Fontys Paramedic University of Applied Sciences

Bachelor Thesis, Department of Physiotherapy

"Is interval exercise superior to continuous exercise in patients with moderate to severe COPD in terms of exercise capacity?"

A systematic literature review

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Preface

This is the last assignment of the four year education at Fontys University of Applied Science. During the four years of education, there have been five internships with several different pathologies being presented to me as a physiotherapy student. One of the most interesting pathologies I encountered was chronic obstructive pulmonary disease. This because the disease in addition to affecting the pulmonary structures also stresses the peripheral structures and presents more as a systemic disorder. So when the persons responsible for this research project presented the list with topics I could write about, and I discovered chronic obstructive pulmonary disease, it was clear to me which one I wanted to apply for.

During this project there have been some obstacles, with some being more challenging than others. To guide me through these obstacles my supervisor Chris Burtin has been there to guide me. It is clear to me that Chris Burtin and my peer reviewers Rolf Stenseth, Domenica Zink and Gard Aslak Patursson deserve a great acknowledgement.

Abstract

Introduction

Chronic obstructive pulmonary disease is the fifth and sixth leading cause of death worldwide in high and middle income countries respectively. 2, 7 million people succumb every year due to the disease. Several systemic changes such as deconditioning, weight loss, respiratory and peripheral muscle weakness and reduced exercise capacity is characteristics often seen in these patients. Exercise is therefore considered a cornerstone in treatment for patients with chronic obstructive pulmonary disease. Endurance exercise is a frequently used exercise modality. However as some patients are not able to sustain the intensity and/or duration of continuous exercise, interval exercise might be used as an alternative.

Objective

To investigate if interval exercise is superior to continuous exercise when wanting to increase exercise capacity.

Method

Systematic search for articles was conducted based on the set inclusion and exclusion criteria. The two online databases PubMed and CINAHL were used for searching literature. The methodological quality was checked by using the PEDro scale.

Results

The primary search yielded six randomized controlled trials with reasonably good to good methodological quality. There were no significant differences between the groups in any of the included studies. Exercise capacity increased significantly in the interval group in two studies, while three studies reported a significant increase in exercise capacity in the continuous groups.

Conclusion

There is no difference between interval exercises and continuous exercise in chronic obstructive pulmonary disease patients when wanting to increase exercise capacity.

Contents

Introduction

The world health organization (WHO) estimates chronic obstructive pulmonary disease (COPD) to be the fifth and sixth leading cause of death in high and middle income countries respectively, and approximately 2,7 million succumb from COPD worldwide per year and it accounts for 4,8% of all deaths.[1] Furthermore it was estimated that COPD patients aged ≥40 years cost the Norwegian health care system €141 million in 2005.[2] The chance of developing COPD increases with age, and in 2003, seven out of 1000 persons in the age between 40-45 and 150 out of 1000 between the ages 80-85 were suffering from COPD in the Netherlands.[3] The major risk factor for COPD is active smoking,[3,4] and it is thought that the attribution to active smoking in COPD is varying from 40 to 70% dependent on the country.[4]

A definition of COPD set by WHO`s Global Initiative for Chronic Obstructive Lung Disease (GOLD) is: *"Chronic Obstructive Pulmonary Disease (COPD), a common preventable and treatable disease, is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. Exacerbations and comorbidities contribute to the overall severity in individual patients".*[5]

COPD is divided into chronic bronchitis (CB) and emphysema.[6] CB is an inflammatory disorder[7] characterised by an increased mucus production, most often of the lower respiratory passageways.[8] The underlying histological cause leads to an increased number of mucus producing cells, which causes cell mediators such as proteases and cytokines to be released, stimulating mucus hyper secretion by activating epidermal growth factor lung receptor.[7] Emphysema is a disorder accompanied by a narrowing of the airways and airflow obstruction[9] characterised by an enlargement of the alveoli, deterioration of the alveolar walls and loss of lung elasticity.[8] When the lungs lose their elasticity the airways will eventually collapse during expiration which in turn will lead to obstruction of the outflow of air.[8] The effect of the pathological changes in CB and emphysema is obstruction of the airways and impairment of lung and gas exchange.[7,8]

COPD patients are characterised by dyspnea, dry mouth, cough, anxiety and depression,[10] in addition to several systemic changes such as deconditioning, weight loss, malnutrition and respiratory and peripheral muscle weakness.[3] As a result of these changes COPD patients experience a reduction in health related quality of life (QoL) and exercise capacity (EC).[11] Reduced EC can turn the most basic activities in daily life (ADL) in to a strenuous task.[12] Focus on reducing or eliminate functional impairments and to improve activities and participation through exercising is therefore a common treatment goal set by COPD patients in collaboration with the physical therapist.[3]

Exercise can, despite the absence of change in pulmonary function,[11] provide several beneficial effects, such as reducing dyspnea, deconditioning and muscle weakness.[13] Optimizing muscle function by means of capacity and efficiency leads to a lower ventilatory requirement for a certain submaximal work, thus increasing EC.[11] Exercise is therefore considered to be a cornerstone in the treatment of COPD patients.[3,11]

Endurance training is frequently used as an exercise modality for COPD patients independent of disease severity,[3,11] and research has reported that high level of continuous exercise (CE) (> 60% maximal work rate) for 20 to 60 minutes per session, three to five times per week will be beneficial for COPD patients in terms of EC.[11,13] However patients with COPD may have difficulties sustaining the intensity and/or duration of CE.[3] For those patients interval exercise (IE) may be prescribed as an alternative.[3,11] A benefit of IE is the opportunity to recover in the less or none active period.[11] It is recommended that IE with an intensity of 90-100% of peak work rate (PWR) achieved in a baseline incremental test should have a work/recovery ratio of 1:2 and that the total work performed resembles that of CE.[3] Furthermore, it is proven that IE has a greater effect than CE on EC in trained people and patients with heart failure.[14,15] This review will therefore evaluate available evidence on the effect of interval exercise compared to continuous exercise in patients with moderate to severe chronic obstructive pulmonary disease in terms of increasing exercise capacity

Method

This systematic literature review comprises scientific articles which investigate IE and CE and its effect on EC in COPD patients. The search was done by one reviewer between March and April 2014.

