups (*n*=7), using either their dominant leg or their non-dominant leg during the exercises. No significant differences in outcome variables were found between the two subgroups, however.

Table 2 Outcome variables of the pre-test and post test for both exercise group

Outcome variables		Scores (mean and SD)		Main effects			Two-way Interaction effects			Three-way Interaction
		Pre-test	Posttest	One leg vs 2 legs	Pretes vs post- test	Exercise bout	One leg vs 2 legs x pre-test vs post-test	Pre-test vs posttest x exercise bout	One leg vs 2 legs x exercise bout	One leg vs 2 legs x pre-test vs posttest x exercise bout
GE (in %)	Total			0.031*	0.004*	0.002*	0.697	0.002*	0.831	0.025*
	One leg	9.2 ± 0.8	10.9 ± 1.7		0.001*	0.083		0.022*		
	Two legs	10.8 ± 2.5	12.2 ± 2.7		0.143	0.011*		0.008*		
VO_2 (L/min)	Total			0.076	<0.001*	<0.001*	0.528	0.007*	0.602	0.103
	One leg	1.29 ± 0.11	1.12 ± 0.14		<0.001*	0.049*		0.066		
	Two legs	1.16 ± 0.26	1.03 ± 0.20		0.072	0.005*		0.041*		
VE (L/min)	Total			0.438	<0.001*	0.002*	0.166	0.002*	0.727	0.397
	One leg	30.5 ± 5.5	26.0 ± 3.1		<0.001*	0.531		0.020*		
	Two legs	29.4 ± 3.8	25.7 ± 2.6		<0.001*	0.479		0.026*		
BF (breaths/ min)	Total			0.46	<0.001*	0.156	0.083	0.082	0.079	0.268
	One leg	20.3 ± 4.8	18.9 ± 4.5		0.033*	0.065		0.071		
	Two legs	22.5 ± 5.0	19.0 ± 4.0		0.004*	0.842		0.211		
HR (beats/min)	Total			0.034*	<0.001*	0.222	0.288	<0.001*	0.672	0.408
	One leg	109.9 ± 12.8	99.1 ± 5.6		0.002*	0.186		0.106		
	Two legs	101.5 ± 9.0	94.1 ± 6.7		<0.001*	0.516		0.004		
RER	Total			0.052	<0.001*	<0.001*	0.057	<0.001*	0.110	0.551
	One leg	0.87 ± 0.04	0.81 ± 0.05		<0.001*	0.036*		<0.001*		
	Two legs	0.82 ± 0.05	0.80 ± 0.03		0.016*	<0.001*		0.033*		
RPE	Total			0.694	<0.001*	0.585	0.120	0.081	0.019*	0.817
	One leg	2.4 ± 1.0	1.2 ± 0.6		0.004*	0.099		0.166		
	Two legs	2.0 ± 1.1	1.4 ± 1.2		0.003*	0.166		0.465		

One versus two legs (mean ±SD scores during the last minute of all three exercise bouts) and the results of a repeated-measures analysis of variance (P values). Main effects for the three main factors (total), 1 versus 2 legs, pre-test versus post-test, exercise bout, and their two-way and three-way interactions. Bonferroni corrected post analyses for all two-legged groups are presented in addition. BF, breathing frequency; GE, gross mechanical efficiency; HR, heart rate; RER, respiratory exchange ratio; RPE, ratings of perceived exertion; VE, ventilation; VO_2, aerobic capacity. *Significant.



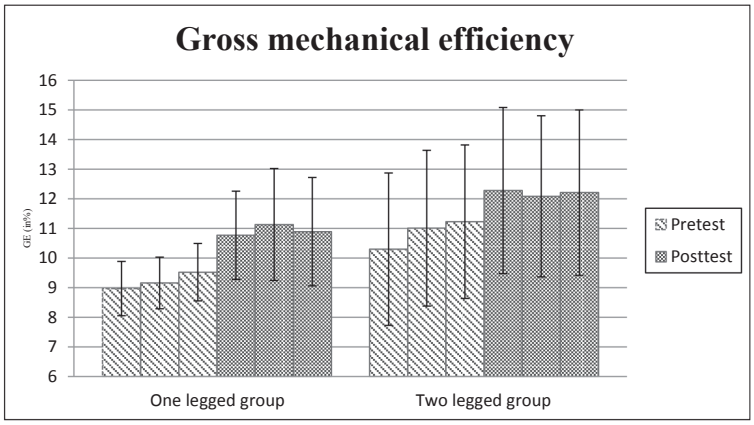

Figure 3: Mean scores and SD of the gross mechanical efficiency during each of the exercise bouts (1-3) for the pre-test and post-test for both groups (n = 14).

Discussion

This is the first study to research the differences between one-legged and two-legged exercise on the combined arm-leg (Cruiser) ergometer. Our study adds to earlier research on the Cruiser ergometer[5,6,7] by showing that one-legged and two-legged exercise on the Cruiser ergometer results in significant differences in HR and GE between the pre- and posttest. The maximum HR during one-legged exercise was higher and one-legged exercise was less efficient than two-legged exercise. After performing a 1-day low-intensity exercise protocol on the Cruiser ergometer, the one-legged exercise group improved significantly in all outcome variables. The two-legged exercise group improved significantly in VE, BF, RER, HR, and RPE, while showing borderline nonsignificant changes in GE and VO_2. GE improved significantly in both groups during the three exercise bouts of the pretest, but it did not improve during the post-test Therefore, it seems motor learning occurs after exercising on the Cruiser ergometer in the short and intermediate term. Furthermore, one-legged exercise on the Cruiser ergometer leads to a greater improvement in motor learning than two-legged exercise. In the one-legged exercise group, no influence of the dominant leg on the outcome variables was found.

Our findings are similar to those reported by Ogita et al.[21], who compared one-legged and two-legged exercise on the cycle ergometer. They found that VO_2 was higher in low-intensity one-legged cycling than in low-intensity two-legged cycling. This is probably because of the fact that postural control muscles have to be more active because of the asynchronic and initially somewhat unbalanced movement[22,23]. Because one-legged exercise requires greater effort, HR was higher compared with two-legged exercise. The same results were found in this study. During one-legged exercise on the Cruiser ergometer, less muscle mass is used, which means that the postural control muscles need to work harder to stabilize the trunk. This could explain why a higher cardiorespiratory strain and a lower GE were found for one-legged exercise compared with two-legged exercise.

Several studies have reported on the increase in GE following practice, which is thought to be indicative of the underlying process of motor learning[11,24,25]. In this study, a significant increase in GE was demonstrated in the one-legged group and a borderline nonsignificant increase in the two-legged group. Cardiorespiratory strain was significantly reduced, especially in one-legged exercise, after practice. Metabolic strain and energy expenditure are reduced with practice when the task constraints remain unchanged[11]. It seems that exercising on the Cruiser ergometer is subject to a process of improved coordination and adaptation, that is, motor learning. To be able to reach a stable metabolic energy expenditure, some practice on the Cruiser ergometer is needed. The motor learning effect was found to be greater for movement with two arms and one leg than for movement with two arms and two legs.

The aforementioned increase in GE can be explained by better coordination of the arms and leg, reduced co-contractions of the dynamic and postural control muscles, and more efficient mechanical power input while exercising on the Cruiser ergometer. A difference was found between both exercise groups for the first 12 min of the exercise protocol. Whereas the two-legged group showed motor learning during the second exercise bout, in the one-legged group motor learning only took place from the third exercise bout onward, 4 min later (Fig. 3). These findings could indicate that one-legged exercise is a more complex movement that requires more (practice) time before motor learning can occur. To our knowledge, this is also the first study to investigate motor learning processes during the first 12 min of exercise on the Cruiser ergometer.

Vegter et al.[13,16] researched the increase in mechanical efficiency during the first 12 min of wheelchair propulsion. The healthy, able-bodied participants in their study increased their mechanical efficiency, indicating that less energy was used to maintain a constant speed and power output. This corresponds with findings from the present study, which demonstrated that motor learning already occurs soon after the start of the more difficult types of exercise. Our findings suggest motor learning did not take place during the posttest. An explanation might be that sometime during the intervention period a steady state was reached, after which no additional motor learning took place. However, given that this study did not measure GE during the intervention period, it is not possible to confirm this.

Another aspect that might influence motor learning is amputation of the dominant leg, which, consequently, does not contribute to the exercise. To test this hypothesis, the one-legged group was further divided into two subgroups in this study. No difference was found, however, between use of the dominant leg or nondominant leg and the occurrence of motor learning. This is in accordance with a review on leg preference in running and cycling[14], which showed that previous studies failed to find a general association between functional asymmetry and lateral preference for the lower limbs. No relationship was found between asymmetries and performance in this study.

A limitation of this study is that only male participants were included. This homogeneous population was chosen to enable comparisons with other research in this area with also only male participants. Previous research[6] showed that female participants exercised seemingly more efficiently on the Cruiser ergometer at identical submaximal absolute power output levels compared with male participants.
Another limitation concerns the lack of data on the seven exercise sessions of the intervention between the pretest and post-test. Therefore, no conclusions can be drawn on outcome variables during the intervention. Future research is needed to clarify at what point during the intervention period a steady state is reached with respect to metabolic costs and GE. Furthermore, to determine whether this steady state is final or only temporary, future studies should consider using a longer intervention period.

Conclusion

This study showed a difference in cardiorespiratory strain and GE between one-legged and two-legged exercise on the Cruiser ergometer. The one-legged and two-legged group showed an increase in GE after the intervention and thus seemed to indicate motor learning. This increase in GE, however, can be mainly attributed to the one-legged group. Motor learning was not influenced by use of dominant leg or nondominant leg. Further research on the use of the Cruiser ergometer in the rehabilitation of patients with a LLA should not only consider differences in cardiorespiratory variables and GE between one and two-legged exercise, but also potential consequences of adaptation over time. Further research should also explore motor learning effects and adaptation in these patients during various periods of practice.

From a clinical perspective, the experimental results suggest that unilateral leg exercise on the Cruiser ergometer is highly feasible, is somewhat more straining, and yet less efficient, and it requires a period of adaptation (in which motor learning takes place) to become familiar with the exercise configuration. Low-intensity practice provides such a period of adaptation, which leads to optimization of efficiency and reduction of metabolic costs at a given power output. This should be taken into account when using the Cruiser in novices for training and/or exercise testing.

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References

1. Blume P, Salonga C, Garbalosa J, et al. Predictors for the healing of transmetatarsal amputations: Retrospective study of 91 amputations. Vascular 2007; 15: 126-133.
2. Chin T, Sawamura S, Shiba R. Effect of physical fitness on prosthetic ambulation in elderly amputees. Am J Phys Med Rehabil 2006; 85:992-996.
3. van Velzen JM, van Bennekom CA, Polomski W, Slootman JR, van der Woude, LH, Houdijk H. Physical capacity and walking ability after lower limb amputation: a systematic review. Clin Rehabil 2006;20:999-1016.
4. Enraf-Nonius, Delft, the Netherlands: operating instructions Cruiser 2011.
5. Simmelink EK, Wempe JB, Geertzen JH, Dekker R. Repeatability and validity of the combined arm-leg (Cruiser) ergometer. Int J Rehabil Res 2009;32:324-330.
6. Simmelink EK, Borgesius EC, Hettinga FJ, Geertzen JH, Dekker R, van der Woude LH. Gross mechanical efficiency of the combined arm-leg (Cruiser) ergometer: A comparison with the bicycle ergometer and handbike. Int J Rehabil Res 2015;38: 61-67.
7. Vestering MM, Schoppen T, Dekker R, Wempe J, Geertzen JH (2005). Development of an exercise testing protocol for patients with a lower limb amputation: Results of a pilot study. Int J Rehabil Res 2005;28: 237-244.
8. Wezenberg D, de Haan A, van der Woude LH, Houdijk H. Feasibility and validity of a graded one-legged cycle exercise test to determine peak aerobic capacity in older people with a lower-limb amputation. Phys Ther 2012;92: 329-338.
9. Wezenberg D, de Haan A, Faber WX, Slootman HJ, van der Woude, LH, Houdijk H. Peak oxygen consumption in older adults with a lower limb amputation. Arch Phys Med Rehabil 2012;93:1924-1929.
10. Bostom AG, Bates E, Mazzarella N, Block E, Adler J. Ergometer modification for combined arm-leg use by lower extremity amputees in cardiovascular testing and training. Arch Phys Med Rehabil 1987;68:244-247.
11. Sparrow,W.A., Newell,K.M. Energy expenditure and motor performance relationships in humans learning a motor task. Psychophysiology 1994;31: 338-346.
12. de Groot S, Veeger HE, Hollander AP, van der Woude LH. Adaptations in physiology and propulsion techniques during the initial phase of learning manual wheelchair propulsion. Am J Phys Med Rehabil 2003; 82: 504-510.
13. Vegter RJ, de Groot S, Lamoth CJ, Veeger DH, van der Woude LH. Initial skill acquisition of handrim wheelchair propulsion: A new perspective. IEEE Trans Neural Syst Rehabil Eng 2014;22: 104-113.
14. Carpes FP, Mota CB, Faria IE. On the bilateral asymmetry during running and cycling - a review considering leg preference. Phys Ther Sport 2010; 11: 136-142.
15. Cardinal BJ, Esters J, Cardinal MK. Evaluation of the revised physical activity readiness questionnaire in older adults. Med Sci Sports Exerc 1996:28: 468-472.
16. Vegter RJ, Lamoth CJ, de Groot S, Veeger DH, van der Woude LH. Inter-individual differences in the initial 80 minutes of motor learning of handrim wheelchair propulsion. PLoS One 2014;9: e89729.

17. van den Berg R, de Groot S, Swart KM, van der Woude LH (2010). Physical capacity after 7 weeks of low-intensity wheelchair training. Disabil Rehabil 2010;32: 2244-2252.
18. Borg GA (1982) Psychophysical bases of perceived exertion. Med Sci Sports Exerc 1982;14: 377-381.
19. Medbo JI, Mamen A, Welde B, von Heimburg E, Stokke R (2002). Examination of the metamax I and II oxygen analysers during exercise studies in the laboratory. Scand J Clin Lab Invest 2002; 62: 585-598.
20. Garby L, Astrup A. The relationship between the respiratory quotient and the energy equivalent of oxygen during simultaneous glucose and lipid oxidation and lipogenesis. Acta Physiol Scand 1987: 129: 443-444.
21. Ogita F, Stam RP, Tazawa HO, Toussaint HM, Hollander AP. Oxygen uptake in one-legged and two-legged exercise. Med Sci Sports Exerc 2000;32:1737-42
22. Sargeant AJ, Davies CT. Forces applied to cranks of a bicycle ergometer during one- and two-leg cycling. J Appl Physiol Respir Environ Exerc Physiol 1977;42:514-518.
23. Neary PJ, Wenger HA. The effects of one- and two-legged exercise on the lactate and ventilatory threshold. Eur J Appl Physiol Occup Physiol 1986;54: 591-595.
24. Almasbakk B, Whiting HT, Helgerud J. The efficient learner. Biol Cybern 2001; 84: 75-83.
25. Vegter RJ, Hartog J, de Groot S, Lamoth CJ, Bekker MJ, van der Scheer JW et al. Early motor learning changes in upper-limb dynamics and shoulder complex loading during handrim wheelchair propulsion. J Neuroeng Rehabil 2015;12:26.



4

Repeatability and validity of the combined arm-leg (Cruiser) ergometer

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Int J Rehabil Res 2009 Dec ; 32 (4): 324-330

Abstract

The measurement of physical fitness of lower limb amputees is difficult, as the commonly used ergometer tests have limitations. A combined arm-leg (Cruiser) ergometer might be valuable. The aim of this study was to establish the repeatability and validity of the combined arm-leg (Cruiser) ergometer. Thirty healthy volunteers carried out three incremental exercise tests, once on the bicycle ergometer and twice on the Cruiser ergometer. The repeatability of the Cruiser ergometer was assessed by studying the mean values of the test–retest and the validity by studying the mean values of the bicycle and the two Cruiser ergometer tests. The intraclass correlation coefficient for repeated measurements on the Cruiser ergometer was 0.84 for the maximal oxygen consumption (VO_2max), and 0.71 for the maximal heart rate (HRmax). The intraclass correlation coefficient for the measurements on the bicycle ergometer and the Cruiser ergometer was 0.86 for the VO_2max and 0.73 for HRmax. Bland and Altman plots for VO_2max and HRmax showed a bias close to zero and a great accuracy. The conclusion of this study is that the Cruiser ergometer provides a repeatable and valid measurement of physical fitness in healthy volunteers. Its value in clinical practice for lower limb amputees needs to be further established.

Keywords: combined arm-leg (Cruiser) ergometer, exercise test, physical fitness, repeatability, validity

Introduction

Patients with a lower limb amputation experience a decline in physical fitness. Walking with a prosthesis expends more energy than walking with two sound legs[1]. To be able to learn to walk with a prosthesis at a practical level of activity, it is very important that the amputee is able to meet the inherent high energy-expenditure demands[2]. Nowadays, the most important element in the rehabilitation of patients with a lower limb amputation is training in walking with a prosthesis. Evidence from Chin et al.[3] suggests that when prosthetic rehabilitation only covers walking training with a prosthesis, maximal aerobic capacity of amputees does not improve to the level of able-bodied persons. Therefore, training in prosthetic walking should be accompanied by some kind of endurance exercise training with the aim of improving the fitness of amputees. Aerobic exercise training comes with some difficulties for lower limb amputees. First, lower limb amputees already have cardiovascular disease or are at risk of developing it[4]. Before commencing aerobic training, an appropriate maximal exercise test is necessary to detect underlying cardiovascular disease, such as ischaemia or heart rhythm problems[5]. Second, the intensity level of exercise training needs to be determined, usually through maximal oxygen uptake (VO_2max) measurement. Many amputees with peripheral vascular disease have altered blood pressure and heart rate (HR) responses to exercise, and most of them take medication such as β-blockers. The consequence of this is that VO_2max cannot be reliably estimated from submaximal oxygen uptake and HR data, and therefore has to be measured during a symptom-limited graded exercise test.

At present, different types of ergometers are available for exercise testing and training: treadmills, bicycle ergometers, arm-ergometers, rowing ergometers, and combined arm-leg ergometers. For a reliable measurement of aerobic capacity and safety, it is best to choose an ergometer on which the patient uses a large muscle mass while exercising, thus reaching higher VO_2max and HRmax[4]. Exercise testing through arm crank ergometry can provide useful data to generate a safe upper extremity exercise program[6]. However, arm ergometry does not stress the cardiovascular and respiratory systems as much as leg cycling or treadmill exercise. During arm ergometry, peak oxygen uptake will approximate 50–70% of that for leg cycling [7,8,9,10]. A combined arm-leg ergometer

might be of value in this respect. In a pilot study, Vestering et al.[11] developed a maximal exercise testing protocol for lower limb amputees using a combined arm-leg ergometer.
Vestering et al.[11] concluded that the Cruiser ergometer can indeed be used in limb amputees for the determination of maximal aerobic capacity, and in fact elicited a higher oxygen uptake and HR than that of arm ergometry.
Currently, no data are present on the repeatability and validity of the combined arm-leg (Cruiser) ergometer. The aim of this study is to establish the repeatability and validity of the Cruiser ergometer.

Methods

Volunteers

Healthy volunteers between 18 and 70 years of age were asked to participate in this study through an advertisement in a newsletter and on the website of the Center for Rehabilitation of the University Medical Center Groningen in the Netherlands. Exclusion criteria for participating in this study were age less than 18 years, a body mass index of more than 30, evidence or serious suspicion of cardiovascular diseases, stress or exercise-related pain in the chest, pulmonary diseases, a resting blood pressure greater than 140/90, viral or bacterial infection for less than 10 days, use of medication for cardiopulmonary diseases, balance disorders, and wounds on the legs and joint diseases. The study was approved by the Ethics Committee of the University Medical Center Groningen, and all volunteers gave written informed consent before testing.

Experimental design

Before testing, the age, height, weight and sex of the volunteers were noted, and spirometry was performed. The protocol consisted of carrying out three incremental exercise tests. The first test was carried out on a bicycle ergometer and the two other tests were carried out on the Cruiser ergometer, a combined arm-leg ergometer. The sequence of the tests was similar for each volunteer. Because the electrocardiogram (ECG) recordings on the Cruiser ergometer were not reliable for every person, the test on the bicycle ergometer was carried out first for safety reasons. The measurements were made at about the same time of day for each individual, with intervals of 1–2 weeks. All participants were asked to refrain from stimulants (caffeine, drugs, cigarettes, etc.), exercise and

alcohol for 12h before testing. Each person was asked to have a light breakfast/ lunch at least 2h before the exercise test, and normal hydration was requested.

Equipment

The Jaeger ER 900L bicycle ergometer was used. On this ergometer, the patient sits in the semirecumbent position and uses both legs to overcome the resistance provided by the ergometer. The accuracy of the power is ±3%. The Cruiser ergometer (Enraf-Nonius, Delft, The Netherlands) is a combined arm-leg ergometer, and is equipped with a comfortable seat. The feet are placed against a nonmoving footrest, which can be adjusted to the patient's height. The footrest is used to push off to make the seat move backwards. The patient can move the seat forward again by pulling the handlebars with the arms. In this way, the arms and legs are used alternatively to overcome the resistance provided by the ergometer. The accuracy of the power of the Cruiser ergometer is ±10%.

Outcome parameters

During testing, the following parameters were measured: maximal load (Wmax) HR, VO_2, carbon dioxide output (VCO_2) and maximal ventilation (VE). VO_2, VCO_2 and VE were recorded by using an Oxycon Delta (Jaeger, Bunnik, The Netherlands). Heart rate was measured with a 12-lead ECG.

The anaerobic threshold (AT) was determined by the V-slope method using VO_2 and VCO_2. Blood pressure was measured every 2 min by an automatic blood pressure meter during the test on the bicycle ergometer. Blood pressure was measured before and after the test with a manual blood pressure meter during the test on the Cruiser ergometer, because it was technically not possible to measure the blood pressure during the test.

When the volunteers were at rest, after the warming-up period and at the point of Wmax ,the Borg 10-point category scale with ratio properties was used to rate the perceived exertion[12] . Dyspnoea, leg muscle fatigue (bicycle and cruiser ergometer) and arm muscle fatigue (Cruiser ergometer) were measured by using the Borg score.

Test protocol

The testing protocol was similar for the three tests. The test started with 3 min of quietly sitting on the ergometer with the ECG recording and the oxygen mouthpiece to asses baseline measurements. After these 3 min, a warm-up was

carried out at 50W for 5 min. After the warm-up, the workload was increased by 20 or 30W every minute upon exhaustion. For men, the workload was increased by 30W every minute and for women by 20W every minute. After the exercise test was terminated, a cooling down of 3min was performed at 20W.
Reasons for terminating the test were inability to maintain a revolution speed of 60 rotations/min on the bicycle ergometer or 50 rotations/min on the Cruiser ergometer, pain in the arms or legs, a painful feeling in the chest, a feeling of dizziness or faintness, severe dyspnoea, paleness, cyanosis, or a cold and clammy feeling of the skin. The test was also stopped by the researcher when there were ECG abnormalities, high systolic (>250mmHg) or high diastolic (>115mmHg) blood pressure or a drop of the systolic blood pressure of more than 10mmHg with an increase in working load in comparison with the systolic blood pressure at rest. After the test, the reason for termination of the exercise test was noted. After performing the three exercise tests, the volunteers were asked to state the test they preferred.