Search strategy

Two online databases; CINAHL and PubMed were used to obtain the relevant articles. After the primary search was conducted, the snowball method was applied to make sure that no articles were excluded

Search terms

The search terms used is to be found in table 1. Medical Subject Headings (MeSH) were used in the online database PubMed.

Search string.

The listed search terms were combined as a boolean search into one search string: ((COPD OR Chronic obstructive airway disease OR Chronic obstructive pulmonary disease) AND (Interval training OR Anaerobic training OR High intensity interval training OR Intermittent training) AND (Endurance training OR Continuous exercise OR Aerobic training) AND (Exercise capacity OR VO2 OR VO2max OR Exercise tolerance OR Physical capacity))

Table 1. Search terms

Pathology	Intervention	Co intervention	Outcome
COPD (MeSH)	Interval training	Endurance training	Exercise capacity
COPD	Anaerobic training	Continuous training	VO2
Chronic obstructive airway disease	High intensity interval training	Aerobic training	VO2max
Chronic obstructive pulmonary disease	Intermittent training		Exercise tolerance
			Physical capacity

COPD: Chronic obstructive pulmonary disease, VO2: oxygen uptake, VO2max: Maximum oxygen uptake, MeSH: Medical Subject Headings

Selection procedure

The selection procedure which took place consisted of three steps (figure 1); I: screening the title. II: screening the abstract and III: screening the full text article. These steps were conducted in accordance with in- and exclusion criteria. (Table 2) If an article was filtered through the aforementioned steps it was included in the review.

Table 2. Inclusion/exclusion criteria

Inclusion criteria	**Exclusion criteria**
Articles with RCT as study design	Studies that had to be purchased
Articles written in English or Norwegian	Studies which had been conducted on animals
Patients who are diagnosed with COPD GOLD stage 2-4 (FEV_1 <79%pred)	Patient which had other pulmonary diseases
Articles in which exercise capacity was measured in VO_2max	
Articles that used both interval exercise and continuous exercise as intervention	

RCT: Randomized controlled trial, COPD: Chronic obstructive pulmonary disease, GOLD: Global initiative for Chronic Obstructive Lung Disease, VO_2max: Maximum oxygen uptake, FEV_1: Forced expiration volume in 1 second, Pred: predicted, Note: VO_2max is used as main outcome as this is considered the gold standard for measuring exercise capacity[16]

Methodological quality

Articles which were found eligible for this review were screened for their methodological quality by using the PEDro scale, a scale which measures the methodological quality of a randomized controlled trial (RCT). It is considered a valid[17] and reliable[18] measure for RCTs. The scale scores 11 items and one point is given per fulfilled item.[17] However as item 1 takes external validity into account this item is not graded.[18] After the overall score is given, it is classified according to the amount of points it has (Table 3)

Table 3. Classification of PEDro score[19]

PEDro score	Methodological quality
0-3	Poor
4-5	Reasonably good
6-8	Good
9-10	Very good

Level of evidence

To evaluate the overall quality and level of evidence in this review, the best evidence synthesis proposed by van Tulder et al was used.[20] This synthesis rates the quality of the systematic review by type of studies used, the methodological quality of the studies used and sample size in the used study.[20] (Table 4) As the PEDro score was used to assess methodological quality in this review, a score of ≥5 was considered by the author to be high quality RCT.

Table 4. Best evidence synthesis[20]

Level of evidence	Description
Strong	Consistent findings among multiple high quality RCTs
Moderate	Consistent findings among multiple low quality RCTs and/or CCTs and/or one high quality RCT
Limited	One low quality RCT and/or CCT
Conflicting	No consistent findings among multiple trials (RCTs and/or CCTs)

RCT: Randomized controlled trail CCT: Clinical controlled trial

Results

The primary search yielded 320 articles in the online databases PubMed and CINAHL. (Figure 1) The included articles were published between 1999 and 2009.[21-26] None of the articles obtained from the online database CINAHL fulfilled the inclusion and/or exclusion criteria's throughout the selection procedure. Therefore, five of the used articles[21-25] was from the online database PubMed while one article was obtained by the use of the snowball method.[26]

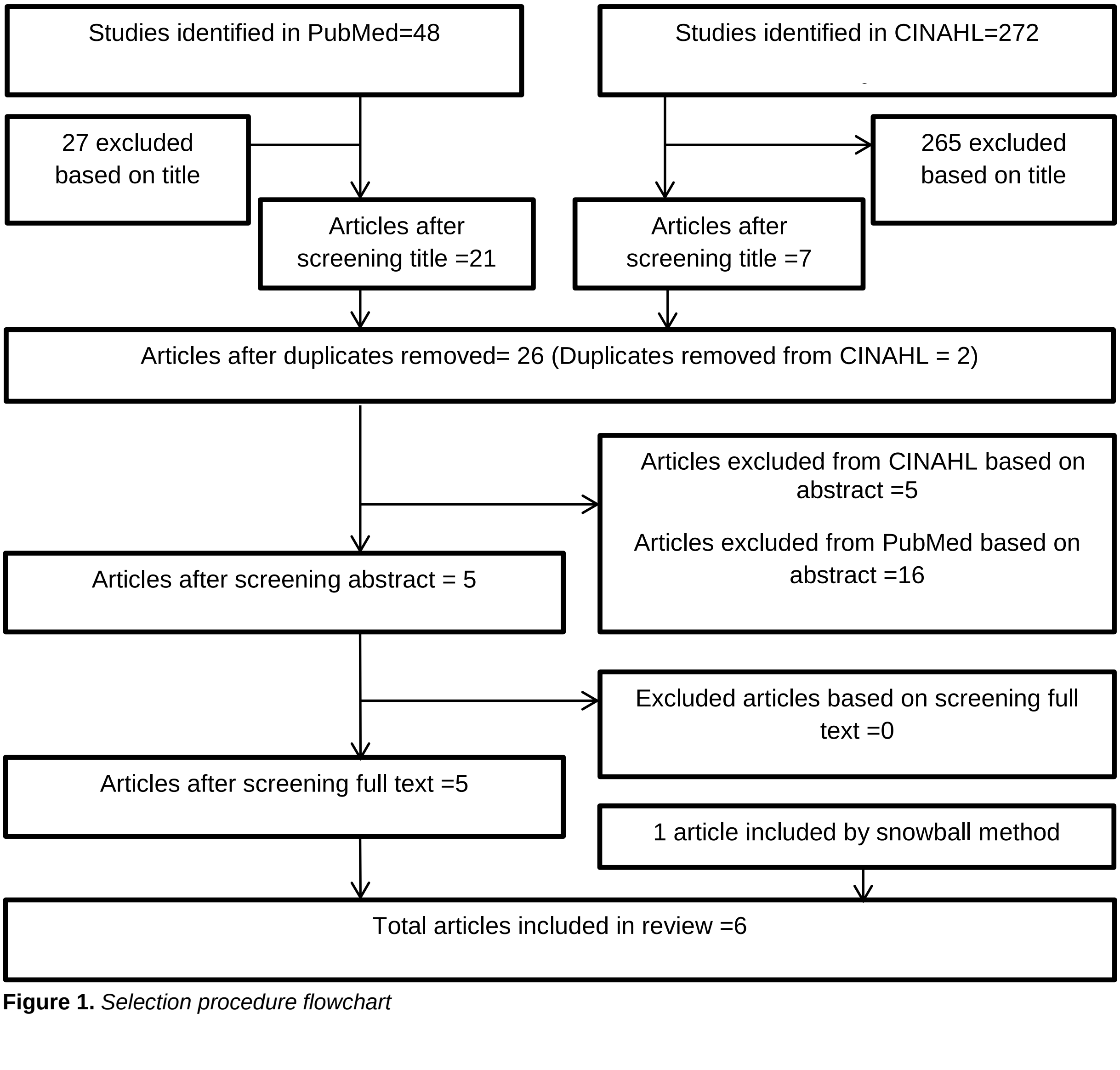

Figure 1. *Selection procedure flowchart*

PEDro score

The methodological quality of the included articles ranged from four[22,23] to seven[26] on the PEDro score. The specific details and grading of the different studies is to be found in appendix (I), while the description of criteria is to be found in appendix (II)

Baseline characteristics

The population ranged from 19[22] participants up to 60[23] in the studies included in this review. The total amount of participants used in this review was 212. The mean age ranged from 60[24] to 72[26] years. The lowest mean of predicted forced expiratory volume in one second (FEV1%pred) was 32%[23] while the highest measured mean of FEV1%pred was 64%.[24] VO_2max were similar at baseline in five of the studies.[21,23-26] and it ranged from 0.87±0.09[25] litres per minute (L/min) to 1.31±0.62[26] L/min The specific details can be found in table 5.

Table 5. Patient characteristics at baseline

Author	Number of participants (Male/female	Age	VO_2max L/min	FEV1%pred
Vogiatzis et al.[21]	(i) =14/4 (c) =16/2	(i) = 67±2 (c) = 69±2	(i) =1.06±0.06 (c) =1.09±0.06	(i)= 45±3 (c)= 44±3
Coppoolse et al.[22]	(i) =10/ (c) =11/	(i) = 63±8 (c) = 67±3	(i) =1.14±0.18 (c) =0.91±0.24	(i)= 36±10 (c)= 37±18
Arnardottir et al.[23]	(i) =3/25 (c) =6/26	(i) = 65±7 (c) = 64±8	(i) =0.98±0.29 (c) =0.97±0.29	(i)= 35±13 (c)= 32±10
Varga et al.[24]	(i) =11/6 (c) =19/3	(i) = 67±10 (c) = 61±12	(i) =1.10±0.31 (c) =1.17±0.40	(i)= 64±29 (c)= 51±16
Vogiatzis et al.[25]	(i) =10¤ (c) =9 ¤	(i) = 64±3 (c) = 67±2	(i) =0.87±0.09 (c) =0.97±0.10	(i)= 44±6 (c)= 39±6
Mador et al.[26]	(i) =21¤ (c) =20¤	(i) = 72±6 (c) = 71±8	(i) =1.22±0.32 (c) =1.31±0.62	(i)= 44±13 (c)= 42±12