Statistical analysis

Data analysis was performed on SPSS version 14.0 for Windows (SPSS, Chicago, Illinois, USA)[13]. Descriptive statistics were generated for all variables. The repeatability of the Cruiser ergometer was assessed by studying the mean values of the test–retest and the validity by studying the mean values of the bicycle ergometer test and the two Cruiser ergometer tests. For analyses, paired (Students) *t*-tests, the one-way random, single measure intraclass correlation coefficient [ICC] and Bland and Altman plots were used[14]. The differences in Borg scores between the tests were assessed by the Wilcoxon signed rank test. Significance level was determined at a P value less than 0.05.

Results

Volunteers

Thirty volunteers participated in this study: 16 men and 14 women, ranging in age from 20 to 61 years. Values of patients' mean (±SD) age, height, weight and forced expiratory volume in 1s (FEV_1) (% of predicted) are presented in Table 1.

Table 1. Characteristics of the 16 men and 14 women

Variable	Mean (±SD)	Range
Age (years)	37.0 (10.0)	20 - 61
Height (m)	1.78 (0.1)	1.6 – 2.0
Weight (kg)	79.0 (13.7)	55 - 109
BMI (kg/m2)	24.7 (2.5)	19.3 - 29.3
FEV_1 (% of predicted)	110.3 (12.23)	81.8 – 136.6

FEV_1, forced expiratory volume in 1 s.

Repeatability of the Cruiser ergometer test

The results of the two tests on the Cruiser ergometer did not show significant differences for the VO_2, VCO_2, HR and AT. A significant difference was found for the VE at 50W and for the Wmax. The Wmax reached at the second test on the Cruiser ergometer was higher than at the first test (Table 2).

The ICC for repeated measurements on the Cruiser ergometer was 0.84 (VO_2max) and 0.71 (HRmax) (Table 3).

In the Bland and Altman plots the bias ±1.96SD of the VO_2max is 0.016 ± 0.74 l/min (Fig. 1) and of the HRmax 2.83 ± 19.85 beats/min (Fig. 2). Both plots show a bias close to zero and high accuracy

Table 2. Comparison of the three exercise tests

	Bicycle	**Cruiser first test**	**Cruiser second test**
mean (SD) n=30			
VO_2 50 W (l/min)	1.00 (0.09)	1.10 (0.15)[a]	1.05 (0.15)
VCO_2 50W (l/min)	0.83 (0.09)[b]	1.00 (0.16)[a]	0.93 (0.13)
VE 50 W (l/min)	25.25 (2.79)[b]	32.08 (4.61)[a]	30.47 (4.26)[c]
HR 50W (beats/min)	101.87 (13.88)	103.73 (12.97)	103.04 (15.30)
VO_2max(l/min)	2.70 (0.60)	2.62 (0.63)	2.64 (0.67)
VCO_2max (l/min)	3.06 (0.68)	2.84 (0.69)[a]	3.00 (0.90)
VEmax (l/min)	91.62 (21.14)	89.89 (22.18)	98.21 (33.11)
HRmax (beats/min)	167.50 (13.94)	164.77 (14.88)	167.60 (12.19)
Maximal load (Wmax)	240.00 (54.20)[b]	196.00 (42.31)[a]	208.67 (48.00)[c]
ATmax	1.70 (0.37)	1.81 (0.42)	1.80 (0.47)

ATmax, anaerobic threshold at maximum load; HRmax, maximum heart rate; HR 50W, heart rate at 50 W; *V*CO_2max, maximum carbon dioxide output; *V*$CO_2$50W, carbon dioxide output at 50W; *V*Emax, maximum ventilation; *V*E 50W, maximum ventilation at 50W; *V*O_2max, maximum oxygen consumption; *V*O_2 50W, oxygen consumption at 50W.

[a]Significant difference between test on the bicycle ergometer and first test on the Cruiser ergometer.

[b]Significant difference between test on the bicycle ergometer and second test on the Cruiser ergometer.

[c]Significant difference between the tests on the Cruiser ergometer.

Table 3. ICC of the two Cruiser ergometer tests

	ICC (single measures)	**95% CI**
VO_2 50 W	0.69	0.45-0.84
HR 50 W	0.70	0.46-0.85
VE 50 W	0.63	0.35-0.80
VO_2max	0.84	0.69-0.92
HR max	0.71	0.48-0.85
VE max	0.59	0.29-0.78

CI, confidence interval; HRmax, maximum heart rate; HR 50W, heart rate at 50 W; ICC, intraclass correlation coefficient; *V*Emax, maximum ventilation; *V*E 50W, maximum ventilation at 50W; *V*O_2max, maximum oxygen consumption; *V*O_2 50W, oxygen consumption at 50W.

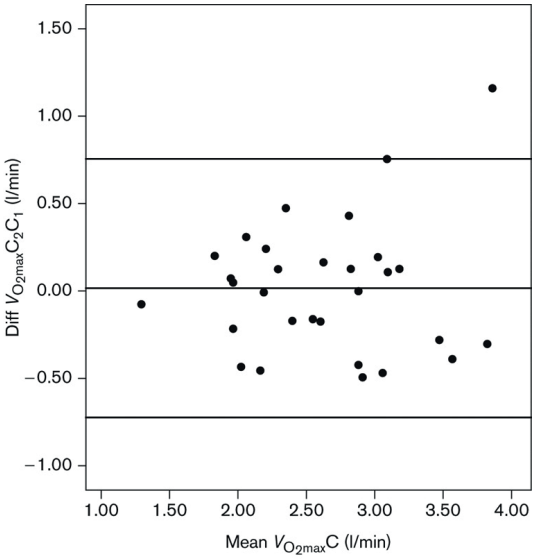

Figure 1. Bland and Altman plot for maximal oxygen consumption (VO_2max) measured on the Cruiser ergometer. Diff $VO_2maxC_2C_1$, difference between the VO_2max in l/min between the first and the second tests on the Cruiser ergometer; Mean VO_2maxC, mean VO_2max in l/min of the two tests on the Cruiser ergometer.

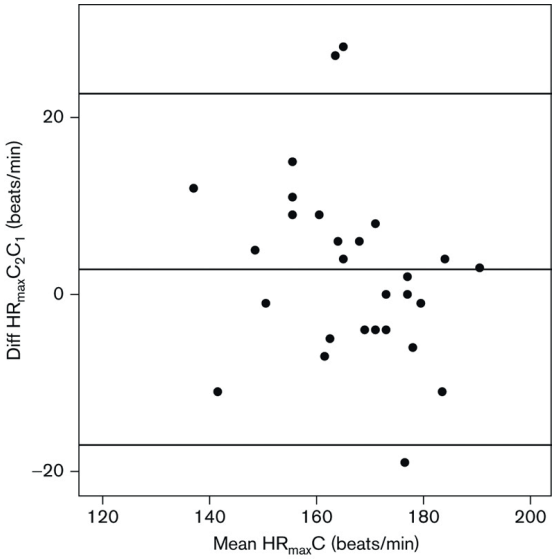

Figure 2 Bland and Altman plot for maximal heart rate (HRmax) measured on the Cruiser ergometer. Diff $HRmaxC_2C_1$, difference between the HRmax in beats/min between the first and the second tests on the Cruiser ergometer; Mean HRmaxC, mean HRmax in beats/min of the two tests on the Cruiser ergometer.

Validity of the Cruiser ergometer test

The results from the two Cruiser tests compared with the bicycle test did not show significant differences for the VO_2max , VEmax, HRmax and ATmax.

At 50W, significant differences were found between the first Cruiser test and the bicycle test for the VO_2, VCO_2 and VE and at Wmax for the VCO_2. At 50W, the VCO_2 and VE were significantly different between the second Cruiser test and the bicycle test (Table 2). The Wmax reached on the bicycle ergometer was higher than on the Cruiser ergometer, and this difference was significant in comparison with the first test ($P<0.001$) and with the second ($P<0.001$) on the Cruiser ergometer.

The ICC for the measurements on the bicycle ergometer and the second test on the Cruiser ergometer was 0.86 (VO_2max) and 0.73 (HRmax) (Table 4).

In the Bland and Altman plots, the bias ±1.96SD of the VO_2max is 0.06 ± 0.67 l/min (Fig. 3), and of the HRmax -1,0 ± 19.21 (Fig. 4). Both plots show a bias close to zero and high accuracy.

Table 4. ICC of the bicycle and Cruiser ergometer tests

	ICC (single measures)	**95% CI**
VO_2 50 W	0.28	-0.08-0.57
HR 50 W	0.74	0.53-0.87
VE 50 W	-0.09	-0.43-0.27
VO_2max	0.86	0.72-0.93
HRmax	0.73	0.51-0.86
VEmax	0.63	0.36-0.80

CI, confidence interval; HRmax, maximum heart rate; HR 50W, heart rate at 50 W; ICC, intraclass correlation coefficient; VEmax, maximum ventilation; VE 50W, maximum ventilation at 50W; VO_2max, maximum oxygen consumption; VO_2 50W, oxygen consumption at 50W.

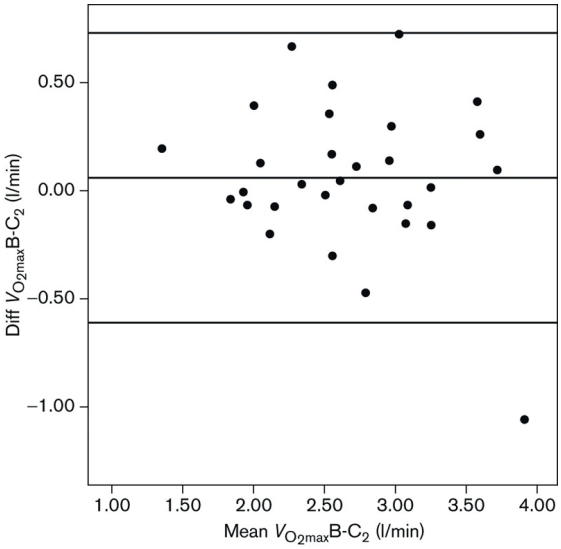

Figure 3. Bland and Altman plot for maximal oxygen consumption (VO_2max) measured on the bicycle and Cruiser ergometer. Diff VO_2maxB-C_2: difference between the VO_2max in l/min between the test on the bicycle ergometer and the second test on the Cruiser ergometer; Mean VO_2maxB-C_2, mean VO_2max in l/min of the test on the bicycle ergometer and the second test on the Cruiser ergometer.

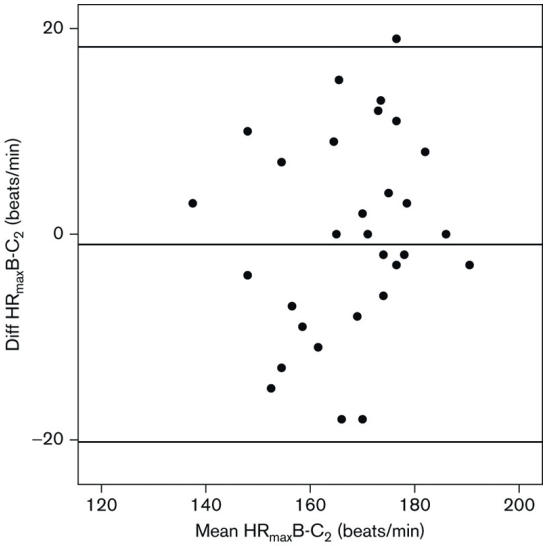

Figure 4. Bland and Altman plot for maximal heart rate (HRmax) measured on the bicycle and Cruiser ergometer. Diff HRmaxB-C_2, difference between the HRmax in beats/min between the test on the bicycle ergometer and the second test on the Cruiser ergometer; Mean HRmaxB-C_2, mean HRmax in beats/min of the test on bicycle ergometer and the second test on the Cruiser ergometer.

Borg score, reason for stopping the test and test of preference

Borg scores for muscle fatigue were significantly higher than for dyspnoea on all tests. On the Cruiser ergometer, maximal Borg score for fatigue of the legs was 4.3 and 4.5 (Cruiser first and second tests), which was significantly lower than on the bicycle (5.5) (Table 5).

Reasons for stopping the test on the bicycle ergometer were leg fatigue (80%), dyspnoea (3%), high blood pressure (13%) and dry mouth (3%). Reasons for stopping the first test on the Cruiser ergometer were leg fatigue (13%), arm fatigue (37%), arm and leg fatigue (37%), dyspnoea (7%) and disturbed coordination (7%). For the second test on the Cruiser ergometer, the reasons for stopping the test were leg fatigue (20%), arm fatigue (30%), arm and leg fatigue (40%) and dyspnoea (10%). The bicycle test was preferred by 80% of the participants, 10% preferred the test on the Cruiser ergometer and 10% had no preference.

Table 5. Borg score

	Bicycle	Cruiser first test	Cruiser second test
mean (SD)			
Dyspne max	2.6 (1.9)	1.8 (2.1)[a]	2.6 (2.7)
Fatigue legs max	5.5 (2.7)[b]	4.3 (2.7)[a]	4.5 (2.5)
Fatigue arms max		4.9 (2.1)	5.0 (2.4)

[a]Significant difference between test on the bicycle ergometer and first test on the Cruiser ergometer.
[b]Significant difference between test on the bicycle ergometer and second test on the Cruiser ergometer

Discussion

This study shows that the Cruiser ergometer provides a repeatable and valid measurement of physical fitness in healthy volunteers. However, accurate ECG recordings were not possible in all volunteers during the Cruiser ergometry because of the movement of the trunk. Automatic measurement of blood pressure was only possible just before and after the test.

It is advocated that an ICC of >0.75 indicates good agreement[15,16]. Laskin et al.[17] found for another frequently used exercise test, the 6-min walk test an ICC for distance, ratings of perceived exertion and HR of 0.78, 0.83 and 0.77,

respectively. The ICC for the repeated measurements on the Cruiser ergometer was 0.84 for the VO_2max and 0.71 for the HRmax, and the Bland and Altman plots were very acceptable with bias close to zero and high accuracy, both reflecting good to reasonable repeatability. Validity, defined by ICC between Cruiser and bicycle, was also reasonable to good: 0.86 for the VO_2max and 0.73 for the HRmax, and the Bland and Altman plots were in agreement with these. We can conclude that there is a good repeatability and validity for the outcome parameter VO_2max and a reasonable repeatability and validity for the outcome parameter HRmax. For individual patient use, we advice using the VO_2max as the primary outcome parameter to measure the physical fitness on the Cruiser ergometer.

The *W*max reached on the bicycle ergometer was significantly higher than that reached on the Cruiser ergometer, despite similar VO_2max. At the end of the steady-state period at 50W, VO_2, VCO_2 and *V*E were significantly higher on the Cruiser ergometer than on the bicycle ergometer. Volunteers experienced more fatigue of the arms than of the legs on the Cruiser ergometer, and the reason for stopping the test was in most cases fatigue of the arms or fatigue of the arms and legs. One explanation for the lower *W*max reached on the Cruiser ergometer can thus be that muscle fatigue of the arms already limits exercise capacity, whereas leg effort is still submaximal. In this respect, Toner et al.[18] evaluated the hemodynamic responses during arm crank and leg exercise during several exercise trials with varying proportions of power from the arms and legs. They found that when exercise was carried out with a 50% combination of the arms and legs, peak VO_2 was similar to leg-only exercise, and there was a significantly lower peak VO_2 when exercise was carried out for 75 or 100% of the arms. In addition, HR and Wmax were higher when a greater percentage of the exercise was carried out by the legs. In this study, we were not able to differentiate how much of the power was delivered by the arms and legs during the Cruiser ergometry. It is possible that in the training or adaptation process, each patient develops a unique exercise pattern, best suited to the individual exercise tolerance of upper and lower extremities.
Another explanation might lie in the precision of the ergometers. However, factory data show an accuracy of power of ±3% for the bicycle ergometer and ±10% for the Cruiser ergometer, which cannot be responsible for the observed differences in *W*max.

A final issue with regard to the lower *W*max reached on the Cruiser ergometer is that the movement on the Cruiser ergometer is definitely less energy efficient than on the bicycle ergometer: volunteers reached a higher *W*max on the bicycle ergometer with similar VO_2. Patients with a lower limb amputation are not able to carry out an exercise test on the bicycle ergometer, and the Cruiser ergometer seems to be a repeatable and valid alternative.
In future when we will develop diagnostic and therapeutic protocols for patients with a lower limb amputation, we have to take into account that the Cruiser ergometer is less energy efficient than the bicycle ergometer.
Feasibility of usage of the Cruiser ergometer in lower limb amputees has already been shown. Vestering et al.[11] tested five patients with a lower limb amputation ranging in age from 15 to 58 years on the Cruiser ergometer and found a VO_2max varying from 1.36 to 2.27l/min and a *W*max reached varying from 65 to 115W. The mean values of two tests, VO_2max (2.63l/min) and *W*max (204W), in our study with healthy volunteers were considerably higher. The difference between our results and Vestering et al.[11] may be because of a considerably lower muscle mass in the leg amputees, but also because of decreased physical condition after amputation, concomitant cardiovascular disease and the older age in the lower limb amputation group. Further research is need Noord Nederland ed to develop appropriate test protocols and normal values for the older age group.

There are some limitations to this study. First, getting used to the Cruiser ergometer may be more important than getting used to the bicycle ergometer, as the movement is more complex and less familiar. This is supported by the higher load on the second Cruiser ergometer test and a lower VO_2 in the second steady-state period. In contrast to this, however, VO_2max and HRmax were comparable, which suggests that a maximal state was reached, providing reliable evaluation of limitation of exercise tolerance and safety issues. Second, our volunteers were all healthy persons. Before using the Cruiser ergometer for patients with a lower limb amputation, we have to adapt our protocol because these patients will reach a lower maximal load. We have to use a protocol with increments of less than the 20 and 30W to achieve a maximal level in 10–12 min, which is recommended for symptom-limited exercise tests. Finally, ECG recordings were not accurate in all volunteers because of excessive noise. Accurate ECG recording is absolutely necessary in patients such as lower limb amputees, who often have concomitant cardiovascular disease. Although it can

be anticipated that these patients may have less disturbing movement of the trunk as they reach lower peak workload, a fair ECG measurement needs to be developed.

In conclusion, this study shows that the Cruiser ergometer provides a repeatable and valid measurement of physical fitness in healthy volunteers. The bicycle ergometer is preferred over the Cruiser ergometer because it is more energy-efficient and ECG recording is possible. However, for patients with a lower limb amputation, the Cruiser ergometer seems to be a good alternative. Further research is needed before the Cruiser ergometer can be used in lower limb amputees, particularly with regard to appropriate diagnostic and therapeutic protocols and a fair ECG measurement.

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References

1. Waters RL, Perry J, Antonelli D, Hislop H (1976). Energy cost of walking of amputees: influence of level of amputation. J Bone Joint Surg Am 1976;58:42–46.
2. Chin T, Sawamura S, Fujita H, Nakajima S, Oyaby H., Nagakura Y, et al. Physical fitness of lower limb amputees. Am J Phys Med Rehab 2002;81:321–325.
3. Chin T, Sawamura S, Fuijta H, Oijma I, Oyabu H, et al. VO_2 max as an indicator of prosthetic rehabilitation outcome after dysvascular amputation. Prosthet Orthot Int *2002;*26:44–49.
4. Bostom AG, Bates E, Mazzarella N, Block E, Adler J. Ergometer modification for combined arm-leg use by lower extremity amputees in cardiovascular testing and training. Arch Phys Med Rehabil 1987;68:244–247.
5. Fletcher GF, Lloyd A, Walling JF, Fletcher BJ. Exercise testing in patients with musculoskeletal handicaps. Arch Phys Med Rehabil 1988;69:123–127.
6. Finestone HM, Lampman RM, Davidoff GN, Westbury L, Islam S, Schultz J. Arm ergometry exercise testing in patients with dysvascular amputations. Arch Phys Med Rehabil 1991; 72:15–19.
7. Bar Or O, Zwiren LD. Maximal oxygen consumption test during arm exercise: reliability and validity. J Appl Physiol 1975;38:424–426.
8. Vokac Z, Nell H, Bautz-Holter E, Rodahl K. Oxygen uptake/heart rate relationship in arm and leg exercise, sitting and standing. J Appl Physiol 1975; 39:54–59.
9. Davis JA, Vodak P, Wilmore JH, Krutz P. Anaerobic threshold and maximal aerobic power for three modes of exercise. J Appl Physiol 1976;41:544–550.
10. Casaburi R, Barstow T, Robinson T, Wasserman K. Dynamic and steady-state ventilatory and gas exchange responses to arm exercise. Med Sci Sports Exerc 1992;24:1365–1374.
11. Vestering MM, Schoppen T, Dekker R, Wempe J, Geertzen JHB. Development of an exercise testing protocol for patients with a lower limb amputation: results of a pilot study. Int J Rehabil Res 2005; 28:237–244.
12. Borg GAV (1982). Psychophysical bases of perceived exertion. Med Sci Sports Exerc 1982*;*14:377–381.
13. Vocht De A. Basic handbook for SPSS 14 for Windows. New York: Utrecht Bijleveld press 2006.
14. Mc Graw KO, Wong SP. Forming inferences about some intraclass correlation coefficicients. Psychol Methods 1996; 1:30–46.
15. Lee J, Koh D, Ong CN. Statistical evaluation of agreement between two methods for measuring quantitative variables. Comput Biol and Med 1989; 19:61–70.
16. Tammemagi MC, Frank JW, LeBlanc M, Artsob H, Streiner DL. Methodological issues in assessing reproducibility – a comparative study of various indices of reproducibility applied to repeat Elisa serological tests for Lyme disease. J Clin Epidemiol 1995;48:1123–1132.

17. Laskin J, Bundy S, Marron H, Moore H, Swanson M, Blair M, Humphrey R. Using a Treadmill for the 6-minute Walk Test. J Cardiopulm Rehabil Prev 2007;27:407–410.
18. Toner MM, Glickman EL, McArdle WD. Cardiovascular adjustments to exercise distributed between the upper and lower body. Med Sci Sports Exerc 1990; 22:773–778.



5

Feasibility, safety, and reliability of exercise testing using the combined arm-leg (Cruiser) ergometer in subjects with a lower limb amputation

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Abstract

Background

Physical fitness of patients with a lower limb amputation predicts their walking ability and may be improved by physical exercise and training. A maximal exercise test is recommended prior to training in order to determine cardiovascular risks and design exercise programs. A potentially suitable ergometer for maximal exercise testing in patients with a lower limb amputation is the combined arm-leg (Cruiser) ergometer. The aim of this study was to determine feasibility, safety, and reliability of (sub)maximal exercise testing on the Cruiser ergometer in subjects with a lower limb amputation.

Methods and Findings

Subjects with a lower limb amputation performed 1 submaximal exercise test and 3 maximal exercise tests on the Cruiser ergometer. Feasibility was determined by examining whether key variables such as power output, heart rate and oxygen uptake were correctly and reliably measured, by determining whether a test was a maximal aerobic performance, by studying reasons for non-completion, and by measuring gross efficiency. Safety was analyzed by recording complications, electrocardiogram results, and blood pressure. Reliability was tested by comparing the results of the second and third maximal exercise test. Seventeen subjects (14 men and 3 women) out of 21 preselected subjects completed the study. In general, the maximal Cruiser exercise test was feasible. Almost 75% of the subjects reached a maximal aerobic performance. The test was also safe because no complications occurred, although electrocardiogram and blood pressure could only be reliably recorded in most subjects just before and after the test. Reliability was good: Intraclass correlation was 0.84 for peak oxygen uptake.

Conclusions

The Cruiser ergometer is a feasible, safe, and reliable ergometer for measuring physical fitness of subjects with a lower limb amputation.

Introduction

Patients who require a lower limb amputation (LLA) are often elderly and have a high prevalence of comorbidities, especially cardiovascular diseases[1]. The presence of cardiovascular diseases reduces the chance of being able to walk with a prosthesis and negatively influences mobility outcomes after LLA[2]. Other factors that influence the ability to walk with a prosthesis are amputation level, age and physical fitness[3]. Most patients with a LLA experience a decline in physical fitness, which in turn negatively influences their functional activity level[4,5,6]. In addition, energy costs of walking with a prosthesis are much higher compared with normal walking and increase proportionally with the level of amputation[4]. It has been demonstrated that maximal aerobic capacity, which is a major constituent of physical fitness, is an important predictor for walking ability in patients with a LLA due to vascular disease[5]. Furthermore, exercise training can improve walking ability[6,7].

Before starting exercise training, a maximal exercise test is not only recommended[8] for reasons of safety, especially with regard to cardiovascular risks, but also for developing individually tailored exercise programs. To achieve the best possible outcomes, the cardiovascular system has to be maximally stressed by using the largest possible muscle mass, i.e., by obtaining the highest possible oxygen uptake (peak VO_2) and/or work capacity[9]. Patients with a LLA have lower functional muscle mass by definition. Previous studies have researched the use of different ergometers by LLA patients, including the arm ergometer[10] and the unilateral bicycle ergometer[5,7]. A disadvantage of the arm ergometer is that only the arms and part of the upper body are used. Similar to the arm ergometer, the bicycle ergometer also only involves the muscle mass of one extremity (the leg) and part of the upper body. Patients with a LLA often need help to make the cycling movement with one leg and have difficulty maintaining balance. A combined arm-leg ergometer, the Cruiser ergometer, is a suitable alternative for testing the physical fitness of patients with a unilateral LLA[11]. The Cruiser ergometer has several advantages for its users: they are seated on the ergometer and their back and residual limb are supported; they can exercise without the help of a therapist; and they use the muscle mass of the trunk and 3 extremities, i.e., 1 leg and 2 arms. The use of relatively high muscle mass during exercise on a combined arm-leg ergometer may lead to a higher peak VO_2 [12-14]. Previous research has demonstrated that the Cruiser ergometer is a

valid, reliable, and safe instrument for measuring the physical fitness of healthy volunteers[12]. The next step is to study the Cruiser ergometer in subjects with a LLA. Therefore, the aims of the current study are 1) to explore the feasibility of the Cruiser ergometer in maximal exercise testing in subjects with a LLA, 2) to evaluate the safety of the Cruiser ergometer, and 3) to study the test-retest reliability of a repeated maximal exercise test on the Cruiser ergometer.

Materials and methods

Population

Twenty-one subjects with a LLA (18 men and 3 women) living in the North of the Netherlands were screened for participation this study. The principal investigator (ES) informed specialists in Rehabilitation Medicine and certified prosthetists working in the North of the Netherlands about this study. These specialists and prosthetists subsequently asked subjects with a LLA to participate in the study and provided them with written information. Following the subjects' agreement to participate, the principal investigator (ES) contacted the subjects to screen for inclusion and exclusion criteria. Inclusion criteria were: age between 18 and 75 years and a LLA (unilateral transfemoral amputation, knee disarticulation, or transtibial amputation). Exclusion criteria were: coronary heart disease, clinically relevant arrhythmia, hypertension (diastolic blood pressure > 100 mm Hg or systolic blood pressure >180 mm Hg), recently diagnosed pulmonary embolism, bilateral LLA, upper limb amputation, and cognitive impairments leading to inability to cooperate or inability to obtain consent[8].

Prior to their participation, subjects signed an informed consent form. All tests were conducted in accordance with the Declaration of Helsinki. The local Medical Ethics Committee (METc UMC Groningen) approved the study (file number METc 2011/123).

Instruments

The Cruiser ergometer (Enraf-Nonius serial number: 3800EN014, ultimo number 10-3013, Delft, The Netherlands) was standardized for use in exercise testing. It is a combined arm-leg ergometer equipped with a comfortable seat (Fig 1). The foot of the user is placed against a fixed footrest, which can be adjusted to the subjects' length. Users can perform tests on the ergometer without

their prosthesis. The residual limb is supported by a special stump support connected to the seat. The footrest is used to push off and make the seat move backward. Users can move the seat forward again by pulling the handlebars. In this way, arms and leg are simultaneously used to overcome the resistance provided by the ergometer. The position of the footrest of the ergometer was adjusted to a fixed setting for each subject during the tests. The ergometer could only be set in a constant power mode of between 35 and 60 revolutions per minute (rpm) and subjects were instructed to maintain 50 rpm[12-14]. The accuracy of the Cruiser ergometer is ± 10% power output (PO in W) and ± 2 rpm speed. Cardiorespiratory parameters were recorded using an Oxycon Delta (Jaeger, Bunnik, the Netherlands). Subjects wore a face mask and ventilation (VE in l/min), oxygen uptake (VO_2 in l/min), and carbon dioxide output (VCO_2 in l/min) were continuously measured. Peak VO_2 and peak VCO_2 were defined as the highest average values obtained over a 30- s period. Blood pressure was measured manually at the beginning of the test, immediately after the test was completed, and after the cooling down period. Heart rate (HR in b/min) was continuously recorded with a 12-lead electrocardiogram (ECG).



Fig 1. The Cruiser ergometer

Study design

All subjects performed 4 exercise tests (1 submaximal and 3 maximal tests) on 3 different days, with an interval of more than 1 week between each test day. On day 1, the principal investigator screened the subjects for contraindications by means of a questionnaire, ECG, and measurement of blood pressure. Next, the subjects started the submaximal test to become acquainted with the Cruiser ergometer and to determine the gross mechanical efficiency (GE). The submaximal exercise test consisted of 3 minutes rest on the Cruiser followed by 3 minutes exercise at 20 W and 3 minutes exercise at 30 W at 50 rpm. GE of the participants was measured during the final 30 seconds of the submaximal blocks of 20 and 30 W. GE was determined to analyze the mechanical efficiency of the movement on the Cruiser ergometer. GE is an important measure because it can be used to evaluate future training effects as well as motor learning effects of the Cruiser ergometer[13,14]. After the submaximal test, subjects had a rest period of more than 10 minutes, which was followed by the first maximal exercise test. The maximal exercise test was repeated on days 2 and 3. The first maximal exercise test was seen as a familiarization test, and tests 2 and 3 were used to determine test-retest reliability. Each maximal exercise test started with 3 minutes rest on the Cruiser and was followed by a 3 minute warm-up at 20 W at 50 rpm. After the warm-up, work load was increased by 10 W per minute, keeping speed at 50 rpm, until the point of exhaustion was reached or until the physician stopped the test. Reasons for terminating the test were inability to maintain 50 rpm, pain in arms or legs, chest pain, dizziness or faintness, severe dyspnea, pallor, cyanosis, or cold and clammy skin. The test was also stopped by the investigator in case of ECG abnormalities. After completing the test, subjects were observed for another 3 minutes. The protocol was derived from an earlier study in healthy volunteers[12]. Taking the lower exercise capacity of subjects with a LLA into account, appropriate adaptations in workload were made. The maximal exercise test protocol was consistent in all subjects over the 3 test days.

Outcome

Feasibility. To evaluate the feasibility of the Cruiser ergometer as an instrument for measuring the physical fitness of subjects with a LLA, this study specifically focused on the indicators acceptability, demand, and practicality[15]. To this end, a 5-step approach was used. First, it was investigated whether all relevant

variables could be measured during the test. Second, subjects who dropped out of the study were analyzed, and this analysis served to refine exclusion criteria for an exercise test on the Cruiser ergometer. Third, when subjects experienced symptoms of dyspnea and fatigue, these symptoms were assessed using a 10-point Borg scale at peak load for dyspnea and for arm and leg muscle fatigue so as to determine the impact of the test[16]. Fourth, the maximal aerobic performance was evaluated for each test. Since no reference data are available of the maximal aerobic performance on the Cruiser ergometer using one leg and two arms, the criteria for the bicycle ergometer were used. A performance was regarded as a maximal aerobic performance when 1 or more of 3 criteria were fulfilled: a heart rate of more than 85% of predicted, maximal ventilation of more than 75% of predicted, or a respiratory exchange rate (RER) of more than 1.1[17]. In addition, it was studied to what extent VO_2peak was related to predicted VO_2peak, which is age and gender dependent (calculated for the bicycle ergometer). Fifth, the GE of movement during the submaximal period of 20 and 30 W was calculated and compared to previous research of Simmelink et. al in healthy volunteers[13,14]. GE (in %) is derived from the ratio between the mechanical power output (Po) and the metabolic power (Pmet), as shown in Eq 1[18].

(1) $GE(\%) = \frac{Po}{Pmet} 100\%$

The metabolic power (Pmet) was calculated using Eq 2.

(2) $P_{met}(w) = VO_2[\frac{(4.940\ RER+16040)}{60}]$

Safety. Subjects became acquainted with the Cruiser ergometer during the submaximal exercise test. When no complications occurred, they started the maximal exercise test. It was studied whether ECG and blood pressure could be reliably recorded prior to, during, and after the (sub)maximal exercise tests. Outcome measures for safety were ECG abnormalities or the occurrence of adverse events during the tests.

Reliability. Test-retest reliability of the maximal exercise test on the Cruiser ergometer was studied by comparing outcome measures of the second and third tests. Outcome measures for reliability were peak oxygen uptake (VO_2), peak heart rate (HR), peak power output (PO), peak ventilation (VE), peak breathing frequency (BF), and respiratory exchange rate (RER).

Statistics

Data analyses were performed using SPSS version 23.0 for Windows (SPSS, Chicago, Illinois, USA). Descriptive statistics were generated for all variables (mean ± SD).

Reliability of the second and third maximal exercise tests was assessed by means of paired t-tests, the one-way random effect model and single measure-intraclass correlation coefficient (ICC), and Bland-Altman plots. Level of significance was set at $p < 0.05$.

Results

Between May 2012 and September 2015 a total of 21 subjects were screened for inclusion. One subject was excluded because of a Syme amputation, which made it impossible to perform the tests without using a prosthesis. Three other subjects dropped out of the study due to medical reasons. Consequently, the complete test results of 17 subjects (14 men and 3 women) could be obtained. Mean age was 54.5 y (SD 18.6, range 25-80), mean BMI 25.2 kg/m^2 (SD 4.0, range 18.4-31.2), and the mean time since amputation was 96.6 months (SD 111.2, range 2-372). Subject characteristics and outcome measures are shown in Table 1.

Feasibility

Three subjects dropped out of the study due to medical reasons. Subject 1 developed an allergic skin reaction located at the site of the ECG suction cups after the first day. The subject recovered within three days but did not perform days 2 and 3 of the protocol. Subject 2 showed signs of cardiac ischemia during the first maximal exercise test and was referred to a cardiologist. This subject withdrew from the study. Subject 3 dropped out after day 2 because of an increase in stump pain. Another subject had hypertension on day 1 (196/103 mmHg) and was referred to his general practitioner. This subject, however, could re-enter the study after treatment. All subjects who completed the protocol (n=17) were able to perform the movement on the Cruiser ergometer. In most cases (second test 9/17 subjects, third test 11/17 subjects), the chosen protocol led to an exercise time of 10-15 minutes, which is considered to be the ideal duration of a maximal exercise test. Monitoring of cardiopulmonary parameters was possible in all subjects.

Table 1. Individual data of the submaximal and 3 maximal exercise tests on the Cruiser ergometer in 17 subjects with a lower limb amputation (mean scores with standard deviation (SD)

Subject Characteristics							GE		1st Cruiser test						
sex	amplevel	time since amp	Reasfor amp	use of B-bloc	Age (y)	BMI (kg/m2)	20W	30W	HR (b/min)	PO (W)	RER	VO_2 (l/min)	VO_2/ VO_2pred (%)	BF (br/min)	VE (l/min)
M	TF	4	cancer	yes	66	27.2	10.3	8.6	142	70	1.18	1.16	49	25	50
M	TF	13	trauma	no	26	20.7		10.3	120	90	1.08	1.49	45	16	38
M	TT	2	vasdi	no	71	23.9	5.4		150	20	1.12	1.59	79	14	59
M	TT	156	trauma	no	48	28.7	8.0	6.8							
M	TF	2	painsy	no	73	23.8	8.0	5.5	145	60	1.09	1.51	75	25	46
F	TT	30	trauma	no	31	18.6	14.4	12.0	165	90	1.2	1.26	69	30	42
M	TF	3	trauma	no	53	27.0	13.8	8.3	156	100	1.01	1.56	65	26	55
M	TF	24	trauma	no	67	27.1	10.6	8.8	126	40	0.95	0.93	46	27	38
M	TT	4	vasdi	no	61	18.4	15.7	9.9	150	70	1	1.12	61	26	42
M	KD	84	neufib	no	33	27.2	9.2	6.9	139	100	1	1.96	40	27	53
F	TF	132	cancer	no	25	26.1	10.0	8.0	184	130	1.1	2.29	117	47	73
F	KD	96	trauma	no	40	19.1	18.1	14.0	165	80	0.96	1.40	87	28	38
M	TF	324	trauma	no	80	28.4	2.7		143	20	1.14	2.23	130	44	80
M	TT	372	trauma	yes	78	27.8	15.0	7.9	186	60	1.04	1.31	71	20	38
M	TT	132	trauma	no	68	31.2	9.7	8.3	152	190	1.1	3.06	142	42	107
M	TT	108	trauma	no	43	23.0	13.2	10.1	117	100	1.05	1.66	59	24	48
M	TF	156	trauma	no	64	30.0	10.3	9.1	102	100	1.13	1.41	64	17	46
Mean		96.6			54.5	25.2	10.9	9.0	146.4	82.5	1.07	1.62	74.9	27.4	53.3
SD		111.2			18.5	4.0	4.0	2.1	22.9	41.7	0.07	0.54	30.3	9.6	18.9

Subject Characteristics							2nd Cruiser test							3rd Cruiser test						
sex	amplevel	time since amp	Reasfor amp	use of B-bloc	Age (y)	BMI (kg/ m2)	HR (b/ min)	PO (W)	RER	VO_2 (l/ min)	VO_2/ VO_2 pred (%)	BF (br/ min)	VE (l/ min)	HR (b/ min)	PO (W)	RER	VO_2 (l/ min)	VO_2/ VO_2 pred (%)	BF (br/ min)	VE (l/ min)
M	TF	4	cancer	yes	66	27.2	95	50	1.00	0.94	40	24	31	148	90	1.20	1.21	52	26	50
M	TF	13	trauma	no	26	20.7	128	100	1.23	1.38	41	16	38	122	100	1.14	1.52	46	19	41
M	TT	2	vasdi	no	71	23.9	158	20	1.22	1.47	73	34	77	133	20	1.25	1.40	69	30	76
M	TT	156	trauma	no	48	28.7	139	140	1.07	2.58	104	33	83	112	100	1.02	1.69	68	28	46
M	TF	2	painsy	no	73	23.8	142	90	1.11	1.82	88	23	53	153	90	1.07	1.87	90	27	51
F	TT	30	trauma	no	31	18.6	147	70	1.12	1.14	62	24	33	171	100	1.24	1.35	56	24	47
M	TF	3	trauma	no	53	27.0	143	100	1.03	1.49	63	23	50	145	100	1.04	1.52	64	25	52
M	TF	24	trauma	no	67	27.1	96	40	0.83	0.76	36	25	27	133	30	0.92	0.84	40	32	38
M	TT	4	vasdi	no	61	18.4	139	70	1.03	0.98	54	25	42	142	80	1.11	1.14	63	26	48
M	KD	84	neufib	no	33	27.2	165	110	0.98	1.92	61	25	55	173	120	1.07	1.92	61	29	71
F	TF	132	cancer	no	25	26.1	186	130	1.01	1.99	102	37	59	184	130	1.08	1.87	96	34	52
F	KD	96	trauma	no	40	19.1	186	90	1.12	1.39	88	25	43	194	100	1.15	1.49	94	29	54
M	TF	324	trauma	no	80	28.4	140	20	1.22	2.02	118	50	82	134	20	1.36	1.82	106	49	70
M	TT	372	trauma	yes	78	27.8	126	70	0.93	1.31	70	21	43	139	70	1.00	1.31	70	21	43
M	TT	132	trauma	no	68	31.2	134	160	0.95	2.56	118	33	72	152	180	1.05	3.05	141	41	97
M	TT	108	trauma	no	43	23.0	105	110	1.01	1.76	63	20	49	122	110	1.00	1.63	58	17	41
M	TF	156	trauma	no	64	30.0	103	100	1.10	1.36	62	18	41	117	110	1.06	1.57	71	19	46
Mean		96.6			54.5	25.2	137.2	86.5	1.06*	1.58	73.1	28.0	51.7	145.5	91.2	1.11*	1.60	73,2	26.8	54.3
SD		111.2			18.5	4.0	27.4	39.5	0.11	0.52	25.9	8.0	17.6	23.6	40.1	0.11	0.47	25.2	8.3	15.5

Abbreviations: GE= Gross Efficiency in percentage (%) ; M= male, F= female; Amp level= amputation level; TF= transfemoral, TT= transtibial, KD=knee disarticulation; time since amp= time since amputation in months; Reas for amp= reason for amputation, vasdi= vascular disease, painsy=pain syndrome, neufib= neurofibromatosis; Age in years; BMI= body mass index in kg/m2; HR = peak heart rate in beats/minute; PO= peak power output in Watt; RER; respiratory exchange rate at the end of the test; VO2= peak oxygen uptake in liter/minute; VO2/VO2pred= peak oxygen uptake in relation to the predicted oxygen uptake in percentage; BF= peak breathing frequency in breaths/minute; VE= peak ventilation in liter/minute.* $p<0.05$ for paired sample test between second and third test

The Borg scores, though relatively low, were fairly consistent for all of the tests (Table 2). The Borg score for arm fatigue was significantly higher for the first maximal test than for the second test. There were no significant differences between the tests with regard to other Borg scores.

Table 2. Borg scores of the 3 maximal exercise tests in 17 subjects with a lower limb amputation.

	Max test 1 Mean (SD)	**Max test 2 Mean (SD)**	**Max test 3 Mean (SD)**
Dyspnea peak	2.9 (3.0)	2.9 (2.0)	3.0 (2.4)
Leg fatigue peak	3.2 (2.8)	2.8 (2.6)	3.6 (2.8)
Arm fatigue peak	3.9 (2.5) *	3.0 (2.6)	3.5 (2.1)

*significant difference between Borg score for fatigue of the arms between first and second test on the Cruiser ergometer

The majority of the subjects had a maximal aerobic performance: 11 of 16 subjects performed maximal at test 1, 12 of 17 subjects performed maximal at test 2, and 14 of 17 subjects performed maximal at test 3. VO_2 peak was 75 % of predicted (SD 30, range 40-140%) for test 1; for test 2 it was 73% of predicted (SD 26, range 36-118%); and for test 3 it was also 73% of predicted (SD 25, range 40-141%) (Table 1). In most cases, the test was stopped because coordination problems of arms and leg, which resulted in an inability to maintain the speed of 50 rpm (Table 3).

The mean GE at 20 W was 10.9 % (SD 4.0, range 2.7- 19.1, n = 16) with one missing data point and 9.0% (SD 2.1, range 5.5-14.0, n = 15) at 30 W with two missing data points (Table 1).

Table 3. Reasons for stopping the maximal exercise test.

	Test 1 n=16	**Test 2** n=17	**Test 3** n =17
Coordination problems (%)	37.5% (6/16)	47.1% (8/17)	52.9% (9/17)
ECG abnormalities (%)	31.3 % (5/16)	23.5% (4/17)	17.7 % (3/17)
Muscle fatigue in the leg (%)	18.8 % (3/16)	17.7% (3/17)	17.7% (3/17)
Muscle fatigue in the arms (%)	6.3% (1/16)	5.9% (1/17)	5.9% (1/17)
Dyspnea (%)	6.3% (1/16)	5.9% (1/17)	5.9% (1/17)

Safety

Most of the tests were performed without complications. As mentioned earlier, three adverse events occurred, resulting in attrition of three subjects. These adverse events were an allergic skin reaction due to the ECG suction cups, an abnormal ECG, and an increase in pain of the stump without physical signs after exercising on the Cruiser ergometer. The ECG could be reliably recorded in all subjects, at least during low to medium workloads. The investigator had to stop a number of tests because the ECG was affected by muscle activity of the arms and thorax (Table 3). Blood pressure could not be reliably measured during exercise, but only before and after the test.

Reliability

The first maximal exercise test was a familiarization trial. Tests 2 and 3 were used for test-retest reliability analysis. No significant differences were present, except in RER (Table 1). A slight learning/ practice effect was seen, especially with regard to the peak workload in the 3 sequential maximal exercise tests.

The ICCs are presented in Table 4. It is advocated that an ICC of > 0.75 indicates good agreement[19,20]. This means there is a good agreement for the outcome measures VO_2peak and POpeak between tests 2 and 3.

Finally, Bland-Altman plots were constructed. The plot for VO_2 shows a bias close to zero with two outliers (Fig 2). Limits of agreement are 0.02 ± 0.58 (mean difference ±2 SD). The plot for HR shows a similar pattern (Fig 3), although this plot has only one outlier. Limits of agreement are -8.4 ±39.5. Furthermore, the Bland-Altman plot for PO (Fig 4) has a bias close to zero with 2 outliners. Limits of agreement are -4.7±34.0.

Table 4. ICC of the second and third test for peak oxygen uptake, heart rate, and power output

	ICC (single measure)	**95% CI**
VO_2, l/min	0.84	0.61 – 0.94
HR, b/min	0.68	0.32 – 0.87
PO, W	0.91	0.77 – 0.97

Abbreviations: VO_2= peak oxygen uptake , HR = peak heart rate, PO=peak power output; ICC= intraclass correlation coefficient, 95% CI= 95% confidence interval.

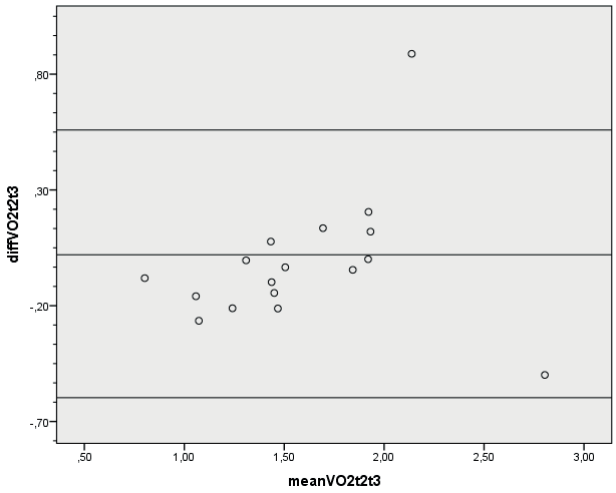

Figure 2. Bland-Altman plot for peak oxygen uptake of 17 subjects with a lower limb amputation during exercise testing on the Cruiser ergometer
diff VO2t2t3 = difference between peak oxygen uptake in l/min between test 2 and test 3 mean VO2t2t3 = mean peak oxygen uptake in l/min of test 2 and test 3.