(i): Interval group, (c): Continuous group, (FEV1%pred): Forced expiration volume in 1 second of predicted value, ¤: Gender not mentioned, VO_2max L/min: maximum oxygen uptake in litres per minute, Note: One study used a continuous home group in addition to the supervised interval exercise and continuous exercise[24]

Exercise protocol

All the studies measured EC at baseline by conducting an incremental test.[21-26] Based on the EC measured the intensity for both CE and IE groups were set. One study set the intensity in the IE group based on the intensity used in the CE group.[26] The intensity of interval work periods varied from ≥80%[23] PWR to 140%[21,25] PWR of baseline measurements between the studies. The duration of the work and recovery periods in the IE groups ranged from 30 seconds[21,25] to three minutes.[23] Two studies used complete rest in the recovery periods[21,25] while four studies used active recovery with intensity ranging from 30-40%[23] to 50%[24] of PWR measured at baseline.[22,23,24,26] In the CE groups the intensity ranged from 50%[21] PWR to 80%[24,26] PWR measured at baseline. Four studies[21-24] used the same duration for both groups per workout session and it varied from 30 minutes[22,25] to approximately 90 minutes.[23] The amount of workouts per week varied from two times/week[21,23] to five times/week[22] and the total length of the studies varied from 8 weeks[22,24,26] to 16 weeks.[23] The specific details is to be found in table 6.

Table 6 Exercise protocol

Author	Interval Load&duration	Continuous Load&duration	Weeks	Frequency	Additional information
Vogiatzis et al.[21]	- 30 s work:30s rest - 100%PWR (40 min)	- 50%PWR (40 min)	12	2 times/week	- (I) Increased 20% in week 4 and 8 each month - (C)Increased 10% in week 4 and 8
Coppoolse et al.[22]	- 1 min work 90%PWR - 2 min at 45% PWR (30min)	- 60% PWR (30min)	8	5 times/week	- (I) did interval 3 times/week and continuous (60%PWR) 2 times/week
Arnardottiret al.[23]	- 3 min work ≥ 80%PWR - 3 min at 30-40% PWR (39min)	- ≥ 65%PWR - (39min)	16	2 times/week	- callisthenics 1 time/week - RT(10 rep 2 sets 70% 1RM) 1 time/week
Varga et al.[24]	- 2 min work 90%PWR - 1 min at 50% PWR (45min)	- 80% PWR (45min)	8	3 times/week	- (CH) Instructed To exercise in their own environment (Stair walking Cycle and walking)
Vogiatzis et al.[25]	- 30 s work 100%PWR - 30 s rest (45min)	- 60% PWR (30min)	10	3 times/week	- (I) increased PWR 20% in week 4 and 7 - (C) increased PWR 10% in week 4 and 7
Mador et al.[26]	- 1 min work 150% of Workload estimated for (C) - 2 min 75% of workload Estimated for (C) (Cycle and Treadmill)	- 50% PWR (Cycle ergometer) - 80% PWR (Treadmill)	8	3 times/week	- Duration not Specified - Intensity in I group was estimated by the Intensity of the (C) Group - patients who could Exercise for 20min (C) And 21 min Without symptoms, The intensity increased by 10% (Cycle) and 5-10% (Treadmill)

Min: Minutes, S: seconds, PWR: Peak work rate, Cycle: Cycle ergometer, (I): Interval group, (C): continuous group, (CH): Continuous home group, 1RM: one repetition maximum, RT: Resistance training, (CH) continuous home group

Data analysis

None of studies included found a significant difference between the two exercise groups.[21-26] Two studies reported a significant improvement in the IE group 6% ($p<0.05$)[23] and 7% ($p<0.05$).[24] Three studies included found a significant improvement in the CE group 17% ($p<0.05$),[22] 13% ($p<0.001$)[23] and 15% ($p<0.05$).[24] The highest improvement in peak VO_2max was 10% ($p>0.05$)[26] and 17% ($p<0.05$)[22] in the IE group and CE group respectively.(Table 7)

Table 7 Data analysis

Author	**(i) VO2 max L/min baseline**	**(i) VO2 max L/min post workout**	**(i) Incr in %**	**(i) P.value within group**	**(c) VO2 max L/min baseline**	**(c) VO2 L/min max post workout**	**(c) Incr in %**	**(c) P.value within group**	**P.value between groups**
Vogiatzis et al.[21]	1.06±0.06	N.S	8%	>0.05	1.09±0.06	N.S	6%	>0.05	>0.05
Coppoolse et al.[22]	1.14±0.18	N.S	6%	>0.05	0.91±0.24	N.S	17%	<0.05	>0.05
Arnardotiret al.[23]	0.98±0.29	1.04±0.30	6%	<0.05	0.97±0.29	1.10±0.30	13%	<0.001	>0.05
Varga et al.[24]	1.10±0.31	1.18±0.36	7%	<0.05	1.17±0.40	1.27±0.40	9%	<0.05	>0.05
Vogiatzis et al.[25]	0.87±0.09	N.S	9%	>0.05	0.97±0.10	N.S	5%	>0.05	>0.05
Mador et al.[26]	1.22±0.32	1.34±0.52	10%	>0.05	1.31±0.62	1.47±0.41	12%	>0.05	>0.05

VO_2max L/min: Maximum oxygen uptake in litres per minute, Incr: Increase, i: Interval group, c: Continuous group

Discussion

The aim of this review was to investigate if IE would be more beneficial than CE to the EC in COPD patients by examining current evidence. After conducting a systematic search and study selection, six RCTs were incorporated in this review.[21-26] The methodological quality of the articles used varied from four[22,23] to seven[26] on the PEDro scale which is considered reasonably good to good quality.[18] The outcome of the literature reviewed in this systematic review suggests that there is no difference between IE and CE in patients with moderate to severe COPD in terms of peak EC. However, IE might be used as an alternative to CE.