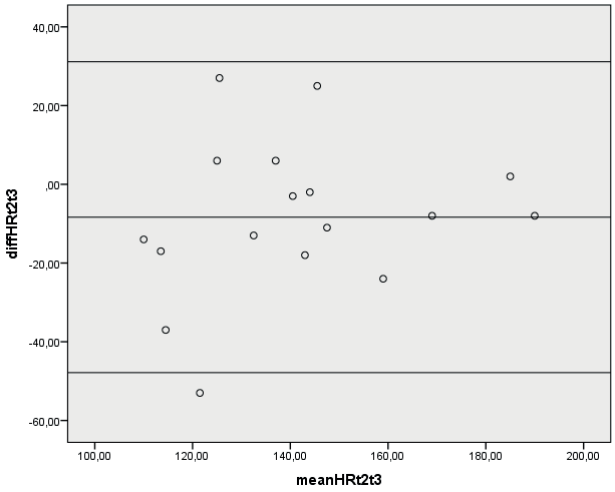

Figure 3. Bland-Altman plot for peak heart rate of the exercise test on the Cruiser ergometer of 17 subjects with a lower limb amputation
diffHRt2t3 = difference between peak heart rate (b/min) between test 2 and test 3 on the Cruiser ergometer. mean HRt2t3 = mean peak heart rate (b/min) of test 2 and test 3 on the Cruiser ergometer

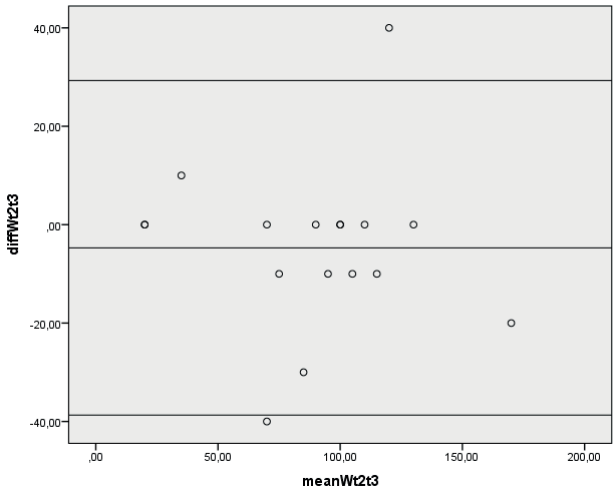

Figure 4. Bland-Altman plot for peak power output of the exercise test on the Cruiser ergometer of 17 subjects with a lower limb amputation
diffWt2t3 = difference between peak power output in Watt between test 2 and test 3 mean Wt2t3 = mean peak power output in Watt of test 2 and test 3

Discussion

In this study, feasibility, safety, and reliability of exercise testing on the combined arm-leg Cruiser ergometer were evaluated in subjects with a LLA. The test procedure was feasible because almost all subjects were able to perform the combined arm-leg movement and managed to reach adequate symptom scores. Furthermore, a large majority of subjects reached a maximal aerobic performance and most variables of interest could be measured appropriately. The test procedure was safe and ECGs could be reliably recorded in most cases. Approximately 20% of ECG recordings were severely influenced by muscle activity of arms and thorax. In addition, blood pressure could not be measured during the tests on the upper arm or on the wrist. Finally, the test-retest reliability was good.

Feasibility

Three subjects dropped out of this study. One subject had an allergic skin reaction to the ECG suction cups. Although the skin reaction healed spontaneously within

a few days, the subject was withdrawn from the study. ECGs are now in clinical practice recorded using self-adhesive electrodes. Another subject dropped out because his pre-existent stump pain worsened after test 2, despite the use of a special stump support attached to the Cruiser. Most subjects, however, felt the stump support was sufficiently comfortable and did not experience pain or discomfort in their stump.

Borg scores for dyspnea and fatigue of the arms and leg were relatively low (mean scores between 2.8 and 3.9). In a study on healthy volunteers, Borg scores for fatigue of the arms (4.9-5.0) and legs (4.3-4.5) were higher[12]. It could be hypothesized that the real maximal aerobic capacity was not measured in our study population. In the study of Wezenberg[21], 93% of subjects reached a RER peak value of more than 1.1. In our study, at least 1 of the following 3 criteria had to be fulfilled in order to consider a test as a maximal aerobic performance: a heart rate of more than 85% of predicted, maximal ventilation of more than 75% of predicted, and a RER of more than 1.1[17]. Following these criteria, at the first test 69% (n=11/16) of subjects had a maximal exercise test and at the second and thirds test 71% (n=12/17) and 82% (n= 14/17) of subjects had a maximal exercise test, respectively. These scores may be explained by several factors. Subjects may have experienced increased symptom perception due to the unfamiliar type of exercise, to coordination problems, and to the relatively large impact of arm exercise in relation to leg exercise. In addition, a few tests were discontinued due to ECG disruptions. Finally, the fixed protocol with relatively large increments of workload may have been less appropriate.

Some learning effects were found, including higher VO_2 and greater power output, which have also been demonstrated in previous research[12]. The GE varied greatly between subjects and ranged between 2.7- 18.1% at 20 W and 5.5- 14.0 %. at 30 W. In earlier research in healthy young subjects, a GE of 13.0 in men and 15.0% in women at 45 W was found[13]. When using the Cruiser ergometer in the future for testing and training, it is important to realize that motor learning effects can vary among subjects.

Safety

Although ECG recordings were possible during the exercise test on the Cruiser, they were hampered by muscle activity of arms and thorax. Nevertheless, ECG abnormalities were found in one subject, who was referred to a cardiologist. Exercise stress testing on the bicycle ergometer has a sensitivity of 33-50 %

and a specificity of 84-96% for detecting coronary artery disease in patients with suspected myocardial ischemia. ECG abnormalities are more easily detected after stopping the exercise. Therefore, in clinical practice, ECGs are recorded 2 minutes after the exercise phase[22,23]. In addition, blood pressure could not be measured during the test, neither with an upper arm monitor or manually measured nor with a pulse monitor This is a limitation of the Cruiser test with respect to safety especially for patients with a LLA with a high risk of cardiovascular disease. In this study, however, no subject had a systolic blood pressure of > 225 mm Hg or a diastolic blood pressure of > 99 mmHg directly after the exercise phase. In future research measurement of blood pressure may be possible, e.g. by using a discontinuous protocol. In addition, further research into the question whether blood pressure measurement before and directly after the test is sufficient, has to be performed. Finally, with the exception of the three subjects who dropped out of the study due to medical reasons, no other subjects experienced medical problems during or after the tests.

Reliability

Reliability was measured by comparing the second and third test on the Cruiser ergometer and was found to be satisfactory in general, as can be deducted from the ICC and Bland-Altman plots. However, the Bland-Altman plots revealed some outliers. The outliers may be explained by a difference in effort of some subjects between the second and third test and by prematurely stopping the test in 7 subjects because of suspected ECG abnormalities. In retrospect, the premature stop of the tests was not necessary, for the abnormalities could be explained by muscle activity in all but one subject. It is recommended that both subject and investigator learn how to use the Cruiser ergometer prior to testing so as to improve reliability.

Limitations of this study

As shown in Table 1, physical fitness of the study population varied greatly. This is to be expected in patients with a LLA, who follow a rehabilitation program to learn to walk with a prosthesis. Most subjects in our study were trauma patients, which is unusual given that peripheral arterial disease is the main reason for performing a LLA[24]. It is likely that selection bias occurred in this study. Specialists in Rehabilitation Medicine and certified prosthetists located in the North of the Netherlands were asked by the principal investigator to recruit subjects with a LLA

for this study. This might have led to a selection bias of motivated and relatively healthy subjects. Consequently, the findings of this study might overestimate the physical fitness of this population The study population was not large enough to perform a comparative analysis between amputees with different causes of the amputation such as trauma, vascular disease, cancer, pain syndrome and neurofibromatosis. The time since amputation varied between 2 to 372 months, which is a large variation. This variation, however, enabled us to study the Cruiser in both inexperienced and experienced subjects. No differences were seen with regard to ease of use and becoming acquainted with the Cruiser ergometer. One protocol was used in all subjects. For some subjects, the submaximal level of 30 W was already the maximal power output they could reach on the Cruiser ergometer. Two subjects only reached a peak power output of 20 W, which was still a maximal aerobic performance when considering the criteria for maximal aerobic exercise. In future studies, individually tailored exercise protocols are needed instead of a one-size-fits-all protocol. These protocols should aim at a test duration of 10-15 minutes[19].

Recommendations for further research

An implementation study is recommended to design patient- specific protocols for using the Cruiser ergometer at the start of the rehabilitation period of patients with a LLA. Also, future research is needed to design exercise training protocols using the data from the baseline Cruiser exercise test.

Conclusions

The Cruiser ergometer is a feasible, safe, and reliable testing instrument for measuring the physical fitness of this study population with a LLA. Adequate practice before actual testing, and the development of individually tailored testing protocols are advised.

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References

1. Remes L, Isoaho R, Vahlberg T, Hiekkanen H, Korhonen K, Viitanen M, et al. Major lower extremity amputation in elderly patients with peripheral arterial disease: incidence and survival rates. Aging Clin Exp Res. 2008;20: 385-393
2. Kaptein S, Geertzen JHB, Dijkstra PU. Association between cardiovascular diseases and mobility in persons with lower limb amputation: a systematic review. Disabil Rehabil. 2018;40: 883-888.
3. Kahle JT, Highsmith MJ, Schaepper H, Johannesson A, Orendurff MS, Kaufman K. Predicting Walking Ability Following Lower Limb Amputation: an Updated Systematic Literature Review. Technol Innov. 2016;18: 125-137.
4. Chin T, Sawamura S, Fujita H, Ojima I, Oyabu H, Nagakura Y, et al. %VO2max as an indicator of prosthetic rehabilitation outcome after dysvascular amputation. Prosthet Orthot Int. 2002;26: 44-49.
5. Wezenberg D, van der Woude, L H, Faber WX, de Haan A, Houdijk H. Relation between aerobic capacity and walking ability in older adults with a lower-limb amputation. Arch Phys Med Rehabil. 2013;94: 1714-1720.
6. van Velzen JM, van Bennekom CA, Polomski W, Slootman JR, van der Woude, L H, Houdijk H. Physical capacity and walking ability after lower limb amputation: a systematic review. Clin Rehabil. 2006;20: 999-1016.
7. Chin T, Sawamura S, Shiba R. Effect of physical fitness on prosthetic ambulation in elderly amputees. Am J Phys Med Rehabil. 2006;85: 992-996.
8. Riebe D, Franklin BA, Thompson PD, Garber CE, Whitfield GP, Magal M, et al. Updating ACSM's Recommendations for Exercise Preparticipation Health Screening. Med Sci Sports Exerc. 2015;47: 2473-2479.
9. Bostom AG, Bates E, Mazzarella N, Block E, Adler J. Ergometer modification for combined arm-leg use by lower extremity amputees in cardiovascular testing and training. Arch Phys Med Rehabil. 1987;68: 244-247.
10. Erjavec T, Vidmar G, Burger H. Exercise testing as a screening measure for ability to walk with aprosthesis after transfemoral amputation due to peripheral vascular disease. Disabil Rehabil. 2014;36: 1148-1155.
11. Vestering MM, Schoppen T, Dekker R, Wempe J, Geertzen JH. Development of an exercise testing protocol for patients with a lower limb amputation: results of a pilot study. Int J Rehabil Res. 2005;28: 237-244.
12. Simmelink EK, Wempe JB, Geertzen JH, Dekker R. Repeatability and validity of the combined arm-leg (Cruiser) ergometer. Int J Rehabil Res. 2009;32: 324-330.
13. Simmelink EK, Borgesius EC, Hettinga FJ, Geertzen JH, Dekker R, van der Woude, L H. Gross mechanical efficiency of the combined arm-leg (Cruiser) ergometer: a comparison with the bicycle ergometer and handbike. Int J Rehabil Res. 2015;38: 61-67.
14. Simmelink EK, Wervelman T, de Vries HS, Geertzen JHB, Dekker R, van der Woude, L H V. One-day low-intensity combined arm-leg (Cruiser) ergometer exercise intervention: cardiorespiratory strain and gross mechanical efficiency in one-legged and two-legged exercise. Int J Rehabil Res. 2017;40: 347-352.

15. Bowen DJ, Kreuter M, Spring B, Cofta-Woerpel L, Linnan L, Weiner D, et al. How we design feasibility studies. Am J Prev Med. 2009;36: 452-457.
16. Borg GA. Psychophysical bases of perceived exertion. Med Sci Sports Exerc. 1982;14: 377-381.
17. Rieger BW. Principles of Exercise Testing and Interpretation: Including Pathophysiology and Clinical Applications, 3rd Edition. Medicine & Science in Sports & Exercise. 2000;32: 1364.
18. Garby L, Astrup A. The relationship between the respiratory quotient and the energy equivalent of oxygen during simultaneous glucose and lipid oxidation and lipogenesis. Acta Physiol Scand. 1987;129: 443-444.
19. Lee J, Koh D, Ong CN. Statistical evaluation of agreement between two methods for measuring a quantitative variable. Comput Biol Med. 1989;19: 61-70.
20. Tammemagi MC, Frank JW, Leblanc M, Artsob H, Streiner DL. Methodological issues in assessing reproducibility--a comparative study of various indices of reproducibility applied to repeat ELISA serologic tests for Lyme disease. J Clin Epidemiol. 1995;48: 1123-1132.
21. Wezenberg D, de Haan A, van der Woude, L H, Houdijk H. Feasibility and validity of a graded one-legged cycle exercise test to determine peak aerobic capacity in older people with a lower-limb amputation. Phys Ther. 2012;92: 329-338.
22. Puelacher C, Wagener M, Abacherli R, Honegger U, Lhasam N, Schaerli N, et al. Diagnostic value of ST-segment deviations during cardiac exercise stress testing: Systematic comparison of different ECG leads and time-points. Int J Cardiol. 2017;238: 166-172.
23. Task Force Members, Montalescot G, Sechtem U, Achenbach S, Andreotti F, Arden C, et al. 2013 ESC guidelines on the management of stable coronary artery disease: the Task Force on the management of stable coronary artery disease of the European Society of Cardiology. Eur Heart J. 2013;34: 2949-3003.
24. Fortington LV, Rommers GM, Postema K, van Netten JJ, Geertzen JH, Dijkstra PU. Lower limb amputation in Northern Netherlands: unchanged incidence from 1991-1992 to 2003-2004. Prosthet Orthot Int. 2013;37: 305-310.



6

Inter-observer and intra-observer reliability of determining aerobic threshold and respiratory compensation point using the combined arm-leg (Cruiser) ergometer in able bodied subjects and subjects with a lower limb amputation

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Abstract

Purpose: To analyze inter-observer and intra-observer reliability of determining first (VT1) and second (VT2) ventilatory thresholds in subjects with a lower limb amputation (LLA) and able bodied (AB) subjects during a peak exercise test on the arm-leg (Cruiser) ergometer.

Materials and Methods: Previously published data of exercise tests on the Cruiser ergometer of subjects with a LLA (n=17) and AB subjects (n=30) were analyzed twice by two observers. The VT1 and VT2 were determined based on ventilation plots . Differences in determining the VT1 and VT2 between the observers for the first and second analysis were analyzed. To quantify variation in measurement a variance component analysis was performed. Bland and Altmann plots were made and limits of agreement were calculated.

Results: The number of observations in which thresholds could not be determined differed significantly between observers and analysis. Variation in VT1 between and within observers was small (0-1.6%) compared to the total variation, for both the subjects with a LLA and AB subjects. The reliability coefficient for VT1 was > 0.75 and limits of agreement were good.

Conclusions: Intra- and inter-observer reliability of determining the VT1 on the Cruiser ergometer is good. Determination of VT2 was less reliable.

Keywords: ventilatory thresholds, ergometer, exercise test, exercise training, lower limb amputation.

Introduction

Most persons with a lower limb amputation (LLA) are elderly with a high prevalence of cardiovascular disease and low physical fitness [1-3]. Low physical fitness results in an undesirable decrease of activities and participation[4,5]. Therefore, it is important for persons with a LLA to start exercising prior to or as soon as possible after amputation in a safe, comfortable, and efficient manner to improve physical fitness. Before starting exercise training, a valid, reliable and safe physical exercise test especially with regard to cardiovascular risks, is required, to design exercise training programs. Additionally, outcomes of exercise tests should help to predict successful ambulation with a prosthesis[6-8]. To stimulate physical fitness as soon as possible after surgery, persons with a LLA have to be able to perform large muscle exercises even in the absence of a prosthesis . Testing and exercising on a bicycle ergometer is limited as persons with a LLA cannot make a complete cycling movement with one leg without help and a limited muscle mass is used because of the amputation[8].
The Cruiser ergometer, a combined arm-leg ergometer, is appropriate for persons with a unilateral LLA to test physical fitness[9-13]. Advantages of the Cruiser ergometer are that persons with a LLA can sit on it with adequate back support and support for the residual limb[13]; they can safely exercise with one leg, both arms and trunk without help of a test assistant and they use relatively large muscle mass.

A protocol for peak cardiopulmonary exercise testing (CPET) can be applied on the Cruiser ergometer[13]. This protocol is used in lung and cardiac rehabilitation for evaluation of exercise intolerance and exercise-related symptoms which cannot be determined by means of resting pulmonary and cardiac function testing or submaximal testing[14,15]. Furthermore, on basis of such a peak exercise test the three-phase model of lactic acid accumulation potentially allows determination of a first (VT1) and second (VT2) ventilatory threshold. VT1 and VT2 are used to individually prescribe exercise training programs[16]. Training prescription based on these thresholds is expected to elicit better responses in improvement of exercise capacity after training than exercise prescription based on maximal oxygen uptake (VO_2max) or maximum heart rate (HR max)[17,18]. The VT1 and VT2 increase with age and are lower in arm exercises compared to leg exercises. Additionally they are protocol and disability specific, in which the

best protocol to reach the maximal exercise capacity within 10-12 minutes has to be individually chosen[14]. It is unknown whether VT1 and VT2 can be reliably determined during peak exercise testing on the Cruiser ergometer. In addition, it is unknown whether differences exist in the level and correct determination of VT1 and VT2 between observers and if there are differences between subjects with a LLA and able bodied (AB) subjects.

The aims of the study were therefore to analyze inter-observer and intra-observer reliability of determining VT1 and VT2 in subjects with a LLA and AB subjects exercising on the Cruiser ergometer by two observers and secondly to analyze differences in VT1 and VT2 between subjects with a LLA and AB subjects.

Materials and Methods

Study design

The current study is based on re-analysis of data of two previous studies regarding standardized peak cardiopulmonary exercise tests on the Cruiser ergometer of subjects with a LLA (transtibial, knee disarticulation or transfemoral level; n=17; men14)[13] and AB subjects (n=30; men16)[10,]. Two experienced observers, a sports physician and a rehabilitation physician determined following a standardized protocol the VT1 and VT2 of both groups on two occasions at least 3 months apart.

The observers independently analyzed data were blinded for the results of each other and for their own results of the first assessment. The Medical Ethics Committee (METc) of the UMC Groningen had approved those studies (METc 2011/123 and METc 2005/237) and gave permission to re-analyze the data for this study.

Instruments and test protocol

The Cruiser ergometer[10,13] (Enraf-Nonius serial number: 3800EN014, Delft, The Netherlands) was used for the peak exercise test in both groups. The test protocol differed somewhat between the groups. Subjects with a LLA started with 3 minutes rest followed by a 3 minute warm-up at 20 W. After the warm-up the work load was increased by 10 W per minute until the point of exhaustion was reached or until the physician stopped the test. After completing the test,

subjects were observed for another 3 minutes[13]. For the AB subjects the test started with 3 minutes rest, followed by a 5 minute warm-up at 50 W. After the warm-up the work load was increased by 30 W per minute for men and 20 W per minute for women until the point of exhaustion was reached or until the physician stopped the test. After the exercise test was terminated, a cooling down of 3 min was performed at 20 W[10]. Reasons to terminate testing were inability to maintain 50 rpm, pain in arms or legs or severe dyspnea. Testing was also stopped by the investigator in case of ECG abnormalities.

The feet of the user were placed against a fixed footrest on the Cruiser ergometer, which can be adjusted to the subjects' length. The subjects with a LLA performed the test without prosthesis. The residual limb rested on a support. The footrest was used to push off and move the seat backward. The handlebars are used to pull the seat forward again. In this way, arms, trunk and leg(s) overcome resistance provided by the ergometer in a cyclic multi-limb movement pattern. The ergometer was set in a constant power mode of between 35 and 60 revolutions per minute (rpm) and subjects were instructed to maintain a cadence of 50 rpm[10,13]. The accuracy of the Cruiser ergometer is within ± 10% power output (W) and ± 2 rpm for cadence. Cardiorespiratory outcomes were recorded using an Oxycon Delta (Jaeger, Bunnik, the Netherlands). Subjects wore a face mask and ventilation (VE, in l/min), oxygen uptake (VO_2, in l/min) and carbon dioxide output (VCO_2, in l/min) were measured breath by breath and plotted. Peak VO_2 and peak VCO_2 were defined as the highest average values obtained over a 30 second period. Blood pressure was measured manually at the beginning of the test, immediately after the test was completed, and after the cooling down period. Heart rate (HR in beats/min) was continuously monitored using a 12-lead electrocardiogram (ECG)[10,13].

Determination of the ventilatory thresholds

The VT1 and VT2 were determined based on ventilation plots as described by Wasserman et al.[19]. The VT1 was determined using three criteria, 1) intersection of a two line regression of the VCO_2 versus VO_2 (V-slope) graph, with a change of the slope from less than one to equal to one or greater than one, 2) first increase of VE/VO_2 versus workload (W) without a simultaneous increase in VE/VCO_2, and 3) first rise of $PETO_2$ (fraction of oxygen in the expired air), while $PETCO_2$ (fraction of CO_2 in the expired air) remains constant or is increasing. The VT2 was determined using three criteria, 1) inflection of VE versus VCO_2 (VE/ VCO_2

slope), 2) nonlinear increase of VE/VCO_2 versus W, and 3) deflection point of the end tidal $PETCO_2$[16]. The criteria are in order of preference: when the first criterion yielded adequately positioning, it was chosen; when the first criterion could not be reasonably applied, the second criterion was chosen, and so further. The observers assessed all three plots for each threshold and based their decision on the V-slope or the ventilatory equivalents; depending on which plot most clearly showed that particular VT1 or VT2. For each VT1 or VT2 determined the Oxycon Delta software calculated the VO_2 and HR. If an observer could not determine VT1 or VT2 it was recorded.

Statistical analysis

Differences between subjects with a LLA and AB subjects were analyzed by means of t-test for independent samples and Chi squared tests. Differences in determining the VT1 and VT2 between the observers for the first and second analysis was analyzed using Cochran's Q test with a post hoc pair wise with Bonferroni correction. To quantify variation in measurement results a variance component analysis (restricted maximum likelihood method) was performed for subjects with a LLA and AB subjects separately. Sources of variation included subjects (persons differ from each other) and observers (observers determine thresholds differently) and repeated analysis (results of the first vs second analysis). Negative variance components were set to 0. Based on the results of the variance components the error variance was calculated as the sum of the variances minus the variance due to subjects with a LLA. The error variance was thereafter divided by the sum of variances, resulting in a reliability coefficient. The following interpretation was used for the reliability coefficient with a minimum reliability 0.7 and clinically relevant at 0.9[20]. For AB subjects a similar procedure was followed. Limits of agreement were calculated and Bland and Altman plots were drawn for the outcomes percentage of VO_2 and HR on the VT1 and VT2. Statistical analyses were performed using SPSS (IBM SPSS Statistics 23).

Results

Baseline data of the subjects are presented in table 1. Subjects with a LLA were significantly older than the AB subjects.