Summary of outcome

It was thought that since IE has a greater effect than CE on EC in trained people and patients with heart failure[14,15] the same could apply for COPD patients. However, based on the studies included in this review this is not the case. Arnardottir et al.[23] and Varga et al.[24] were the only authors who reported significant improvement in peak EC in both exercise groups. Coppoolse et al.[22] showed a significant improvement in peak EC in the CE group. The other studies used did not find a significant improvement in peak EC in any of the groups.[21,25,26] Furthermore, it should be emphasized that none of the studies included reported a significant difference between the exercise groups.[21-26] The reason for a non-significant difference in peak EC between IE and CE in COPD patients is not clear.

Exercise protocol

The heterogeneity in the exercise protocols between the studies reveal that there is no clear universal definition of IE.[27] The intensity, duration and frequency varied considerably between the different studies used. In the study conducted by Arnardottir et al. the intensity in the work period in the IE group were set to 80% PWR achieved in a baseline incremental test throughout the entire study[23], while Vogiatzis et al.[21] and Vogiatzis et al.[25] increased the intensity in the work period in the IE group from 100-140% of PWR achieved in a baseline incremental test. Interestingly, despite the great difference in intensity there was a small difference in peak EC improvement with 6% ($p<0.05$)[23], 8% ($p>0.05$)[21] and 9% ($p>0.05$)[25] respectively. Arnardottir et al. also incorporated calisthenics and strength exercises twice/week in addition to the IE.[23] However, the American Thoracic Society (ATS) and European Respiratory Society (ETS) and Bernard et al. reported that despite improvement in peripheral muscle strength, strength exercise in addition to CE do not offer extra improvement in overall EC in COPD patients,[11,28] indicating that the increased peak EC is not influenced by the additional exercise modalities. The reason for a significant increase in the study by Arnardottir et al. is not clear.[23] However, a considerable larger study population was seen in that study (n=60) compared to Vogiatzis et al.[21] (n=36) and Vogiatzis et al.[25] (n=19) which might have influenced the significance of the outcome. Furthermore, this suggest that an intensity of 80% PWR achieved in a baseline incremental test is sufficient to increase peak EC. Nonetheless, duration of the work periods in the IE groups might have influenced the outcome to. Varga et al.[24] and Arnardottir et al.[23] which had the longest work duration in the IE group (2x1 minutes and 3x3 minutes respectively), were the only ones who reported a significant improvement in peak EC in the IE groups by 6% ($p<0.05$) and 7% ($p<0.05$) respectively. This suggests that the duration of the work periods might be an important factor in the improvement of EC.

Vogiatzis et al. set the intensity in the CE group to 50% PWR achieved in a baseline incremental test.[21] The intensity increased by 10% every 4 weeks throughout the intervention period (12 weeks). However, ATS and ETS recommends an intensity of >60% PWR when performing CE[11] which gives 8 weeks with a recommended intensity. This indicates that the outcome 6% ($p>0.05$) increase in peak EC could have been different with a higher intensity from the beginning.

In the study conducted by Varga et al. the intensity was set to 80% of PWR in the CE group.[24] Seven of 22 subjects in that group were allowed to take breaks every 10 min the first nine sessions, and some patients had to start at an intensity of 65%, 15% lower than the target intensity. This suggests that the intensity was too high. Furthermore, it implies that exercise programs should be adjusted to each individual patient. This is also recommended by the ATS and ETS.[11] The same author set the intensity in the IE group during the work period to 90% of PWR. This is a minor difference compared to the CE group when put into Watts (W). The IE group during their work periods had a mean of 79 W while the CE group had a mean of 74 W. This indicates that the constant workload in the CE group gave a greater stimulus than the IE group. However, despite the high constant workload in the CE group both groups improved relatively similar with 7% ($p<0.05$) and 9% ($p<0.05$) in the IE and CE group respectively. Assuming that the seven subjects who were allowed to take breaks and those subjects who started at a lower intensity would have managed the target intensity from the beginning, the outcome could have been different.

Another factor in regards to the exercise protocol in the included studies is the frequency. The ATS and ETS recommend a frequency of three to five times per week.[11] Vogiatzis et al.[21] and Arnardottir et al.[23] exercised two times per week. Interestingly, Arnardottir et al. reported significant improvement in peak EC 6%, ($p<0.05$) and 13% ($p<0.001$) in the IE group and CE group respectively.[23] However, the duration of that intervention was 16 weeks which was the longest intervention of all studies included. This might be a factor for the improvement as it is thought that exercise programs with longer duration yield greater gains.[11]

In the study conducted by Varga et al. the continuous home group was instructed to exercise (climb stairs, cycle and walk in their own environment) at home.[24] That group did not demonstrate a significant improvement in PWR or EC. These findings indicate that exercising for COPD patients should be performed in a supervised environment. This also corresponds with the recommendations by KNGF.[3]

All studies reviewed conducted a symptom limited incremental test at the outset of the experiment to measure peak physiological responses and PWR so that the intensity could be set.[21-26] This type of test is considered to be a “gold standard” test in patients with COPD.[29] However, as symptoms are measured subjectively,[11] the outcome might not always be accurate. This also correspond with the findings of Rossiter et al. who reported that peak EC is not consistently revealed in an incremental test despite apparent maximum effort.[30]

Benefits of exercising

Despite the non-significant findings in peak EC between IE and CE in this review, there were other interesting findings which might be relevant in the rehabilitation of COPD patients. Five of the six studies used showed a significant improvement in PWR in both CE groups and IE groups.[21,23-26] Casaburi et al. reported that higher PWR induce a greater exercise effect by increasing the blood lactate threshold and reducing the ventilatory capacity required to perform exercise.[31] This also resembles the findings in the studies conducted by Varga et al.[24] and Vogiatzis et al.[25] which showed a significant improvement in lactate production in both groups. This indicates that muscle capacity and/or oxygen utilization improvement is independent of the exercise modality.

In relation to minute ventilation (VE), there was a great difference in outcome between the studies. Vogiatzis et al.[21] and Mador et al.[26] showed a significant decrease in VE to an identical work rate exercise test (pre/post rehabilitation) in both groups, with no difference seen between groups. Vogiatzis et al. reported a significant reduction in VE in the IE group to an identical work rate exercise test (pre/post rehabilitation).[25] Arnardottir et al. reported a significant improvement in peak VE in the CE group[23] while two studies did not report significant improvement.[22,24] This suggest that both exercise modalities increase general condition, as deconditioning contribute to excess ventilation, which in turn results in an earlier ventilatory limitation.[11] Another relevant health outcome of the physical rehabilitation for COPD patients is QoL.[3] Five studies incorporated in this review investigated either QoL, dyspnea, fatigue or all three.[21,22,23,25,26] All of these studies reported a significant improvement in both groups during and after exercise in one of the aforementioned parameters.[21,22,23,25,26] This suggests that both exercise modalities will benefit COPD patients in terms of QoL. This also correspond with the findings of Wijkstra et al.[32]

Dropouts

Five authors reported dropouts,[21-24,26] and the dropout rates ranged from 0%[24,26] to 40%.[23] Arnardottir et al. reported that the majority of dropouts was due to exacerbations n=24.[23] Besides that, the overall dropout rate was relatively low which indicate that both modalities are well tolerated by COPD patients.

Clinical relevance

As the one of the goals in the rehabilitation of COPD patients is to reduce the limitations of ADL[3] IE might be an alternative to CE, this because it resembles ADL more than CE.[33] Another relevant clinical aspect is that despite the same benefits, IE seems to be better tolerated by COPD patients.[34] This is might be due to the recovery periods. Furthermore, it is suggested that IE is associated with more enjoyment.[35] This should be considered before prescribing one of the compared exercise modalities as COPD patients tend to have a decreased exercise motivation[11] With all these factors in consideration, IE might be preferred by COPD patients.

PEDro score

The methodological quality of studies used in this review ranged from reasonably good to good. As item five and six is considering blinding of subjects and therapists and this is not possible in the topic investigate on in this review, the RCTs automatically loses two points on the overall quality. However, one study[25] achieved a point in item five in the original score but not by the author of this paper. (APPENDIX I)

Best evidence synthesis

All articles used in this systematic review showed consistent findings in terms of IE compared to CE. Five of the used studies achieved reasonably good to good score on the PEDro scale making them high quality RCTs. This in turn suggests that there is strong evidence that there is no difference between the two exercise modalities.

Strengths, limitations and future research

The strengths of the studies used in this systematic review are that all used articles achieved reasonably good to good methodological quality which in turn contributed to the strong evidence. Furthermore, this systematic review has been supervised by an experienced researcher throughout the project and it has been peer reviewed by three external persons which is considered to be a strong point. Some weaknesses in this review are to be considered. Four of the studies included in this systematic review had a relatively small study population with less than 45 participants.[21,22,25,26] This is a point which should be taken into account in future research. It should also be investigated into the optimal exercise protocol to establish which protocol yield the best result. The same accounts for the duration of the studies. 16 weeks was the longest trial while the shortest lasted for six weeks. A longer duration might yield better outcome.[11]

Conclusion

There is strong evidence suggesting that there is no difference between continuous exercise and interval exercise when wanting to improve exercise capacity in chronic obstructive pulmonary disease patients. However, both exercise modalities shows improvement in peak exercise capacity. Interval exercise might therefore be used as an alternative to continuous exercise.