Table 1. Subject characteristics

	Subjects with a LLA (n=17)	AB subjects (n=30)	Significance (p)	95 % confidence interval of the difference
Men/ women	14/3	16/14	0.06*	
Mean (SD) age in years	54.5 (18.6)	37.0 (10.0)	<0.001	(9.4; 25.7)
Mean (SD) BMI in kg/m^2	25.2 (4.0)	24.7 (2.5)	0.60	(-1.4; 2.4)
Median(IQR) time since amputation (months)	84.0 (4;144)	NA		

LLA= lower limb amputation, AB= able bodied, SD= standard deviation, BMI= Body Mass Index, NA= not applicable, IQR= interquartile range, *based on Fisher exact, all other p values based on independent sample t-test.

The number of observations in which thresholds could not be determined differed significantly between observers and tests (Cochran's Q test, p= <0.001). The number of observations in which the thresholds could not be determined was higher for VT2 than for VT1. The number of observations in which thresholds could not be determined was significantly lower for observer 1 compared to observer 2 in analysis 1 (p=0.008) and analysis 2 (p=0.001) (table 2).

Table 2. Number of observations in which observers could not determine the first ventilatory threshold (VT1) and/or the second ventilatory threshold (VT2) for all subjects (n=47)

	Observer 1		Observer 2	
	Analysis 1	Analysis 2	Analysis 1	Analysis2
VT1	2	2	3	4
VT2	6*	4#	16*	12#

*Difference between observer 1 and 2 is significant (p=0.008) # Difference between observer 1 and 2 is significant (p=0.001) Based on Cochran's Q test (P<0.001) and post hoc pair wise comparison with a Bonferroni correction for pairwise comparison.

Inter-observer and intra-observer reliability

Variation between and within observers was small (0-1.6%) compared to the total variation, for both subjects with a LLA and AB subjects (table 3). The reliability coefficients for VT1, expressed as VO_2 and HR at that threshold were respectively 0.89 and 0.75 respectively for the subjects with a LLA and 0.81 and 0.84 for the AB subjects. For VT1 expressed as VO_2 variation between observers contributed 0.0% (subjects with a LLA) and 3.9% (AB subjects) to the error variation. For the variation within observers these values were 6.6% (subjects with a LLA)

and 0.0% (AB subjects). For VT1 expressed as HR variation between observers contributed 1.2 % (subjects with a LLA) and 10.1% (AB subjects) to the error variation. For within observers variation these values were 0.0% (subjects with a LLA) and 0.0% (AB subjects) respectively. Variance components for VT2 were also calculated (table 3), but were based on a limited number of observations. Therefore these variance components estimation are difficult to interpret.
The limits of agreement for the VO_2 and HR at VT1 and VT2 for the subjects with a LLA and AB subjects are shown in table 4 and in the figures in the appendix (Fig S1-S8). There were varying differences in the limits of agreements between the subjects with a LLA and the AB subjects. In the plots there were no obvious differences between the observers (inter observer reliability) and between the analysis (intra observer reliability).
All the outcome parameters at VT1 and VT2 were significantly higher for the AB subjects than for subjects with a LLA (table 5).

Table 3. Variance component analysis (Restricted Maximum Likelihood Method) for subjects with a lower limb amputation (LLA) and able bodied subjects (AB)

Sources of variation	LLA	LLA % of total var	LLA % of error var	AB	AB % of total var	AB % of error var
VT1 VO_2 (l/min)						
Subject	114.42	88.6		192.38	81.1	
Observer	0.0*	0.0	0.0	1.77	0.7	3.9
Analysis	0.97	0.7	6.6	0.0*	0.0	0.0
Observer x Subject	5.58	4.3	37.9	0.0*	0.0	0.0
Subject x Analysis	0.0	0.0	0.0	21.08	8.9	46.9
Observer x Analysis	0.20	0.2	1.4	0.0*	0.0	0.0
Residual	7.95	6.2	54.1	22.11	9.3	49.2
Sum of var. comp.	129.12			237.34		
Reliability coeff.	0.89			0.81		
VT1 HR (beats/min)						
Subject	263.6	74.6		221.1	84.0	
Observer	1.1	0.3	1.2	4.3	1.6	10.1
Analysis	0.0*	0.0	0.0	0.0*	0.0	0.0
Observer x Subject	27.7	7.8	30.8	9.4	3.6	22.3
Subject x Analysis	6.7	1.9	7.4	7.1	2.7	16.8
Observer x Analysis	0.0*	0.0	0.0	0.0*	0.0	0.0
Residual	54.4	15.4	60.6	21.5	8.2	50.8
Sum of var. comp.	353.4			265.4		
Reliability coeff.	0.75			0.84		

Sources of variation	LLA	LLA % of total var	LLA % of error var	AB	AB % of total Var	AB % of error var
VT2 VO2 (ml/min)						
Subject	258.11	99.4		327.59	93.7	
Observer	0.0*	0.0	0.0	0.0*	0.0	0.0
Analysis	0.0*	0.0	0.0	0.0*	0.0	0.0
Observer x Subject	0.0*	0.0	0.0	4.96	1.4	22.3
Subject x Analysis	0.04	0.0	2.4	5.54	1.6	25.0
Observer x Analysis	0.0*	0.0	0.0	0.0*	0.0	0.0
Residual	1.49	0.6	97.6	11.71	3.3	52.7
Sum of var. comp.	259.64			349.80		
Reliability coeff.	0.99			0.94		
VT2 HR (beats/min)						
Subject	1028.6	99.6		181.7	82.3	
Observer	0.0*	0.0	0.0	0.0	0.0	0.0
Analysis	0.0*	0.0	0.0	1.3	0.6	3.4
Observer x Subject	0.0*	0.0	0.0	6.4	2.9	16.3
Subject x Analysis	0.0*	0.0	0.0	13.9	6.3	35.6
Observer x Analysis	0.0*	0.0	0.0	0.25	0.1	0.6
Residual	4.1	0.4	100.0	17.2	7.8	44.0
Sum of var. comp.	1032.7			220.8		
Reliability coeff.	1.00			0.82		

VT1= first ventilatory threshold, VT2= secondary ventilatory threshold, VO2= oxygen uptake, HR= heart rate, sum of var.comp= sum of variance component analysis, reliability coeff= reliability coefficient.

Table 4. Limits of agreement of the Bland and Altman plots

Limits of agreement (± 1.96 SD)	LLA subjects	AB subjects
VT1 VO_2 (l/min)	0.19	0.33
VT1 HR (beats/min)	15.08	10.04
VT2 VO_2 (l/min)	0.07	0.23
VT2 HR (beats/min)	3.36	9.19

VT1= first ventilatory threshold, VT2= second ventilatory threshold, VO_2= oxygen uptake, HR= heart rate, SD= standard deviation, LLA= lower limb amputation, AB= able bodied

Table 5. Differences of the outcome parameters between able bodied subjects and subjects with lower limb amputation

	Subjects with a LLA (n=17) Mean (SD)	AB subjects (n=30) Mean (SD)	Significance (p)	95 % confidence interval of the difference
VT1 VO_2 (l/min)	1.12 (0.35)	1.82(0.46)	<0.001	(0.45; 0.96)
VT1HR (beats/min)	117.9 (17.2)	136.9.1(15.3)	<0.001	(9.2; 28.9)
VT2 VO_2 (l/min)	1.42 (0.51)	2.33 (0.58)	<0.001	(0.56; 1.26)
VT2HR (beats/min)	130.9 (32.1)	156.2 (14.1)	0.001	(11.2; 39.3)

AB= able bodied, LLA= lower limb amputation, SD= standard deviation VT1= first ventilatory threshold, VT2= second ventilatory threshold, VO_2= oxygen uptake, HR= Heart rate

Discussion

Inter- and intra-observer reliability of determining the VT1 during CPET on the Cruiser ergometer was good for subjects with a LLA and AB subjects. For the VO_2 at VT1 the reliability coefficient for the subject with a LLA was 0.89 and for AB subjects 0.81. In contrast, the reliability coefficient for HR at VT1 was lower for the subjects with a LLA (0.75) compared to the AB subjects (0.84). The reliability coefficients of VT1 were all above the minimally required 0.7 but not above 0.9 which is a requirement for clinically application[20]. The values of VO_2 and HR at VT1 and VT2 were higher for the AB subjects than for the subjects with a LLA.

VT1 could be determined more reliably than VT2. Because VT2 could not be determined in all subjects, the number of observations involved in the variance components analysis and Bland and Altman analysis was considerably smaller (table 2) and the analysis of the inter- and intra-observer reliability of the VT2 was limited. In a similar study determining ventilatory thresholds in individuals with spinal cord injury, also about 10% of the ventilatory thresholds could not be determined, particularly for the VT2 in individuals with tetraplegia[21]. In that study intra-observer reliability for determining ventilatory thresholds was good, as in our study for the VT1. In a study determining ventilatory threshold in persons with a stroke the VO_2 at ventilatory threshold had a good inter-observer reliability with an ICC of 0.93[22]. However, in that study only VT1 was determined, on a treadmill. The VO_2 peak in that study was probably influenced by motor dysfunction after stroke resulting in low values of aerobic capacity, this effect was less pronounced

for the VO_2 at ventilatory threshold[22]. In the current study the VO_2 at VT1 and VT2 was higher for the AB subjects in comparison with the subjects with a LLA. In addition to age, probably the LLA had not only an effect on VO_2peak[13], but also on ventilatory thresholds. Subjects with a LLA performed the exercise test on the Cruiser ergometer with one leg and two arms and the AB subjects with two legs and two arms. During upper body exercise ventilatory threshold can be reached at lower absolute VO_2 than during lower body exercise, whereas VT1 and VT2 occur at similar percentage of VO_2 max for both modes of exercise performed[23]. Subjects with a LLA use one leg and they had to exercise relatively more with their upper body. This difference in upper body exercise may explain lower values of VO_2 at VT1 and VT2 for subjects with a LLA compared to AB subjects.

A study limitation is the age difference between subjects with a LLA and AB subjects. As mentioned above, it was expected that the VO_2 at VT1 and VT2 was higher for the AB subjects than for subjects with a LLA because of the difference in performing the exercise test with one or two legs. However, the difference in age between the subjects with a LLA and AB subjects can also be an influencing factor on the difference in VO_2. Furthermore, the sample size of persons with a LLA was small and especially for the determining of inter- and intra-observer reliability of the VT2 the calculations were limited due to missing data (not being able to determine VT2).
Another limitation of this study was that data of performing CPET on the Cruiser ergometer twice in the same circumstances were not analyzed, so test-retest reliability of determining the VT1 and VT2 was not investigated. In addition, the outcome measure power output or work rate expressed in Watt was not used as an outcome measure because the software of the Oxycon Delta was not linked to the Cruiser ergometer and, consequently, the power output was not automatically described on VT1 and VT2. This shortcoming is a limitation, since power output can be important as an outcome measure in exercise intensity prescription, especially if the heart rate is influenced by medication[19]. Furthermore, a limitation was the difference in test protocol between the subjects with a LLA and the AB subjects. The warm-up period for subjects with a LLA was 3 minutes on 20 Watt and for AB subjects 5 minutes at 50 Watt. All the subjects with a LLA had the same test protocol, and for AB subjects there was a difference in test protocol for men and women. For some of the subjects with a LLA VT1 was determined during or soon after the warming up period of 3

minutes on 20 Watt.
For exercise prescription it is mostly recommended to use the VT1 and VT2[16]. Based on the results of this study for the Cruiser ergometer the use of only the VT1 is recommended, but further research to the clinically application is needed because the reliability coefficients were not above 0.9. To use the VT2, more research is needed to establish the reliability of determining VT2 in a larger sample of subjects with a LLA performing a CPET on the cruiser ergometer. Based on a CPET at the start of the rehabilitation after a LLA an individualized exercise intensity program can be composed to improve physical fitness, as an important cornerstone of recovery. In the present study, it was not investigated whether such an exercise intensity prescription based on VT1 or VT2 is more favorable to exercise prescription based on other variables as rate of perceived exertion, percentage of heart rate reserve or percentage of peak power output. This difference should be investigated in future research. Also training regimens based on VT1 and VT2, resulting from CPET on a Cruiser ergometer should be clinically evaluated on individual level.

Conclusion

The intra- and inter-observer reliability of determining VT1 during CPET on the Cruiser ergometer in this study is good for subjects with a LLA and AB subjects. In the current study populations determination of VT2 was less reliable. VT1 determined after an exercise test on the Cruiser ergometer can be helpful in prescribing the exercise intensity for a training program after a lower limb amputation.

References

1. Chin T, Sawamura S, Fujita H, Nakajima S, Oyabu H, Nagakura Y, et al. Physical fitness of lower limb amputees. Am J Phys Med Rehabil 2002 May;81(5):321-325.
2. Wezenberg D, de Haan A, Faber WX, Slootman HJ, van der Woude, L H, Houdijk H. Peak oxygen consumption in older adults with a lower limb amputation. Arch Phys Med Rehabil 2012 Nov;93(11):1924-1929.
3. Kaptein S, Geertzen JHB, Dijkstra PU. Association between cardiovascular diseases and mobility in persons with lower limb amputation: a systematic review. Disabil Rehabil 2018 Apr;40(8):883-888.
4. Chin T, Sawamura S, Shiba R. Effect of physical fitness on prosthetic ambulation in elderly amputees. Am J Phys Med Rehabil 2006 Dec;85(12):992-996.
5. van Velzen JM, van Bennekom CA, Polomski W, Slootman JR, van der Woude, L H, Houdijk H. Physical capacity and walking ability after lower limb amputation: a systematic review. Clin Rehabil 2006 Nov;20(11):999-1016.
6. Erjavec T, Presern-Strukelj M, Burger H. The diagnostic importance of exercise testing in developing appropriate rehabilitation programmes for patients following transfemoral amputation. Eur J Phys Rehabil Med 2008 Jun;44(2):133-139.
7. Klenow TD, Mengelkoch LJ, Stevens PM, Rabago CA, Hill OT, Latlief GA, et al. The role of exercise testing in predicting successful ambulation with a lower extremity prosthesis: a systematic literature review and clinical practice guideline. J Neuroeng Rehabil 2018 Sep 5;15(Suppl 1):64-z.
8. Wezenberg D, de Haan A, van der Woude, L H, Houdijk H. Feasibility and validity of a graded one-legged cycle exercise test to determine peak aerobic capacity in older people with a lower-limb amputation. Phys Ther 2012 Feb;92(2):329-338.
9. Vestering MM, Schoppen T, Dekker R, Wempe J, Geertzen JH. Development of an exercise testing protocol for patients with a lower limb amputation: results of a pilot study. Int J Rehabil Res 2005 Sep;28(3):237-244.
10. Simmelink EK, Wempe JB, Geertzen JH, Dekker R. Repeatability and validity of the combined arm-leg (Cruiser) ergometer. Int J Rehabil Res 2009 Dec;32(4):324-330.
11. Simmelink EK, Borgesius EC, Hettinga FJ, Geertzen JH, Dekker R, van der Woude, L H. Gross mechanical efficiency of the combined arm-leg (Cruiser) ergometer: a comparison with the bicycle ergometer and handbike. Int J Rehabil Res 2015 Mar;38(1):61-67.
12. Simmelink EK, Wervelman T, de Vries HS, Geertzen JHB, Dekker R, van der Woude, L H V. One-day low-intensity combined arm-leg (Cruiser) ergometer exercise intervention: cardiorespiratory strain and gross mechanical efficiency in one-legged and two-legged exercise. Int J Rehabil Res 2017 Dec;40(4):347-352.
13. Simmelink EK, Wempe JB, Geertzen JHB, van der Woude, L. H. V., Dekker R. Feasibility, safety, and reliability of exercise testing using the combined arm-leg (Cruiser) ergometer in subjects with a lower limb amputation. PLoS One 2018 Aug 13;13(8):e0202264.
14. American Thoracic Society, American College of Chest Physicians. ATS/ACCP Statement on cardiopulmonary exercise testing. Am J Respir Crit Care Med 2003 Jan 15;167(2):211-277.

15. Guazzi M, Arena R, Halle M, Piepoli MF, Myers J, Lavie CJ. 2016 Focused Update: Clinical Recommendations for Cardiopulmonary Exercise Testing Data Assessment in Specific Patient Populations. Circulation 2016 Jun 14;133(24):694.
16. Binder RK, Wonisch M, Corra U, Cohen-Solal A, Vanhees L, Saner H, et al. Methodological approach to the first and second lactate threshold in incremental cardiopulmonary exercise testing. Eur J Cardiovasc Prev Rehabil 2008 Dec;15(6):726-734.
17. Wolpern AE, Burgos DJ, Janot JM, Dalleck LC. Is a threshold-based model a superior method to the relative percent concept for establishing individual exercise intensity? a randomized controlled trial. BMC Sports Sci Med Rehabil 2015 Jul 4;7:16-z. eCollection 2015.
18. Mezzani A, Hamm LF, Jones AM, McBride PE, Moholdt T, Stone JA, et al. Aerobic exercise intensity assessment and prescription in cardiac rehabilitation: a joint position statement of the European Association for Cardiovascular Prevention and Rehabilitation, the American Association of Cardiovascular and Pulmonary Rehabilitation and the Canadian Association of Cardiac Rehabilitation. Eur J Prev Cardiol 2013 Jun;20(3):442-467.
19. Wasserman K, Hansen JE, Sue DY, Stringer WW, Sietsema KE, Sun X, et al. Principles of Exercise Testing and Interpretation. 5th ed. Philadelphia USA: Lippincott Wiliiams and Wilkins; 2011.
20. Streinder David L, Norman Geoffrey R. Health measurement scales. A practical guide to their development and use. fourth ed. Oxford: Oxford University Press; 2008.
21. Kouwijzer I, Cowan RE, Maher JL, Groot FP, Riedstra F, Valent LJM, et al. Interrater and intrarater reliability of ventilatory thresholds determined in individuals with spinal cord injury. Spinal Cord 2019 Aug;57(8):669-678.
22. Boyne P, Reisman D, Brian M, Barney B, Franke A, Carl D, et al. Ventilatory threshold may be a more specific measure of aerobic capacity than peak oxygen consumption rate in persons with stroke. Top Stroke Rehabil 2017 Mar;24(2):149-157.
23. Dekerle J, Dupont L, Caby I, Marais G, Vanvelcenaher J, Lavoie JM, et al. Ventilatory thresholds in arm and leg exercises with spontaneously chosen crank and pedal rates. Percept Mot Skills 2002 Dec;95(3 Pt 2):1035-1046.

Appendix

Table S1. Results of the two analyses of the 2 observers of the first (VT1) and second (VT2) ventilatory threshold

	1st analysis				2ndanalysis			
	1stobserver		2nd observer		1stobserver		2nd observer	
	LLA	AB	LLA	AB	LLA	AB	LLA	AB
VT1 VO_2	1.19	1.85	1.12	1.76	1.10	1.86	1.10	1.80
Mean (SD)	(0.36)	(0.51)	(0.38)	(0.45)	(0.33)	(0.50)	(0.37)	(0.49)
N valid	16	30	17	29	17	30	17	29
VT1 HR	120.3	138.4	115.7	135.0	117.8	138.1	117.2	135.7
Mean (SD)	(20.4)	(14.4)	(19.8)	(17.9)	(17.8)	(16.2)	(17.3)	(16.9)
N valid	16	29	17	27	17	28	17	26
VT2 VO_2	1.43	2.31	1.46	2.31	1.42	2.33	1.44	2.38
Mean (SD)	(0.51)	(0.54)	(0.56)	(0.62)	(0.51)	(0.60)	(0.59)	(0.67)
N valid	16	25	12	19	16	28	12	24
VT2 HR	130.8	157.2	137.5	157.7	131.0	154.2	132.8	155.6
Mean (SD)	(33.0)	(16.1)	(26.0)	(14.0)	(31.3)	(15.3)	(35.9)	(14.5)
N valid	16	25	12	19	16	27	12	23

VT1= first ventilatory threshold, VT2= second ventilatory threshold, VO_2 =oxygen uptake in l/min, HR= Heart rate in beats/min, SD= standard deviation, AB= Able bodied subjects, LLA= subjects with a lower limb amputation N valid= number of subjects who are involved in the analysis.

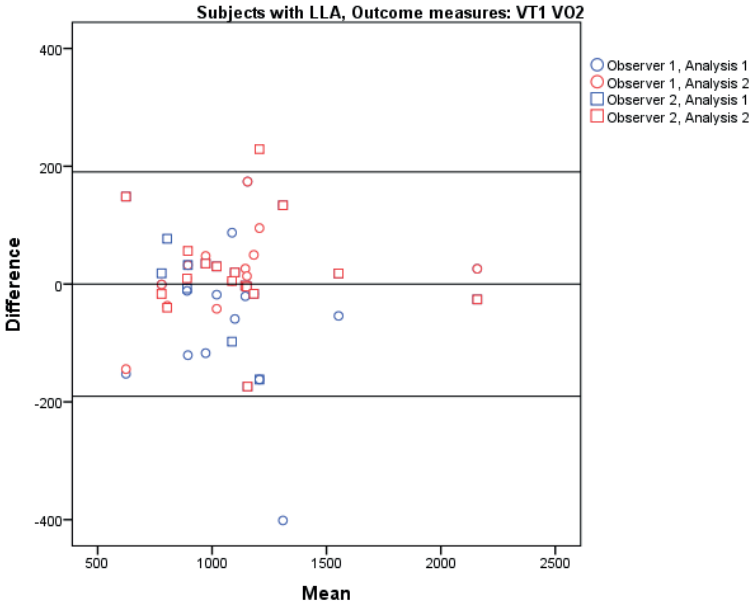

Figure S1

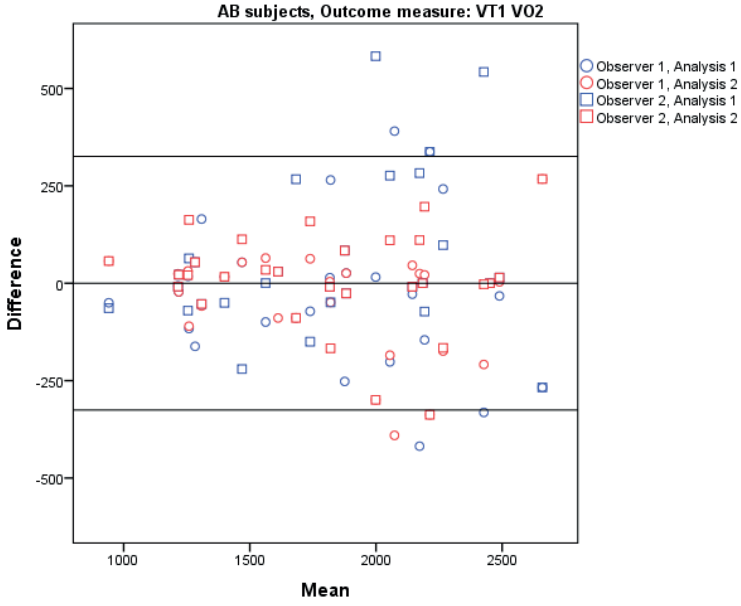

Figure S2

Figure S1 and S2: Bland and Altman plots for oxygen uptake (VO_2) at the the first ventilatory threshold (VT1) during the test on the Cruiser ergometer for subjects with a lower limb amputation (figure S1) and for the able bodied subjects (figure S2)

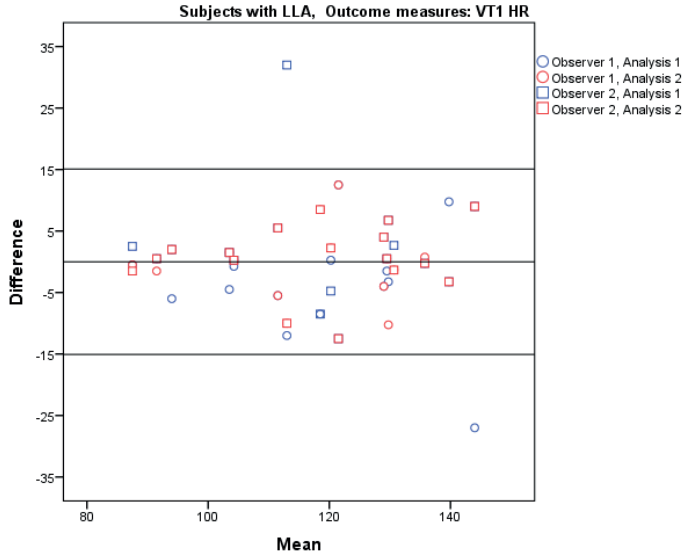

Figure S3

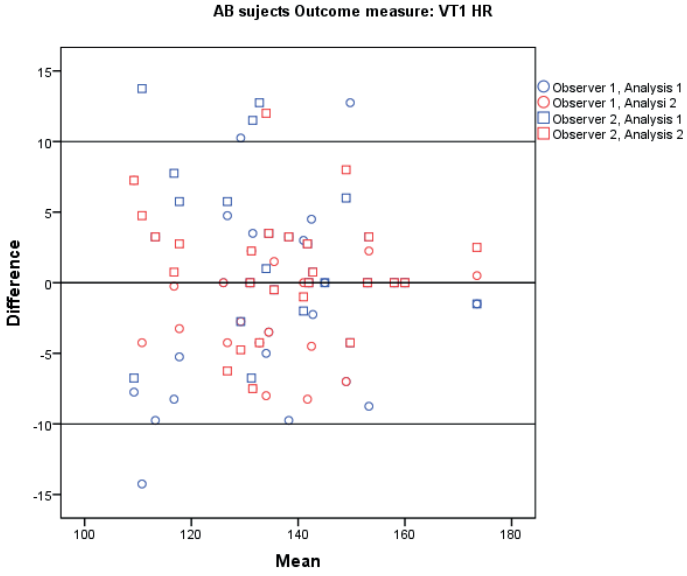

Figure S4

Figure S3 and S4: Bland and Altman plots for Heart rate(HR) at the first ventilatory threshold (VT1) during the test on the Cruiser ergometer for subjects with a lower limb amputation (figure S3) and able bodied subjects (figure S4)

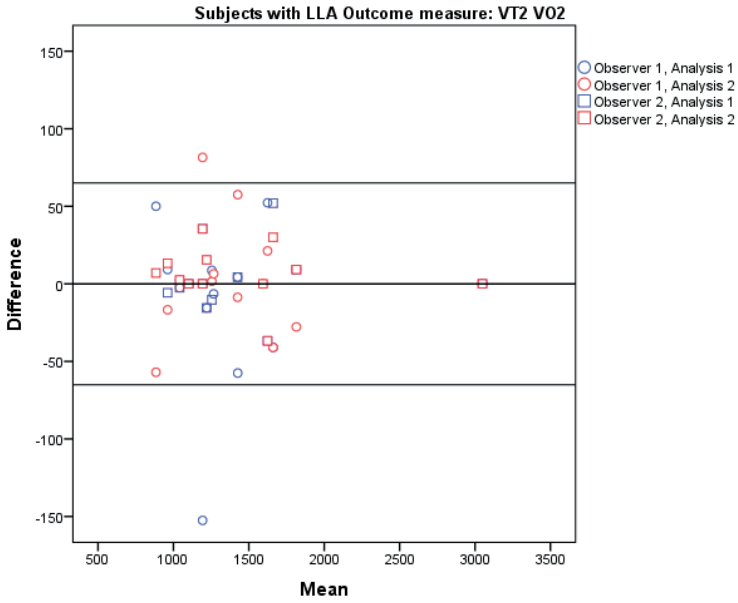

Figure S5

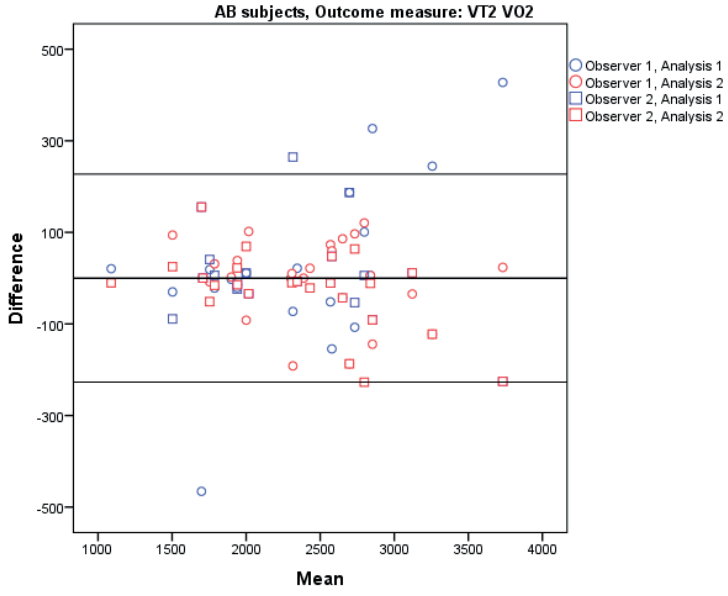

Figure S6

Figure S5 and S6: Bland and Altman plots for oxygen uptake (VO_2) at the second ventilatory threshold (VT2) on the Cruiser ergometer subjects with a lower limb amputation (figure S5) and for the able bodied subjects (figure S6).

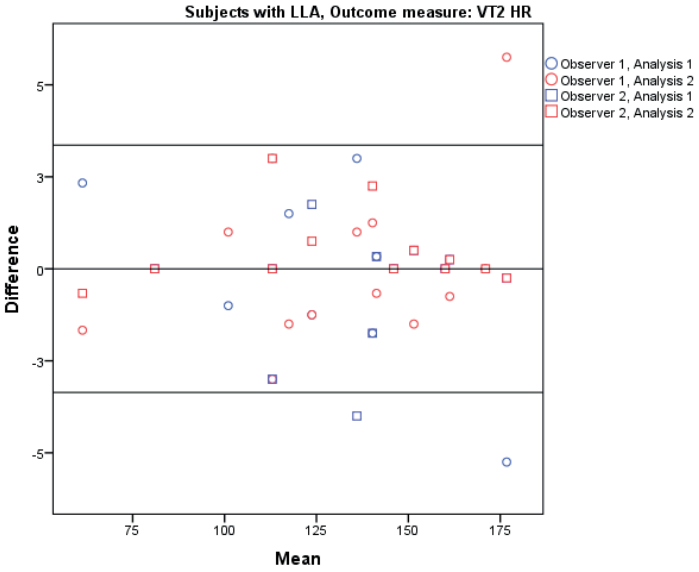

Figure S7

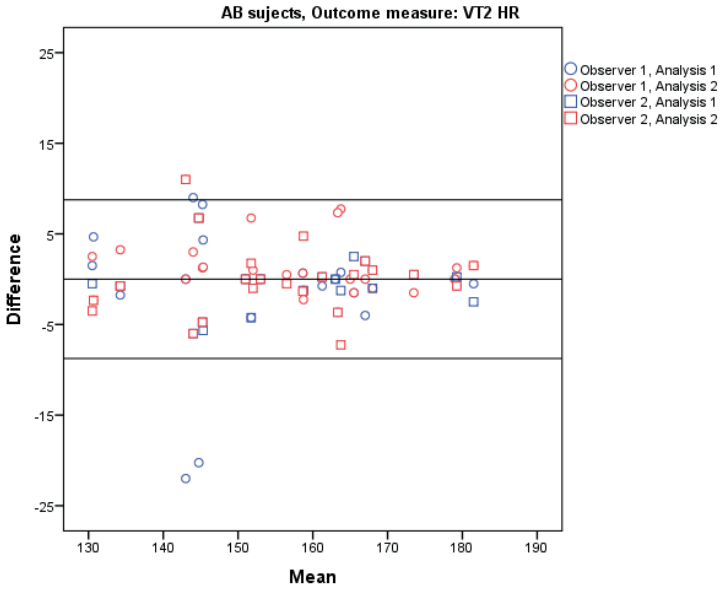

Figure S8

Figure S7 and S8: Bland and Altman plots for heart rate (HR) at the second ventilatory threshold (VT2) on the Cruiser ergometer subjects with a lower limb amputation (figure S7) and for the able bodied subjects (figure S8).



7

General discussion

Improving the cardiorespiratory fitness through testing and training is important in persons with a lower limb amputation (LLA) in rehabilitation and beyond[1,2]. With respect to testing and training, the Cruiser ergometer (Enraf Nonius) is a combined arm-leg ergometer, on which the tested person sits in supine position with back support and the arms, legs and trunk actively involved in cyclic work. With a small adaptation, a leg support connected to the seat, it is assumed to be a safe and accessible device for exercise testing and training in persons with a LLA already in early rehabilitation. The Cruiser ergometer is used by physiotherapists for years as an instrument for improving physical fitness, but research into measurement properties and effects on change of cardiorespiratory fitness in persons with a LLA has, up to now, not been performed. The substantiation of feasibility, safety, reliability and validity of the Cruiser ergometer in the measurement of cardiorespiratory fitness was performed and is reported in this thesis.

More specifically, the general aim of this thesis was to determine whether the Cruiser ergometer is clinically applicable as an instrument for cardiopulmonary exercise testing in persons with a LLA. In this respect, five studies were performed in order to reach this general aim.

Sub-aims of this thesis are:

- To compare and understand the physiology of submaximal cyclic exercise on the Cruiser ergometer, regular cycling and treadmill hand cycling on cardiorespiratory variables, gross mechanical efficiency (GE) and perceived exertion in healthy persons.
- To study potential motor learning effects during low-intensity submaximal steady state one-legged and two-legged practice on the Cruiser ergometer in healthy persons with respect to GE and cardiorespiratory strain.
- To establish the repeatability and validity of peak exercise testing on the Cruiser ergometer in a population of healthy persons.
- To determine the feasibility, safety, and reliability of (sub)maximal exercise testing on the Cruiser ergometer in a study population with a LLA.
- To determine the inter-observer and intra-observer reliability of the first (VT1) and second (VT2) ventilatory thresholds in persons with a unilateral LLA and healthy persons during a peak exercise test on the Cruiser ergometer.

In the next paragraphs the main findings of this thesis will be reviewed and specific topics are discussed in more detail, including clinical implications and suggestions for future research.

Main findings

The first aim was addressed in Chapter 2, revealing that during submaximal exercise no differences were found in GE and cardio-respiratory strain between Cruiser ergometer tests (GE at power output (PO) 45 W: male 13.0%, female 15%) and bicycle ergometer tests (GE at PO 45 W: male 13.2%, female 14.6%). The GE of the hand bike tests (GE at PO 45 W: male 11.2%, female 12.2%) was lower compared to the Cruiser and bicycle ergometer test results, while cardio-respiratory strain in hand cycling was consistently higher. Under the testing conditions in this study, males appeared less efficient than females ($P<0.05$), which may be due to the higher absolute PO in males. A PO of 45W is probably relatively lower to the men's peak PO, which may lead to a lower GE that is curvilinear associated to PO. The results suggest that the Cruiser ergometer test at identical submaximal effort has a comparable efficiency as the regular bicycle test, indicating that a relatively large muscle mass is engaged in an equally efficient motor pattern at the same energetic cost. Continued research should verify similar questions at higher submaximal intensities.

The second aim was on motor learning (Chapter 3). In healthy participants, a small degree of motor learning was indeed identified during low-intensity one-legged and two-legged exercises on the Cruiser ergometer meaning that such task-related cyclic exercises slightly optimized towards a lower energetic cost over practice time. We hypothesized that lower cardiovascular strain and higher muscular efficiency is underlying this process of motor optimization. Motor learning turned out to be more explicit in one-legged exercise as compared with two-legged exercise. Future research is required to understand in more detail how one-legged exercise on the Cruiser ergometer is optimized in clinical practice, since balance and force direction are potentially more critical in one-legged exercise, while the strain per muscle mass unit will be higher compared to two-legged exercise.

In Chapter 4 and 5 (in line with the third and fourth aim of the thesis) it was demonstrated that the Cruiser ergometer could safely and feasible be used for

peak exercise testing in healthy persons and persons with a LLA. The validity of the Cruiser ergometer was good. This was based on the fact that outcome of the VO_2peak on the Cruiser ergometer was corresponding with the VO_2peak obtained by testing on the bicycle ergometer in healthy persons, which can be considered as the gold standard. From the test-retest analysis in both healthy persons and persons with a LLA it was concluded that the Cruiser ergometer is a reliable measurement instrument. No complications occurred during the exercise tests and most persons could perform the exercise test until exhaustion. Further research was recommended to design tailor-made patient protocols for using the Cruiser ergometer as a measure instrument for exercise testing in the rehabilitation after a LLA.
To elaborate the final aim, in Chapter 6, based on the inter- and intra-observer reliability results, it is described that ventilatory thresholds can mostly be determined using the Cruiser ergometer. The inter- and intra-observer reliability of determining VT1 during a cardiopulmonary exercise test on the Cruiser ergometer in this study was sufficient for subjects with a LLA and healthy subjects in which VT1 could be assessed successfully. Determination of VT2 was less reliable in both subject groups and for both observers. Future research should address determination of peak aerobic capacity, ventilatory thresholds and their validity in and sensitivity to training interventions on the Cruiser ergometer among a wider, more variable population of persons with a LLA.

Implications

In the introduction a patient history was reported to illustrate the clinical aspect of the thesis. It concerns Mr. X, 62 years old, who has undergone a lower limb amputation, and who experienced, following the amputation and a period of perioperative inactivity, a decline in physical fitness. The physiotherapist who is involved in the exercise training program to improve physical fitness needs to know the level of physical fitness at the start of the rehabilitation and has to make choices with regard to training intensity and duration. With the results of this thesis we want to give the physiotherapist involved in the rehabilitation of Mr. X the tools and advices to perform a safe, feasible and reliable exercise

test to determine the physical fitness of the patient. Based on the outcome of this test, the physiotherapist can make choices with regard to the composition of exercise training in the rehabilitation program of Mr. X.

Ergometry in persons with a lower limb amputation

As described in the introduction of this thesis, physical fitness is defined in several ways. A generally accepted definition is: 'the ability to carry out daily tasks with vigor and alertness, without undue fatigue, and with ample energy to enjoy leisure-time pursuits and meet unforeseen emergencies'[3]. In this concept, cardiorespiratory fitness is one of the elements of physical fitness and can be determined by measuring cardiovascular and pulmonary parameters during a cardiopulmonary exercise test (CPET)[3,4]. It is known that most persons with a LLA have a low cardiorespiratory fitness and that undergoing conventional prosthetic rehabilitation does not necessarily result in improvement in their cardiorespiratory fitness[5-7]. On top of that, walking with a prosthesis costs considerably more energy than walking with two healthy legs[8]. The percentage of persons with an amputation who regain walking ability with a prosthesis varies from 56% to 97%[9]. Also it is known that persons with a LLA due to vascular reasons have more walking problems than persons with a LLA due to a trauma. In addition, it is known that persons with a LLA due to a vascular reasons in general are older, and an older age also affects walking ability in a negative way[9]. A specific exercise program during the rehabilitation to improve cardiorespiratory fitness can probably increase the chance of achieving walking ability after a LLA. Another purpose of improving the cardiorespiratory fitness after a LLA due to vascular reasons is to preclude or abate the pathogenesis of diabetes, atherosclerosis, or both.

For persons with a LLA due to other reasons improving the cardiorespiratory fitness focuses on risk reduction for developing secondary disabilities such as cardiovascular disease, diabetes, high blood pressure, and obesity. In fact persons with a LLA have a higher risk for developing secondary cardiovascular related disabilities than nondisabled individuals because of the LLA predisposition toward living a sedentary lifestyle[1].

Pre-operative rehabilitation (also called pre-rehabilitation) could be considered in a selected small group of (mostly) younger persons without comorbidities who are scheduled for an elective, non-dysvascular lower extremity amputation.

In these situations, the preoperative rehabilitation is focused on improving the physical fitness prior to surgery. From literature and from clinical experience, however, it is known that pre-operative rehabilitation is hard to apply in the majority of persons with a dysvascular LLA because of the older age, multiple comorbidities, a lack of motivation for behavioral change and, in particular, a short time window prior to surgery[10,11].

In this thesis we focused us on testing the cardiorespiratory fitness after a LLA. For improving the cardiorespiratory fitness persons with a LLA should use a mode that 1) incorporates enough muscle mass to produce improvements in cardiorespiratory fitness and 2) will not cause overuse injuries, skin breakdowns, and joint pain or inflammation in the non-amputated or amputated limbs[1]. Based on the outcome of this thesis we assume that the Cruiser ergometer is suitable for this purpose because the muscles of arms, trunk and one leg are cyclically involved in the exercise and shows comparable results to bicycling exercise (chapter 2 and 4). Furthermore, the amputated leg is not involved in the exercise and can be supported during the exercise: as a consequence, there is no chance for overuse injuries and skin breakdowns in the residual limb. Before starting an exercise program after a LLA it is important to be able to provide a good exercise prescription for a rehabilitation program and to give a prediction about the walking ability after the rehabilitation program. Another goal of the peak cardiopulmonary exercise test is to investigate if there are cardiopulmonary contra-indications for a person to exercise[2].
In this thesis we studied the clinical application of the Cruiser ergometer and compared this ergometer with the common used bicycle ergometer and, on submaximal level, with the handbike. In chapter 2 of this thesis we found during submaximal exercise in healthy persons no differences in GE and cardio-respiratory strain between the submaximal exercise test on the Cruiser ergometer and the bicycle ergometer. In chapter 4 the VO_2peak on the Cruiser ergometer was found to be corresponding with the VO_2peak on the bicycle ergometer in healthy persons. From these studies we conclude that a peak exercise test on the Cruiser ergometer seems a good alternative for a peak exercise test on the bicycle ergometer. However further research is expedient for understanding the relation of cardiorespiratory fitness measured using the Cruiser ergometer and the successful regain of walking ability.

Motor learning on the Cruiser ergometer

In chapter 2 no differences were found between the two Cruiser ergometer tests on the seven different power output levels for efficiency and most of the cardiorespiratory outcomes, except for the rate of perceived exertion (RPF). On the other hand, in chapter 3 motor learning was found in a healthy study population, especially for one-legged exercise on the Cruiser ergometer. Also a low-intensity, 7-week training protocol on a wheelchair has a beneficial effect on the mechanical efficiency and metabolic cost of wheelchair propulsion in able-bodied participants in a wheelchair study[12]. Possibly, the duration of the sessions of the seven different power output levels on the Cruiser ergometer, as described in chapter 2 was too short and the exercise not intensive enough to notice differences in GE. After one day practice on the Cruiser ergometer, as described in chapter 3, this motor learning effect was noted as an improvement in GE after practice, especially in the one-legged group. In addition, when repeating a peak exercise test on the Cruiser ergometer with the same protocol under the same circumstances and without any change in physical fitness, a higher not significant different VO_2 and greater power output were seen in the 2nd measurement in healthy persons (chapter 4) and in the 2nd and 3rd measurement in persons with a LLA (chapter 5).

In chapter 5 it is also described that a maximal aerobic performance was determined when one of the following criteria was fulfilled: a heart rate of more than 85% of predicted, maximal ventilation of more than 75% of predicted and a respiratory exchange ratio (RER) of more than 1.1[13]. Following these criteria at the first test 69% of persons had a maximal exercise test and at the second and third test 71% and 82% respectively, what may rise the idea that there is a motor learning effect.

In literature movement economy is defined as the metabolic energy expended to achieve the objective or goal[14,15]. There is a principal of least metabolic energy expenditure: organisms select the least effortful coordination and control function and with practice the selected control parameters are refined to attain the task goal with less metabolic energy expenditure. Also there is thought to be a relation between cardiovascular responses to exercise and timing characteristics of limb movement[14,16].

We hypothesize that by practice the movement on the Cruiser ergometer will be done with less energy expenditure and that the cardiovascular responses

to exercise will initially slightly drop. We found that when the peak exercise test on the Cruiser ergometer is done for the 2nd and 3rd time the cardiovascular responses improved. Also for bicycle ergometry a familiarization effect is described for cardiovascular variables, with persistently better values on the second test[17]. Probably this familiarization effect will be greater for an exercise test on the Cruiser ergometer because exercising on a bicycle ergometer is for most people in the Netherlands a more familiar movement which they have practiced already for a very long time and since early age. The movement on the Cruiser ergometer however is for most persons less familiar and somewhat complicated by the potentially three or four limbs actively involved in a consecutive cyclic order. We therefore expect that more changes in metabolic energy expenditure, as well as in muscle activation and force production patterns, will potentially be seen by practice. Probably this change in metabolic energy expenditure and motor behavior as consequence of an innate drive to minimize the cost of movement (i.e. motor learning) already happens continuously when the patient exercises on the Cruiser ergometer. Therefore, before performing the peak exercise test, exercising on the Cruiser ergometer is advised in order to get used to this specific movement with the arms and leg.

Feasibility, safety and reliability of the Cruiser ergometer

Based on earlier research[5,18-21] it is important to test the cardiorespiratory fitness as soon as possible after the amputation. Therefore it is important that the test procedure, on the Cruiser ergometer with one leg and two arms and good support for the residual limb, is feasible, safe and reliable. In chapter 5 the feasibility and safety of the Cruiser ergometer is described.

To evaluate the feasibility in this study the indicators acceptability, demand and practicality were used[22]. Three of the 21 preselected persons with a LLA dropped out of this study. One person had an allergic skin reaction to the ECG suction cups, which were used in this period. To solve this problem, ECGs are now in clinical practice recorded using self-adhesive electrodes. Another person showed signs of cardiac ischemia during the first maximal exercise test and was referred to a cardiologist. This can be seen as a positive point in relation to the safety of the Cruiser ergometer, because one of the goals of the exercise test is to screen for contra-indications for exercising. The third person dropped out because his pre-existent stump pain worsened after test 2, despite the use of a

special residual limb support attached to the Cruiser. Most subjects, however, felt the stump support was sufficiently comfortable and did not experience pain or discomfort in their stump. The Borg scores were relatively low and the majority of the subjects had a maximal aerobic performance. Based on these outcomes, application of the Cruiser ergometer is likely to be feasible.