References

1. Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJL. Global burden of disease and risk factors. Illustrated ed. Washington (DC): World Bank; 2006.
2. Nilsen R, Johannessen A, Benediktsdottir B, Gislason T, Buist AS, Gulsvik A, et al. Present and future costs of COPD in Iceland and Norway: results from the BOLD study. Eur Respir J. 2009 October; 34 (4): 850-857.
3. Gosselink R, Langer D, Burtin C, Probst V, Hendriks HJM, van der Schans, et al. KNGF-Guideline for physical therapy in patients with chronic obstructive pulmonary disease. Dutch Journal of Physical Therapy. 2008; 118: (4) (Suppl)
4. Raherison C, Girodet P-O. Epidemiology of COPD. Eur Respir Rev. 2009 December; 18 (114): 213-221.
5. Global strategy for the Diagnosis, Management and Prevention of COPD. Global Initiative for chronic obstructive lung disease (GOLD) 2014. Available from: http://www.goldcopd.org/.
6. Higginson R. COPD: pathophysiology and treatment. Nurse Prescribing. 2010 March; 8 (3): 102-10.
7. Lan LTT, Dinh-Xuan AT. Pathophysilogy updates for chronic obstructive pulmonary disease. Curr Respir Care Rep. 2013 September; 2 (3): 139-144.
8. Marieb EN, Hoehn K. Human anatomy & physiology. ed. 8. San Francisco: Pearson education, publishing as Pearson Benjamin Cummings; 2010.
9. Mattison S, Christensen M. The pathophysiology of emphysema: considerations for critical care nursing practice. Intensive and Critical Care Nursing. 2006 December; 22 (6): 329-337.
10. Blinderman CD, Homel P, Billings A, Tennstedt S, Portenoy RK. Symptom distress and quality of life in patients with advanced chronic obstructive pulmonary disease. J Pain Sympt Man. 2009 July; 38 (1):115-123.
11. Spruit MA, Sing SJ, Garvey C, ZuWallack R, Nici L, Rochester C, et al. An official american thoracic society/european respiratory society statement: key concepts and advances in pulmonary rehabilitation. AM J Respir Crit Care Med. 2013 Oktober; 188 (8): 13-64.
12. Belfer MH, Reardon JZ. Improving exercise tolerance and quality of life in patient with chronic obstructive pulmonary disease. J Am Osteopath Assoc. 2009 May; 109 (5): 268-278
13. Spruit MA, Gosselink R, Troosters T, De Paepe K, Decramer M. Resistance versus endurance training in patients with COPD and peripheral muscle weakness. Eur Respir J. 2002 June; 19 (6): 1072-1078.
14. Laursen PB, David GJ. The scientific basis for high-Intensity interval training: optimising training programmes and maximising performance in highly trained endurance athletes. Sports Med. 2002; 32 (1): 53-73.
15. Wisløff U, Støylen A, Lonnechen JP, Bruvold M, Rognmo Ø, Haram PM, et al. Superior cardiovascular effect of aerobic interval training versus moderate continuous training in heart failure patients: a randomized study. Circulation. 2007 June; 115 (24): 3086-3094.

16. LoRusso TJ, Belman MJ, Elashoff JD, Koerner SK. Prediction of maximal exercise capacity in obstructive and restrictive pulmonary disease. Chest. 1993 December; 104 (6): 1748-1754.
17. De Morton NA. The PEDro scale is a valid measure of the methodological quality of clinical trials: a demographic study. Aust J Physiother. 2009; 55 (2): 129-133.
18. Maher CG, Sherrington C, Herbert RD, Moseley AM, Elkins M. Reliability of the PEDro scale for rating quality of randomized controlled trials. Phys Ther. 2003 August; 83 (8): 713-721.
19. van Peppen RPS, Kwakkel G, Harmeling-van der wel BC, Kollen BJ, Hobbelen JSM, Buurke JH, et al. KNGF Clinical Practice Guideline for physical therapy in patients with stroke. Dutch Journal of Physical Therapy. 2004; 114 (5) (Suppl)
20. van Tulder M, Furlan A, Bobardier C. Updated method guidelines for systematic reviews in the cochrane collaboration back review group. Spine. 2003 June; 28 (12): 1290-1299.
21. Vogiatzis I, Nanas S, Roussos C. Interval training as an alternative modality to continuous exercise in patients with COPD. Eur Respir J. 2002 July; 20 (1): 12-21.
22. Coppoolse R, Schols AM, Baarends EM, Mostert R, Akkermans MA, Janssen PP, et al. Interval versus continuous training in patients with severe COPD: a randomized clinical trial. Eur Respir J. 1999 August; 14 (2): 258-263.
23. Arnardottir RH, Boman G, Larsson K, Hedenstrom H, Emtner M. Interval training compared with continuous training in patients with COPD. Respir Med. 2007 June; 101 (6): 1196-1204.
24. Varga J, Porszasz J, Boda K, Casaburi R, Somfay A. Supervised high intensity continuous and interval training vs. self-paced training in COPD. Respir Med. 2007 November; 101 (11): 2297-2304.
25. Vogiatzis I, Terzis G, Nanas S, Stratakos G, Simoes DC, Georgiadou O, et al. Skeletal muscle adaptations to interval training in patients with advanced COPD. Chest. 2005 December; 128 (6): 3838-3845.
26. Mador MJ, Keawza M, Alhajhusian A, Khan AL, Shaffer M, Kufel TJ. Interval training versus continuous training in patients with chronic obstructive pulmonary disease. J Cardiopulm Rehabil Prev. 2009 March-April; 29 (2): 126-132.
27. *Gibala MJ.* High-intensity interval training: new insight. *Sports Science Exchange.* 2007; 20 (2).
28. Bernard S, Whittom F, LeBlanc P, Jobin J, Belleau R, Berube C, et al. Aerobic and strength training in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 1999 March; 159 (3): 896-901.
29. Turner SE, Eastwood PR, Cecins NM, Hillman DR, Jenkins SC. Physiologic responses to incremental and self-paced exercise in COPD: a comparison of three tests. Chest. 2004 September; 126 (3): 766-773.
30. Rossiter HB, Kowalchuk JM, Whipp BJ. A test to establish maximum O2 uptake despite no plateau in the o2 uptake response to ramp incremental exercise. J Appl Physiol. 2006 March; 100 (3): 764- 770.

31. Casaburi R, Patessio A, Loli F, Zanaboni S, Donner CF, Wasserman K. Reductions in exercise lactic acidosis and ventilation as a result of exercise training in patients with obstructive lung disease. Am Rev Respir Dis. 1991 January; 143 (1): 9-18.

32. Wijkstra PJ, Van Altena R, Kraan J, Otten V, Postma DS, Koeter GH. Quality of life in patients with chronic obstructive pulmonary disease improves after rehabilitation at home. Eur Respir J. 1994 February; 7 (2): 269-273.