Relevant outcomes for safety among the currently studied group of persons with a LLA as described in chapter 5 were the occurrence of ECG abnormalities or the occurrence of adverse effects during the test. No adverse events or complications occurred however during the peak exercise tests on the Cruiser ergometer.
Although, in general, the risk of cardiovascular complications resulting from a CPET is low[4,23], it is still important to monitor ECG, blood pressure and the well-being of the person who performs the CPET. At peak performance, measurement of the ECG and blood pressure was complicated by the movement of the trunk and arms. In some subjects the test leader had to stop the test because the interpretation of the ECG was not possible anymore. For the first test this percentage was higher (31.3%; 5/16) than for the second (23.5%; 4/17) and third test (17.7%; 3/17). Because of movement of the arms and trunk and contractions of trunk muscles, resulting in artifacts in ECG registration during the exercise on the Cruiser ergometer, a fully adequate ECG registration was not possible, especially at peak exercise. Although the heart rate can be measured during the procedure, it is not possible to assess other important aspects of the ECG pattern, like ST-depressions. Directly after stopping the test these ECG abnormalities can be seen on a rest ECG[24]. To put these findings in perspective, in other forms of ergometry like arm ergometry, rowing ergometry and treadmill tests the ECG registration is also affected by the movement of the trunk and arm muscles[1]. Already in 1984 Van Alste et al. found difficulties in adequate ECG registration during their research into the clinically applicability of rowing ergometry in persons with a LLA[25]. Even in leg ergometry, applying a bicycle-ergometer, clear ECG registration is sometimes not achievable. In order to address this issue, Wezenberg et al used a discontinuous one-legged cycle exercise test[26]. In the rest phase between active blocks an ECG and blood pressure was interpreted. A discontinuous protocol for the Cruiser ergometer was tried and tested, but turned out to be impractical while using the iso-power mode, since starting the movement at zero speed on the Cruiser ergometer at

the high resistance is too hard to accomplish. In other words, the discontinuous protocol was demanding too much effort during the re-start phases from the subjects and was therefore not applicable. Maybe in future the Cruiser ergometer can be adapted , e.g. by using a power assisted mode as discussed in the paragraph future developments and research, to make it possible to use also a discontinuous protocol as in the study of Wezenberg et al.[26]. For now, in clinical practice it is advised to perform an ECG registration in rest prior to testing and subsequently just after termination of the peak exercise test for an additional 2 minutes in order to detect exercise-related ECG abnormalities[24,27].
Blood pressure measurement during the peak exercise test on the Cruiser ergometer was not possible because of movement of the arms and the exertion of the muscles of the arms. It has to be noted that also in other forms of ergometry when the arms are involved in the movement, measuring of the blood pressure during the exercise test is not possible due to the same reasons[28,29]. Further research has to be done into the question whether an alternative measure of the blood pressure is possible, for example on another location, like the wrist[30,31]. And as mentioned above maybe in future the Cruiser ergometer can be adapted to a power assisted mode to make it possible to use a discontinuous protocol. With this adaptation the blood pressure can be measured in the rest phase when the arms are not involved in the exercise. Another point of view is that, as we did in our research, before the test all subjects are screened on cardiovascular risk factors by a questionnaire and measuring ECG and blood pressure in rest. When there are no major cardiovascular contra-indications as a history of a stroke or ischemic heart disease and it will not be expected that a high blood pressure will be a reason to stop the exercise test, the blood pressure can be measured directly after the exercise test[29].

Reliability of the peak exercise test on the Cruiser ergometer in the test-retest analysis in both healthy persons and persons with a LLA was good (chapter 4 and 5), but there was a not significant change in VO_2peak for the 2nd and 3rd test. This is the same as for the CPET on the bicycle ergometer, in literature also a familiarization effect for bicycle ergometry is described, unlikely to be of clinical relevance[17]. Consequently, the reliability of the peak exercise test on the Cruiser ergometer is corresponding with the bicycle ergometer.

Training prescription for exercising on the Cruiser ergometer

It is important to test and train cardiorespiratory fitness on the same type of ergometer because VO_2peak and ventilatory thresholds can vary between different modes of exercise[32]. An advantage of the Cruiser ergometer in the rehabilitation after a LLA is that it can be used both as a testing and training instrument. The Cruiser ergometer can be used as a testing instrument at the start of the rehabilitation program, for monitoring during the rehabilitation and at the end to evaluate the program. In addition, the Cruiser ergometer can be used as a training instrument during the rehabilitation, which is facilitated by the fact that a person with a LLA is able to exercise on the Cruiser ergometer with two arms and one leg without help and also without the prosthesis. Moreover, training load of the Cruiser ergometer and bicycle ergometer are comparable, with respect to GE and cardiorespiratory strain in the healthy individuals. In chapter 3 we studied the difference in submaximal exercise on the Cruiser ergometer with one and two legs in healthy persons. We found that the GE was lower for the one-legged group and the heart rate (HR) was higher for the one-legged group. We assume that balance and force direction are potentially more critical in one-legged exercise, while the strain per muscle mass unit will be higher in one-legged exercise, compared to two-legged exercise. Furthermore, it could be hypothesized that in one-legged exercise on the Cruiser ergometer the arms, during a lower training load, are more involved than during two-legged exercise. However, the current Cruiser ergometer does not produce output of each extremity separately, and therefore, the difference in output specifically of the arms in one-legged and two-legged exercise on the Cruiser ergometer cannot be measured. If it is possible to measure the output of the arms and legs separately with the use of sensor technology, it will allow us to understand the involvement of separate legs and arms in power production and thus to give more sharp training instructions for the exercise on the Cruiser ergometer for each of the limbs.

Training prescription for exercising on the Cruiser ergometer is possible when ventilatory thresholds are available[33]. In chapter 6 it is described that the first ventilatory threshold (VT1) could be determined in the majority of the healthy subjects and subjects with a LLA, but determination of the second ventilatory threshold (VT2) was less reliable. However when the first ventilatory threshold is known, an exercise program can be designed[33]. Further research into the effects

of a different rehabilitation programs after a LLA with this training prescription is needed.

Implications for Mister X: Taken the results of this thesis together, we can recommend the physiotherapist of mister X to compose a training prescription based on a CPET performed on the Cruiser ergometer. Before the cardiopulmonary exercise test is started it is advised that mister X will exercise on the Cruiser ergometer to get acquainted with this ergometer, if possible a couple of days before the CPET. Mister X can perform the CPET even before a prosthesis is developed and placed, because the exercise on the Cruiser ergometer can be safely done with two arms and one leg and the residual limb can be supported. The CPET reveals whether is it necessary to investigate underlying problems with heart or lungs, and enables the composition of a training program, especially in the presence of the first ventilatory threshold.

Limitations

A limitation of the thesis is that we only focused on measuring cardiorespiratory fitness on the Cruiser ergometer. Physical fitness is a much broader concept, consisting of strength, flexibility, coordination, anaerobic and aerobic capacity, which could all be the focus of training and the basis for daily life activities in rehabilitation and beyond[34]. It is generally acknowledged that these different aspects of physical fitness should be improved after a LLA[3,8]. Consequently, a training program after a LLA should include exercise modes to improve not only cardiorespiratory fitness but also the other aspects of physical fitness. Future research into the possibilities of the Cruiser ergometer as an instrument to measure and improve for example anaerobic capacity and muscular strength should be considered.

A second limitation is the fact that we used the same test protocol for all persons with a LLA. For some of the subjects the warming up on 20W was already strenuous whereas others had to exercise more than 10 minutes to reach VO_2 peak. In chapter 5 the protocol for subjects with a LLA is described. Each peak exercise test started with 3 minutes rest on the Cruiser ergometer and was

followed by a 3 minutes warm-up at 20W at 50 rpm. After the warm-up, workload was increased by 10W per minute, keeping speed at 50 rpm, until the point of exhaustion was reached or until the physician stopped the test. Consequently, it is advised to use a protocol in which the workload is increased dependent of the age, gender and activity level of the subject.

A technical limitation of the Cruiser ergometer was, that the lowest accurate workload setting on the Cruiser ergometer was 20 Watt. As mentioned above for some of the subjects the warming up on 20W was already strenuous. We therefor suggest that in developing a new version of the Cruiser, lower workloads should be possible. Furthermore the iso-power mode of the Cruiser used in the current experiments are typical in clinical ergometry applications. It means that the system regulates a constant power output (W); based on the definition of power output as the product of resistance force and speed: when the speed goes down, the resistance goes up and vice versa. A more natural - real life mode – is the iso-inertial mode where the eventual power output is dependent on the actual speed. When speed drops, power output will drop. Future research should focus on such mode related characteristics and the (dis)continuity of the protocol and the feasibility.
Another technical limitation was that the workload of the Cruiser ergometer had to be noted manually because it was not connected to the machinery and software that controls the cardiorespiratory variables.

Also a limitation was that only in chapter 5 and 6 persons with a LLA were involved in the study. In chapter 2 and 3 research was done to the cardiorespiratory strain, GE and motor learning on the Cruiser ergometer in healthy persons. It is quite possible that GE and motor learning are different in elderly subjects with a LLA, in particular as cardiorespiratory physical fitness is diminished as a result of decreased activity pattern, age, and chronic disease. These aspects require considerable continued research in the rehabilitation setting, both cross-sectional as well as longitudinal. The latter provides indications of time-(i.e. rehabilitation and age) associated changes in performance capacity.
For individual training-related exercise prescription, it is often recommended to use VT1 and VT2[33]. However, VT2 could not be determined in the majority of our subjects. It is obviously possible to compose training programs just on the VT1, and further study should focus on the efficacy of such programs. A limitation

in this study is that it was not investigated whether such an exercise intensity prescription based on VT1 or VT2 is favorable to exercise prescription based on other parameters as rate of perceived exertion, percentage of heart rate reserve or percentage of peak power output. Such studies are advised to be conducted in future rehabilitation contexts, for instance, in multicenter collaborations with larger numbers of patients with a LLA.

Future developments and research (Cruiser 2.0)

We demonstrated that de Cruiser ergometer is useful in testing cardiorespiratory fitness in persons with a LLA. Based on our experience with the Cruiser ergometer, we hypothesize that this ergometer is also useful in exercise training as component of a rehabilitation program. In addition, the Cruiser ergometer is possibly useful in other persons with unilateral impairments (i.e. stroke) or persons with limited balance control or capacity to stand or walk, i.e. elderly or people with overweight.

The Cruiser ergometer is currently out of production. Initiatives are undertaken to develop and produce an updated version of the Cruiser ergometer, stimulated by the outcome of this thesis that arm-leg ergometry should be used in favor of one-leg bicycle ergometry in persons with a LLA. The benefits of the Cruiser ergometer above the one-leg bicycle ergometer as mentioned in the introduction are evident. The Cruiser ergometer can be used as a testing and probably also as a training instrument in persons with a lower limb impairment, possibly also in those with stroke or other fragile patient populations. The latter is of even greater value in the concept of testing and training with the same equipment[32].
Based on the outcome of this thesis and taking the reported limitations into account, when developing a new ergometer the following points as mentioned earlier are important: 1) adequate and reliable ECG registration; 2) blood pressure measurement; 3) connection with the software to enable control of Cruiser load from the software that also controls the cardiorespiratory variables; 4) possibility of accurate and low loads from 0W upwards obviously in smaller steps as well as discontinuous patterns in an iso-inertial mode; 5) provide the user with isometric, iso-power as well as iso-inertial modes of operation; and 6) being able to measure the effort of the arms and leg(s) separately with the use

of sensor technology .

For some populations of patients starting levels of work or power may be too high, which suggests the use of a power-assist technology that support personal effort. Because of movements of trunk and contraction of trunk muscles a discontinuous protocol which enables ECG and blood pressure monitoring is advised, but therefore the iso-power function has to be changed to, for example, a function in which power-assistance is possible in the rest phase when ECG registration and blood pressure monitoring can be done. When developing this new Cruiser ergometer, technical innovations from the power assisted wheelchair[35] or Servo-Driven Dual-Roller Handrim (Essada) Wheelchair Ergometer[36] could be considered.

We expect that there will be a motor learning effect when exercising on the Cruiser ergometer. Because the movement on the Cruiser ergometer is a less natural movement than, for instance, the movement on the bicycle ergometer it is important that the person with a LLA has tried the Cruiser ergometer before performing the exercise test. When developing a testing protocol for this new ergometer it is important to take into account motor learning effects. Also different protocols have to be developed for the exercise test dependent on the age, gender and activity level of the person. We suggest a test protocol starting with 2 minutes rest, followed by a warm-up of 3-5 minutes at a low level, under the VT1. Thereafter, an incremental load should be applied, 1 minute per step, aiming at a duration of this phase of 8-12 minutes, which is in accordance with current protocols. After reaching the maximal level, subjects should be observed for 2-3 minutes, with continuation of measurement of ECG, blood pressure and ventilation. These testing protocols for the Cruiser ergometer should be tested on validity, reliability, feasibility and safety in a population of persons with a LLA especially in older persons with cardiovascular risk factors.

Further research into the clinical use of the ventilatory thresholds that can be determined from the results of the exercise test on this new version of the Cruiser ergometer, has to be done. With these thresholds an individually tailored training protocol can be developed to improve the cardiorespiratory fitness during the rehabilitation after a LLA. Research on the effects of such a training protocol applied on the newly developed Cruiser ergometer should be performed before this new version of the ergometer can be used as a training instrument in the rehabilitation after a LLA.

General conclusion

It can be concluded that the Cruiser ergometer is useful as an instrument for clinical exercise testing in persons with a LLA and probably in future also for training. Suggestions for innovation of the Cruiser ergometer emanated from the experiments. Based on these outcomes, recommendations are made to develop and produce an updated version of the Cruiser ergometer.

References

1. Durstine JL, Moore GE, Painter PL, Roberts SO. ACSM's Exercise management for persons with chronice diseases and disabilities.Third edition: Human Kinetics; Champaign, United States of America 2009.
2. Frontera WR, Dawson DM, Slovik DM. Exercise in Rehabilitation Medicine. Human Kinetics; Champaign, United States of America 1999.
3. American College of Sports Medicine. ACSM Guidelines for Exercise Testing. Chapter 1.Benefits and Risks Associated with Physical Activity. ninth edition: Wolter Kluwer / Lippincot Williams & Wilkins; Philadelphia 2014.
4. American Thoracic Society, American College of Chest Physicians. ATS/ACCP Statement on cardiopulmonary exercise testing. Am J Respir Crit Care Med 2003;167(2):211-277.
5. Chin T, Sawamura S, Fujita H, Ojima I, Oyabu H, Nagakura Y, et al. %VO2max as an indicator of prosthetic rehabilitation outcome after dysvascular amputation. Prosthet Orthot Int 2002;26(1):44-49.
6. Wezenberg D, Dekker R, van Dijk F, Faber W, van der Woude L, Houdijk H. Cardiorespiratory fitness and physical strain during prosthetic rehabilitation after lower limb amputation. Prosthet Orthot Int 2019;43(4):418-425.
7. Cruts HEP. Cardiac condition and the success of rehabilitation programs in the treatment of leg amputees. Technische Hogeschool Twente; Enschede, The Netherland 1986.
8. van Schaik L, Geertzen JHB, Dijkstra PU, Dekker R. Metabolic costs of activities of daily living in persons with a lower limb amputation: A systematic review and meta-analysis. PLoS One 2019;14(3):e0213256.
9. van Velzen JM, van Bennekom CA, Polomski W, Slootman JR, van der Woude, L H, Houdijk H. Physical capacity and walking ability after lower limb amputation: a systematic review. Clin Rehabil 2006;20(11):999-1016.
10. Dekker R, Hristova YV, Hijmans JM, Geertzen JHB. Pre-operative rehabilitation for dysvascular lower-limb amputee patients: A focus group study involving medical professionals. PLoS One 2018;13(10):e0204726.
11. Hijmans JM, Dekker R, Geertzen JHB. Pre-operative rehabilitation in lower-limb amputation patients and its effect on post-operative outcomes. Med Hypotheses 2020;143:110134.
12. de Groot S, de Bruin M, Noomen SP, van der Woude, L. H. Mechanical efficiency and propulsion technique after 7 weeks of low-intensity wheelchair training. Clin Biomech (Bristol, Avon) 2008;23(4):434-441.
13. Rieger BW. Principles of Exercise Testing and Interpretation: Including Pathophysiology and Clinical Applications, 3rd Edition. Medicine & Science in Sports & Exercise 2000;32(7):1364.
14. Sparrow WA, Newell KM. Metabolic energy expenditure and the regulation of movement economy. Psychonomic Bulletin & Review 1998;2(5):173-196.
15. Sparrow WA, Newell KM. Energy expenditure and motor performance relationships in humans learning a motor task. Psychophysiology 1994;31(4):338-346.

16. Vegter R. Wheelchair skill acquisition: motor learning effects of low-intensity handrim wheelchair practice. University of Groningen; 2015.
17. Barron A, Dhutia N, Mayet J, Hughes AD, Francis DP, Wensel R. Test-retest repeatability of cardiopulmonary exercise test variables in patients with cardiac or respiratory disease. Eur J Prev Cardiol 2014;21(4):445-453.
18. Chin T, Sawamura S, Fujita H, Nakajima S, Oyabu H, Nagakura Y, et al. Physical fitness of lower limb amputees. Am J Phys Med Rehabil 2002;81(5):321-325.
19. Chin T, Sawamura S, Shiba R. Effect of physical fitness on prosthetic ambulation in elderly amputees. Am J Phys Med Rehabil 2006;85(12):992-996.
20. Erjavec T, Vidmar G, Burger H. Exercise testing as a screening measure for ability to walk with aprosthesis after transfemoral amputation due to peripheral vascular disease. Disabil Rehabil 2014;36(14):1148-1155.
21. Klenow TD, Mengelkoch LJ, Stevens PM, Rabago CA, Hill OT, Latlief GA, et al. The role of exercise testing in predicting successful ambulation with a lower extremity prosthesis: a systematic literature review and clinical practice guideline. J Neuroeng Rehabil 2018;15(Suppl 1):64.
22. Bowen DJ, Kreuter M, Spring B, Cofta-Woerpel L, Linnan L, Weiner D, et al. How we design feasibility studies. Am J Prev Med 2009;36(5):452-457.
23. Skalski J, Allison TG, Miller TD. The safety of cardiopulmonary exercise testing in a population with high-risk cardiovascular diseases. Circulation 2012;126(21):2465-2472.
24. Puelacher C, Wagener M, Abacherli R, Honegger U, Lhasam N, Schaerli N, et al. Diagnostic value of ST-segment deviations during cardiac exercise stress testing: Systematic comparison of different ECG leads and time-points. Int J Cardiol 2017;238:166-172
25. Van Alste JA. Exercise electrocardiography in the rehabilitation of leg amputees. Technische Hogeschool Twente; Enschede, The Netherlands 1984.
26. Wezenberg D, de Haan A, van der Woude, L H, Houdijk H. Feasibility and validity of a graded one-legged cycle exercise test to determine peak aerobic capacity in older people with a lower-limb amputation. Phys Ther 2012;92(2):329-338.
27. Task Force Members, Montalescot G, Sechtem U, Achenbach S, Andreotti F, Arden C, et al. 2013 ESC guidelines on the management of stable coronary artery disease: the Task Force on the management of stable coronary artery disease of the European Society of Cardiology. Eur Heart J 2013;34(38):2949-3003.
28. Sharman JE, LaGerche A. Exercise blood pressure: clinical relevance and correct measurement. J Hum Hypertens 2015;29(6):351-358.
29. Schultz MG, La Gerche A, Sharman JE. Blood Pressure Response to Exercise and Cardiovascular Disease. Curr Hypertens Rep 2017;19(11):89.
30. Validation and Acceptability of a Cuffless Wrist-Worn Wearable Blood Pressure Monitoring Device Among Users and Health Care Professionals: Mixed Methods Study. JMIR Mhealth Uhealth 2019;;7(10):e14706
31. Melville S, Teskey R, Philip S, Simpson JA, Lutchmedial S, Brunt KR. A Comparison and Calibration of a Wrist-Worn Blood Pressure Monitor for Patient Management: Assessing the Reliability of Innovative Blood Pressure Devices. J Med Internet Res 2018;20(4):e111.

32. Dekerle J, Dupont L, Caby I, Marais G, Vanvelcenaher J, Lavoie JM, et al. Ventilatory thresholds in arm and leg exercises with spontaneously chosen crank and pedal rates. Percept Mot Skills 2002;95:1035-1046.
33. Binder RK, Wonisch M, Corra U, Cohen-Solal A, Vanhees L, Saner H, et al. Methodological approach to the first and second lactate threshold in incremental cardiopulmonary exercise testing. Eur J Cardiovasc Prev Rehabil 2008;15(6):726-734.
34. Bull FC, Al-Ansari SS, Biddle S, Borodulin K, Buman MP, Cardon G, et al. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. Br J Sports Med 2020;54(24):1451-1462.
35. Pavlidou E, Kloosterman MG, Buurke JH, Rietman JS, Janssen TW. Rolling resistance and propulsion efficiency of manual and power-assisted wheelchairs. Med Eng Phys 2015;37(11):1105-1110.
36. de Klerk R, Vegter RJK, Veeger HEJ, van der Woude, LHV. Technical Note: A Novel Servo-Driven Dual-Roller Handrim Wheelchair Ergometer. IEEE Trans Neural Syst Rehabil Eng 2020;28(4):953-960.



Summary

Nederlandse samenvatting

Dankwoord

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Summary

A lower limb amputation (LLA) is one of the main patient categories in rehabilitation medicine and is in about 90% related to peripheral arterial disease and diabetes mellitus (DM). Having a LLA mostly results in a severe decline in physical fitness. Poor physical fitness influences the progress of rehabilitation in a negative way. Often the physical strain during rehabilitation is insufficient to elicit potential improvements in cardiorespiratory fitness. It is suggested that gait training with a prosthesis should be accompanied by some kind of endurance exercise training to improve the overall cardiorespiratory and muscular systems of physical fitness. Individualized training requires individualized goal setting, based on a safe, feasible, valid and reliable cardiopulmonary exercise test (CPET). Cardiorespiratory fitness or aerobic exercise capacity can be measured with CPET by determining different parameters as peak oxygen uptake (VO_2peak), peak power output and peak heart rate.

Different ergometers were used in the past to measure the cardiorespiratory fitness in persons with a LLA like a motor driven treadmill (only in those with walking ability with a prosthesis), one-legged cycle ergometer, arm ergometer, rowing ergometer or a combined arm-leg ergometer. In order to measure the cardiorespiratory fitness validly and freliably, it is important to apply a testing protocol that involves the largest possible active muscle mass during exercise. When using a large muscle mass during testing, more oxygen is consumed which allows a more reliable estimate of peak VO_2 and heart function.

In persons with a LLA combined arm-leg ergometry with the Cruiser ergometer seems suitable to use for exercise testing because a lot of muscle mass is involved. Other advantages of the Cruiser ergometer are that persons with a LLA can perform the test in a safe relatively low sitting position with proper back support and with support for the residual limb, while using one leg, both arms and trunk, without external help.

However the movement on the Cruiser ergometer is for most people an unknown form of cyclic multi-limb exercise. This implicates that the movement may be subject to natural motor learning, i.e. learning through practice. Before developing the studies described in this thesis, it was not clear which learning effects are existent when exercising on the Cruiser ergometer and whether there are differences between one-legged and two-legged exercise. When using the Cruiser ergometer for exercise testing in persons with a LLA, it is important that it enables evaluation of undiagnosed exercise intolerance, exercise-related

symptoms and determination of peak aerobic capacity is possible in a feasible, safe, reliable and valid way. In addition, with the results of the exercise test, individual prescription of the optimal training dose during the rehabilitation program after a LLA should be possible.

The general aim of this thesis is to determine whether the Cruiser ergometer is clinically applicable as an instrument for cardiopulmonary exercise testing in persons with a LLA.
In this respect, the following sub-aims are formulated:

- To compare and understand the physiology of submaximal cyclic exercise on the Cruiser ergometer, regular cycling and treadmill hand cycling on cardiorespiratory variables, gross mechanical efficiency (GE) and perceived exertion in healthy persons.
- To study potential motor learning effects during low-intensity submaximal steady state one-legged and two-legged practice on the Cruiser ergometer in healthy persons with respect to GE and cardiorespiratory strain.
- To establish the repeatability and validity of peak exercise testing on the Cruiser ergometer in a population of healthy persons.
- To determine the feasibility, safety, and reliability of (sub)maximal exercise testing on the Cruiser ergometer in a study population with a LLA.
- To determine the inter-observer and intra-observer reliability of the first (VT1) and second (VT2) ventilatory thresholds in subjects with a unilateral LLA and able bodied subjects during a peak exercise test on the Cruiser ergometer.

Chapter 2 describes the GE, cardiorespiratory strain and perceived exertion of low-intensity Cruiser ergometer exercise and these results are compared with leg cycling and hand cycling. Ten healthy able-bodied men and 12 healthy able-bodied women enrolled in 4 discontinuous submaximal graded exercise tests on respectively the Cruiser ergometer, a bicycle ergometer, a handbike on a motor driven treadmill and again the Cruiser ergometer. Each test was following the same protocol and consisted of seven bouts of 3 min exercise ranging from 20 to 45W. GE measured on the Cruiser ergometer did not differ from cycling but was higher than in handcycling. A comparable cardiorespiratory strain was established between the Cruiser ergometer test and bicycle test, but

a significantly higher cardiorespiratory strain was found for handcycling. The repeated test on the Cruiser ergometer showed no differences compared to the initial test. Under the current testing conditions, men appeared less efficient than woman. We conclude that GE and cardiorespiratory strain in submaximal exercise on the Cruiser ergometer is comparable to exercise on the bicycle ergometer under the current submaximal testing conditions. This suggests that the Cruiser ergometer can be a suitable instrument to use in training and exercise testing in persons with a LLA.

Chapter 3 describes a low-intensity practice study on the Cruiser ergometer among healthy individuals. The aim was to study whether differences exist in cardiorespiratory variables and GE comparing one-legged and two-legged exercise on the Cruiser ergometer and whether motor learning occurs over time. Twenty-eight healthy male subjects participated in this one-day randomized controlled trial. One group (n=14) used one leg and both arms during the exercise and the other group (n =14) used both legs and both arms. All subjects performed a one-day low-intensity exercise protocol. This included a standardized pre- and posttest of 3 bouts of 4 minutes exercise at 40W and an exercise intervention of 7 bouts of 2 x 4 minutes exercise at 40W. The one and two-legged group significantly differed regarding heart rate and GE between the pre- and posttest. The one-legged group showed more motor learning effects than the two-legged group. GE improved significantly in both groups over the duration of the 3 exercise bouts of the pretest, but it did not improve during the posttest. The conclusion of this study is that there are expected differences in cardiorespiratory variables and GE between one and two-legged exercise on the Cruiser ergometer. It seems that motor learning occurs and the one-legged group showed more motor learning effects than the two-legged group. From a clinical perspective, the experimental results suggest that unilateral leg exercise on the Cruiser ergometer is highly feasible, is somewhat more straining, and yet less efficient, and it requires a period of adaptation to become familiar with the exercise configuration.

Chapter 4 describes a study to the repeatability and validity of the cardio-respiratory fitness measured on the Cruiser ergometer. Thirty healthy volunteers carried out 3 incremental exercise tests, once on the bicycle ergometer and twice on the Cruiser ergometer. The repeatability of the Cruiser ergometer was assessed by studying the results of the test-retest and the validity by studying

the results of the bicycle and the mean of the 2 repeated Cruiser ergometer tests. The intraclass correlation coefficient for repeated measurements on the Cruiser ergometer was 0.84 for the maximal oxygen consumption (VO_2max), and 0.71 for the maximal heart rate (HRmax). The intraclass correlation coefficient for the measurements on the bicycle ergometer and the Cruiser ergometer was 0.86 for the VO_2max and 0.73 for HRmax. Bland and Altman plots for VO_2max and HRmax showed a bias close to zero and a great accuracy. The conclusion of this study is that the Cruiser ergometer provides a repeatable and valid measurement of cardiorespiratory fitness in healthy volunteers. For persons with a LLA, an exercise test on the Cruiser ergometer seems to be a good alternative for an one-legged cycle exercise test. Further research was advised before the Cruiser ergometer can be used in persons with a LLA, particularly with regard to diagnostic and therapeutic protocols and reliable ECG measurement.

This research into the feasibility, safety and reliability of (sub)maximal exercise testing on the Cruiser ergometer in a population with a LLA is presented in **chapter 5.** Seventeen persons with a LLA performed one submaximal exercise test and three maximal exercise tests on the Cruiser ergometer. Fourteen men and 3 women out of 21 preselected subjects completed the study. In general, the maximal Cruiser exercise test was feasible. Almost 75% of the subjects reached a maximal aerobic performance. The test was also safe because no complications occurred, although electrocardiogram and blood pressure could only be reliably recorded in most subjects just before and after the test. The reliability of this exercise protocol was good. The conclusion of this chapter is that the Cruiser ergometer is a feasible, safe, and reliable testing instrument for measuring the cardiorespiratory fitness of this study population with a LLA. Adequate practice before actual testing, and the development of individually tailored testing protocols are advised.

Chapter 6 describes the inter-observer and intra-observer reliability of determining the ventilatory thresholds in subjects with a LLA and able bodied (AB) subjects during a peak exercise test on the Cruiser ergometer. Two observers determined two ventilatory thresholds of the exercise tests performed in the studies described in **chapters 4 and 5**. The first (VT1) and second (VT2) ventilatory threshold were determined based on ventilation plots. The number of observations in which thresholds could not be determined differed significantly between observers and analyses. The inter- and intra-observer reliability of

determining VT1 in this study was sufficiently good (reliability coefficient > 0.75) for subjects with a LLA and AB subjects in which VT1 could be successfully assessed. However, limits of agreement were relatively wide, which makes individual assessment sensitive to error. Determination of VT2 was less reliable than the VT1 in both subject groups and for both observers. For clinical practice, VT1 determined after an exercise test on the Cruiser ergometer can be helpful in prescribing exercise intensity for a training program after a LLA.

In **chapter 7** the most remarkable findings of this thesis are summarized and discussed. The conclusion is that the Cruiser ergometer is suitable for measuring the cardiorespiratory fitness in persons with a LLA. There is evidence for motor learning when using the Cruiser ergometer for the first time in exercise testing. Before the peak exercise test, sufficient practice on the Cruiser ergometer is advised in order to get used to this movement with the arms and leg.
A person with a LLA can safely, without help and comfortable perform an exercise test on the Cruiser ergometer. Another advantage of the Cruiser ergometer that in future it can be used both as a testing and training instrument in the early phase after a LLA.
However, the Cruiser ergometer is out of production. Initiatives are taken to develop and produce an updated version of the Cruiser ergometer, stimulated by the outcome of this thesis that arm-leg ergometry should be used in favor of one-leg bicycle ergometry in persons with a LLA. Based on the outcomes of this thesis and taking the reported limitations into account, when developing a new ergometer the following points are important: 1) adequate and reliable ECG registration during the exercise test; 2) blood pressure measurement during the exercise test; 3) connection with the software to enable control of the ergometer load from the software that also controls the cardiorespiratory variables; 4) possibility of accurate and low loads from 0 W upwards obviously in smaller steps as well as discontinuous patterns in an iso-inertial mode; 5) provide the user with isometric, iso-power as well as iso-inertial modes of operation; and 6) being able to measure the effort of the arms and leg(s) separately with the use of sensor technology.
With this new updated version of the Cruiser ergometer testing and training protocols for persons with a LLA can be developed. Further research on the clinical use of the ventilatory thresholds, has to be done focused on improvement of accuracy of determination of the thresholds and on the usefulness of these thresholds for individually tailored training protocols.

Nederlandse samenvatting

Een beenamputatie is een veel voorkomende aandoening binnen de revalidatiegeneeskunde en in ongeveer 90 procent gerelateerd aan perifeer vaatlijden en diabetes mellitus (DM). Bij de meeste mensen met een beenamputatie is er sprake van een verminderde fysieke fitheid. Dit heeft een negatief effect op de revalidatie na een beenamputatie. Vaak is de fysieke inspanning tijdens de revalidatie onvoldoende om een verbetering te geven in cardiorespiratoire fitheid. Daarom wordt aanbevolen om naast looptraining met een prothese een vorm van training aan te bieden om de cardiorespiratoire fitheid en de spierkracht te verbeteren. Individuele training vraagt om individuele doelen gebaseerd op een veilige, uitvoerbare, valide en betrouwbare cardiopulmonale maximale inspanningstest. De cardiorespiratoire fitheid of aerobe inspanningscapaciteit kan bepaald worden door middel van een maximale inspanningstest waarbij onder andere de piek zuurstofopname (VO_2piek), het piek vermogen en de piek hartslag gemeten worden.

Verschillende ergometers zijn al eerder uitgeprobeerd om de maximale inspanningscapaciteit te bepalen bij mensen met een beenamputatie, zoals een lopende band (alleen voor mensen met loopfunctie met prothese), éénbenige fietsergometer, armergometer, roei-ergometer en gecombineerde arm-been ergometers. Om de VO_2piek valide en betrouwbaar te kunnen bepalen, is een inspanningsvorm nodig waarbij een zo groot mogelijke spiermassa gebruikt wordt tijdens inspanning. Als veel spieren actief zijn zal meer zuurstof verbruikt worden, waardoor de VO_2piek en de hartfunctie nauwkeuriger bepaald kunnen worden.

Bij mensen met een beenamputatie lijkt de Cruiser ergometer, een gecombineerde arm-been ergometer waarbij beide armen en 1 been gebruikt worden, een geschikt meetinstrument voor een maximale inspanningstest omdat dan veel spiermassa actief is. Andere voordelen van de Cruiser ergometer zijn dat mensen met een beenamputatie de test kunnen doen in een veilige laag zittende positie met ondersteuning voor de rug en ondersteuning voor de stomp, terwijl ze 1 been, beide armen en de romp gebruiken zonder verdere hulp.

De beweging op de Cruiser ergometer is voor de meeste mensen een ongewone cyclische beweging met meerdere ledematen. Dit betekent dat er bij deze beweging sprake kan zijn van een natuurlijk proces van motorisch leren, oftewel leren door oefening. Voor het uitvoeren van de studies, beschreven

in dit proefschrift, was niet duidelijk of er sprake is van motorisch leren bij het bewegen op de Cruiser ergometer en welke verschillen tussen één- en tweebenige inspanning bestaan. Als de Cruiser ergometer wordt gebruikt voor inspanningstesten bij mensen met een beenamputatie is het belangrijk dat het mogelijk is om de inspanningstolerantie te meten, dat inspanning gerelateerde klachten opgespoord worden en dat het bepalen van de maximale aerobe capaciteit uitvoerbaar, veilig, betrouwbaar en valide is. Verder moet het mogelijk zijn om op basis van de resultaten van de inspanningstest een individueel trainingsadvies te geven wat gebruikt kan worden tijdens de revalidatie na een beenamputatie.

Het hoofddoel van dit proefschrift is het vaststellen of de Cruiser ergometer klinisch toepasbaar is als meetinstrument voor cardiopulmonale inspanningstesten bij patiënten met een beenamputatie. De volgende subdoelen zijn geformuleerd:

- Vergelijken en begrijpen van de fysiologie van submaximale cyclische inspanning bij gezonde mensen op de Cruiser ergometer, fietsergometer en handbike (op een lopende band) ten aanzien van cardiorespiratoire variabelen, mechanische efficiëntie (GE) en ervaren inspanning.
- Bestuderen van mogelijke leereffecten tijdens laag-intensieve submaximale éénbenige en tweebenige inspanning op de Cruiser ergometer bij gezonde mensen door het bepalen van de mechanische efficiëntie en cardiorespiratoire inspanningsintensiteit.
- Bepalen van de betrouwbaarheid en validiteit van een maximale inspanningstest op de Cruiser ergometer in een populatie van gezonde mensen.
- Bepalen van de toepasbaarheid, veiligheid en betrouwbaarheid van een (sub)maximale inspanningstest op de Cruiser ergometer in een studie populatie van mensen met een beenamputatie.
- Het bepalen van de inter-beoordelaar en intra-beoordelaar betrouwbaarheid van de eerste (VT1) en tweede (VT2) ventilatoire drempel bij mensen met een éénzijdige beenamputatie en gezonde proefpersonen tijdens een maximale inspanningstest op de Cruiser ergometer.

Hoofdstuk 2 beschrijft de GE, cardiorespiratoire inspanningsintensiteit en ervaren inspanning van een laag-intensieve inspanning op de Cruiser ergometer.

Deze resultaten worden vergeleken met de inspanning op hetzelfde vermogen op de fietsergometer en de handbike. Tien gezonde mannen en 12 gezonde vrouwen namen deel aan 4 discontinue submaximale inspanningstesten op respectievelijk de Cruiser ergometer, fietsergometer, handbike op een lopende band en opnieuw de Cruiser ergometer. Elke test vond plaats volgens hetzelfde protocol en bestond uit 7 blokken van 3 minuten inspanning variërend tussen de 20 tot 45 W. De GE gemeten op de Cruiser ergometer verschilde niet van de fietsergometer, maar was hoger bij de test op de handbike. Een vergelijkbare cardiorespiratoire inspanningsintensiteit werd vastgesteld tussen de Cruiser ergometer test en fietsergometer test, maar een significant hogere cardiorespiratoire inspanningsintensiteit werd gevonden voor de handbike test. De herhaalde test op de Cruiser ergometer toonde geen verschillen vergeleken met de 1e test. Onder de beschreven test omstandigheden bleken mannen minder efficiënt dan vrouwen. De conclusie is dat GE en cardiorespiratoire inspanningsintensiteit tijdens inspanning op de Cruiser ergometer vergelijkbaar zijn aan de inspanning op de fietsergometer onder de beschreven submaximale test omstandigheden. Deze studie toont aan dat de Cruiser ergometer geschikt kan zijn om te gebruiken als test- en trainingsinstrument voor mensen met een beenamputatie.

Hoofdstuk 3 beschrijft een onderzoek naar laag-intensieve inspanning op de Cruiser ergometer bij gezonde individuen. Het doel van dit onderzoek was te bestuderen of er verschillen optraden in cardiorespiratoire variabelen en GE tussen éénbenige en tweebenige inspanning op de Cruiser ergometer en of er sprake was van een motorisch leereffect. Achtentwintig gezonde mannen namen deel aan deze ééndaagse gerandomiseerde gecontroleerde studie. Eén groep (n=14) gebruikte één been en beide armen tijdens de beweging en de andere groep (n=14) gebruikte beide armen en beide benen. Alle proefpersonen volgden een laagintensief oefenprotocol. Dit hield in een gestandaardiseerde test voor en na de interventie waarbij 3 blokken van 4 minuten inspanning op 40 W, de interventie bestaand uit 7 blokken van 2 x 4 minuten inspanning op 40 W. De éénbenige en tweebenige groep verschilde significant wat betreft hartslag en GE tussen de voor- en nameting. Bij de éénbenige groep was er een groter motorisch leereffect dan bij de tweebenige groep. GE verbeterde significant in beide groepen tijdens de 3 inspanningssessies van de voormeting, maar verbeterde niet tijdens de nameting. De conclusie van deze studie is dat er

verschillen waren in cardiorespiratoire variabelen en GE tussen de éénbenige en tweebenige inspanning op de Cruiser ergometer. Er trad een motorisch leerproces op en dit effect was groter bij de éénbenige groep dan bij de tweebenige groep. Vanuit een klinisch perspectief laat dit onderzoek zien dat een éénbenige beweging op de Cruiser ergometer goed mogelijk is, echter meer inspannend en minder efficiënt is dan de tweebenige beweging en dat een langere periode nodig is om te wennen aan deze vorm van inspanning.

Hoofdstuk 4 beschrijft een studie naar de reproduceerbaarheid en de validiteit van de maximale inspanningscapaciteit gemeten op de Cruiser ergometer. Dertig gezonde proefpersonen ondergingen 3 maximale inspanningstesten, één keer op de fietsergometer en twee keer op de Cruiser ergometer. De reproduceerbaarheid werd vastgesteld door de resultaten van de test-hertest te vergelijken en de validiteit door resultaten van de fietsergometer test en het gemiddelde van de 2 herhaalde Cruiser ergometer testen met elkaar te vergelijken. De intraclass correlatie coëfficiënt (ICC) voor de herhaalde metingen op de Cruiser ergometer was 0.84 voor de maximale zuurstof opname (VO_2 max) en 0.71 voor de maximale hartslag (HRmax). De intraclass correlatie coëfficiënt voor de metingen op de fietsergometer en de Cruiser ergometer was 0.86 voor de VO_2max en 0.73 voor de HRmax. Bland en Altman grafieken voor VO_2max en HRmax lieten een bias van bijna nul zien en een grote nauwkeurigheid. De conclusie van deze studie is dat de Cruiser ergometer een reproduceerbaar en valide meetinstrument is om de maximale inspanningscapaciteit te bepalen bij gezonde proefpersonen. Voor mensen met een beenamputatie lijkt een inspanningstest met de Cruiser ergometer een goed alternatief te zijn voor de éénbenige fietstest. Vanuit deze studie werd verder onderzoek geadviseerd voordat de Cruiser ergometer gebruikt kan worden bij mensen met een beenamputatie, met name ten aanzien van diagnostische en therapeutische protocollen en betrouwbare ECG registratie.

Dit onderzoek naar de toepasbaarheid, veiligheid en betrouwbaarheid van (sub)maximale inspanningstesten op de Cruiser ergometer in een populatie met een beenamputatie wordt beschreven in **hoofdstuk 5**. Zeventien mensen met een beenamputatie hebben 1 submaximale inspanningstest en 3 maximale inspanningstesten uitgevoerd op de Cruiser ergometer. Veertien mannen en 3 vrouwen van de 21 voorgeselecteerde proefpersonen hebben deze studie

voltooid. In het algemeen was de inspanningstest op de Cruiser ergometer goed uitvoerbaar. Ongeveer 75% van de proefpersonen heeft een maximale aerobe inspanning verricht. De test was veilig omdat er geen complicaties optraden, hoewel ECG en bloeddruk bij de meeste proefpersonen alleen betrouwbaar gemeten konden worden voor en direct na de test. De betrouwbaarheid van het inspanningsprotocol was goed. De conclusie vanuit deze studie is dat de Cruiser ergometer een toepasbaar, veilig en betrouwbaar meetinstrument is om de inspanningscapaciteit te meten bij deze onderzoekspopulatie met een beenamputatie. Wennen aan het apparaat voor de uitvoer van de test en de ontwikkeling van individueel te bepalen test protocollen wordt geadviseerd.

Hoofdstuk 6 beschrijft de inter-beoordelaar en intra-beoordelaar betrouwbaarheid van het bepalen van de ventilatoire drempels bij mensen met een beenamputatie en bij gezonde proefpersonen tijdens een maximale inspanningstest op de Cruiser ergometer. Twee beoordelaars bepaalden twee ventilatoire drempels van de inspanningstesten beschreven in **hoofdstuk 4 en 5**. De eerste (VT1) en tweede (VT2) ventilatoire drempel werden bepaald op basis van de ventilatie plots. Het aantal observaties waarbij de drempels niet bepaald kon worden verschilde significant tussen de beoordelaars en tussen de analyses. De inter-beoordelaar en intra-beoordelaar betrouwbaarheid van het bepalen van VT1 in dit onderzoek was redelijk goed (betrouwbaarheid coëfficiënt > 0.75) voor de proefpersonen met een beenamputatie en de gezonde proefpersonen waarbij de VT1 goed bepaald kon worden. Echter de grenzen van overeenstemming (limits of agreement) waren relatief groot, wat een individuele bepaling gevoelig maakt voor fouten. Het bepalen van VT2 was minder betrouwbaar dan van VT1 in beide onderzoekspopulaties en voor beide beoordelaars. Voor de klinische praktijk, kan het bepalen van VT1 na een inspanningstest op de Cruiser ergometer ondersteunen in het voorschrijven van de juiste intensiteit van de revalidatie na een beenamputatie.

In **hoofdstuk 7** worden de meest belangrijke bevindingen van dit proefschrift samengevat en bediscussieerd. De conclusie is dat de Cruiser ergometer bruikbaar is om de cardiorespiratoire fitheid te meten bij mensen met een beenamputatie. Er is bewijs voor motorisch leren als de Cruiser ergometer voor het eerst wordt gebruikt voor het meten van de inspanningscapaciteit. Voor de uitvoer van een maximale inspanningstest wordt het oefenen op de Cruiser

ergometer geadviseerd om te wennen aan deze beweging met de armen en het been.

Op de Cruiser ergometer kan een persoon met een beenamputatie veilig, zelfstandig en comfortabel zittend een inspanningstest uitvoeren. Een bijkomend voordeel is dat de Cruiser ergometer zowel als test- en trainingsinstrument in de vroege fase na een beenamputatie gebruikt kan worden.

Echter de Cruiser ergometer wordt niet meer geproduceerd. Initiatieven worden ondernomen om een vernieuwde versie van de Cruiser ergometer te ontwikkelen, gestimuleerd vanuit de conclusie van dit proefschrift waarbij de arm-been ergometer meer geschikt lijkt dan de éénbenige fietsergometer bij mensen met een beenamputatie. Op basis van de uitkomsten van dit proefschrift en rekening houdend met de beschreven beperkingen zijn de volgende punten belangrijk bij het ontwikkelen van een nieuwe ergometer: 1) adequate en betrouwbare ECG registratie tijdens de inspanningstest; 2) bloeddrukmeting tijdens de inspanningstest; 3) verbinding met de software om het mogelijk te maken dat de weerstand van de ergometer verbonden wordt met de software die ook de cardiorespiratoire variabelen meet; 4) de mogelijkheid van accurate en lage weerstand niveaus vanaf 0 W en oplopend met kleine stapjes en ook met de mogelijkheid tot een discontinu patroon in een iso-inertiële stand; 5) mogelijk maken voor de gebruiker om te kiezen uit een isometrische, iso-power en iso-inertiële stand; en 6) het mogelijk maken van het meten van de inspanning van de armen en het been of benen afzonderlijk door gebruik te maken van sensortechnologie.

Met deze vernieuwde versie van de Cruiser ergometer kunnen test- en trainingsprotocollen voor mensen met een beenamputatie ontwikkeld worden. Meer onderzoek naar de klinische toepasbaarheid van het bepalen van de ventilatoire drempels moet worden gedaan, gericht op het verbeteren van de nauwkeurigheid van het bepalen van de drempels en de bruikbaarheid van deze drempels voor individueel te bepalen trainingsprotocollen.

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Curriculum Vitae



Liesbeth Simmelink werd geboren op 12 september 1979 te Ermelo en verhuisde op haar 9e naar Dronten. In 1997 behaalde zij haar VWO diploma aan het Ichthus College te Kampen. Van 1997 tot 2003 studeerde zij Geneeskunde aan de Rijksuniversiteit in Groningen. Tijdens haar studie deed ze een keuze coschap Revalidatiegeneeskunde waar haar interesse voor dit vakgebied werd gewekt. Van 2003 tot 2004 was zij werkzaam als AGNIO neurologie in het Martiniziekenhuis in Groningen. In 2004 kon zij starten met de opleiding tot revalidatiearts in het UMCG. Tijdens haar opleiding tot revalidatiearts is zij begonnen met dit huidige promotie onderzoek. In 2008 heeft zij haar opleiding tot revalidatiearts afgerond. Zij kon blijven werken in het UMCG waarbij zij als revalidatiearts in eerste instantie werkzaam was op locatie Beatrixoord en in het OZG locatie Delfzicht. Sinds 2014 is zij volledig werkzaam binnen de neurorevalidatie in het UMCG met als aandachtsgebieden Niet aangeboren hersenletsel (NAH), Multipele Sclerose (MS) en Bewegen & Sport. Zij is lid van de werkgroep MS en de werkgroep Bewegen & Sport van de Vereniging voor Revalidatieartsen (VRA).

Zij is getrouwd met Bas Moekotte en heeft 2 dochters Valerie en Daphne.

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