33. Rochester CL. Exercise training in chronic obstructive pulmonary disease. JRRD. 2003 October; 40 (5): 59-80.

34. Puhan MA, Busching G, Schunemann HJ, vanOort E, Zaugg C, Frey M. Interval versus continuous high-intensity exercise in chronic obstructive pulmonary disease: a randomized trial. Ann Intern Med. 2006 December; 145 (11): 816-825.

35. Bartlett JD, Close GL, Maclaren DP, Gregson W, Drust B, Morton JP. High intensity interval running is perceived to be more enjoyable than moderate-intensity continuous exercise: implications for exercise adherence. J Sports Sci. 2011 March; 29 (6): 547-553.

Appendix I. PEDro score

The PEDro scale assess RCTs for the methodological quality. It is considered a valid (REF and reliable (REF) measure. It consists of 11 items. As item one takes external validity into account, this item is excluded when rating, leaving 10 items left for scoring the RCT (REF same som reliable) One point was given if the criteria was specifically stated in the RCT. Depending on the score achieved the RCT was graded as Poor (score 0-3), Reasonably good (score 4-5), Good (score 6-8) and very good (score 9-10)[3]

Table 8. PEDro score

Author	1	2	3	4	5	6	7	8	9	10	11	Score	Overall quality
Vogiatzis et al[21]	Y	Y	N	Y	N	N	Y	N	N	Y	Y	5/10	Reasonably good
Coppoolse et al[22]	Y	Y	N	N	N	N	N	N	Y	Y	Y	4/10	Reasonably good
Arnardottir et al[23]	Y	Y	Y	Y	N	N	N	N	N	Y	Y	4/10	Reasonably good
Varga et al[24]	Y	Y	N	Y	N	N	N	Y	N	Y	Y	5/10	Reasonably good
Vogiatzis et al[25]	Y	Y	N	Y	N	N	N	Y	N	Y	Y	5/10	Reasonably Good
Mador et al[26]	Y	Y	Y	Y	N	N	Y	Y	N	Y	Y	7/10	Good ‘

Appendix II - PEDro scale criteria

Criterion 1	This criterion is satisfied if the report describes the source of subjects and a list of criteria used to determine who was eligible to participate in the study.
Criterion 2	A study is considered to have used random allocation if the report states that allocation was random. The precise method of randomisation need not be specified. Procedures such as coin-tossing and dice-rolling should be considered random. Quasi-randomisation allocation procedures such as allocation by hospital record number or birth date, or alternation, do not satisfy this criterion.
Criterion 3	Concealed allocations means that the person who determined if a subject was eligible for inclusion in the trial was unaware, when this decision was made, of which group the subject would be allocated to. A point is awarded for this criteria, even if it is not stated that allocation was concealed, when the report states that allocation was by sealed opaque envelopes or that allocation involved contacting the holder of the allocation schedule who was “off-site”.
Criterion 4	At a minimum, in studies of therapeutic interventions, the report must describe at least one measure of the severity of the condition being treated and at least one (different) key outcome measure at baseline. The rater must be satisfied that the groups’ outcomes would not be expected to differ, on the basis of baseline differences in prognostic variables alone, by a clinically significant amount. This criterion is satisfied even if only baseline data of study completers are presented.
Criteria 4, 7-11	Key outcomes are those outcomes which provide the primary measure of the effectiveness (or lack of effectiveness) of the therapy. In most studies, more than one variable is used as an outcome measure.
Criterion 5-7	Blinding means the person in question (subject, therapist or assessor) did not know which group the subject had been allocated to. In addition, subjects and therapists are only considered to be “blind” if it could be expected that they would have been unable to distinguish between the treatments applied to different groups. In trials in which key outcomes are self-reported (eg, visual analogue scale, pain diary), the assessor is considered to be blind if the subject was blind.
Criterion 8	This criterion is only satisfied if the report explicitly states both the number of subjec initially allocated to groups and the number of subjects from whom key outcome measures were obtained. In trials in which outcomes are measured at several points in time, a key outcome must have been measured in more than 85% of subjects at one of those points in time.
Criterion 9	An intention to treat analysis means that, where subjects did not receive treatment (or the control condition) as allocated, and where measures of outcomes were available, the analysis was performed as if subjects received the treatment (or control condition) they were allocated to. This criterion is satisfied, even if there is no mention of analysis by intention to treat, if the report explicitly states that all subjects received treatment or control conditions as allocated.
Criterion 10	A between-group statistical comparison involves statistical comparison of one group with another. Depending on the design of the study, this may involve comparison of two or more treatments, or comparison of treatment with a control condition. The analysis may be a simple comparison of outcomes measured after the treatment was administered, or a comparison of the change in one group with the change in another (when a factorial analysis of variance has been used to analyse the data, the latter is often reported as a group × time interaction). The comparison may be in the form hypothesis testing (which provides a “p” value, describing the probability that the groups differed only by chance) or in the form of an estimate (for example, the mean or median difference, or a difference in proportions, or number needed to treat, or a relative risk or hazard ratio) and its confidence interval.
Criterion 11	A point measure is a measure of the size of the treatment effect. The treatment effect may be described as a difference in group outcomes, or as the outcome in (each of) all groups. Measures of variability include standard deviations, standard errors, confidence intervals, interquartile ranges (or other quantile ranges), and ranges. Point measures and/or measures of variability may be provided graphically (for example, SDs may be given as error bars in a Figure) as long as it is clear what is being graphed (for example, as long as it is clear whether error bars represent SDs or SEs). Where outcomes are categorical, this criterion is considered to have been met if the number of subjects in each category is given for each group.