Blood flow restriction training for people with chronic obstructive pulmonary disease or heart failure; A scoping review

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Abstract:

**Background:** Blood flow restriction training (BFRT) is an effective way of training that enables training with low external load while receiving similar effects to high load training. The lack of knowledge of BFRT for people with chronic obstructive pulmonary disease (COPD) or heart failure (HF) led to the making of this scoping review.

**Objective:** This scoping review aims to map the existing knowledge, effects, safety, and feasibility of BFRT for people with COPD or heart failure HF.

**Method:** The review followed PRISMA’s structure for scoping review. Selection involved title and abstract screening, followed by full text analysis and peer-review by both authors.

**Results:** A wide variety of study designs was included in this scoping review. Of 11 included studies all were original intervention studies, whereof 8/11 studies were focused on HF. A large majority of participants were male. Training methods used in intervention studies varied from exercises like leg extensions, leg press and cycling, all while using vascular blood flow restriction. All studies followed different training protocols. The reported outcomes indicated promising improvements like increased functional exercise capacity, muscle strength, reduced symptom burden, and several positive physiological changes for both people with COPD and HF. Some concerns remain regarding the safety of BFRT, but no serious adverse events were reported directly linked to BFRT.

**Conclusion:** With many reported improvements, BFRT could be a safe and feasible alternative rehabilitation method for people with COPD or HF. Furthermore, with minimal reported adverse events, the method appears safe for both groups. Despite this, the included studies all had small sample sizes, so more high-quality studies with larger sample sizes are needed to give a better understanding on BFRTs effects on both short- and long term. Better studies including females are also needed.
Svensk sammanfattning:

**Bakgrund:** Ocklusionsträning är en effektiv träningsmetod som möjliggör träning på låg yttre belastning samtidigt som det ger effekter liknande högbelastande träning. Bristen på kunskap om ocklusionsträning för personer med kronisk obstruktiv lungsjukdom (KOL) eller hjärtsvikt ledde till denna litteraturstudie.

**Syfte:** Syftet med denna översiktsstudie var att kartlägga befintlig kunskap, effekter, säkerhet och genomförbarhet gällande ocklusionsträning för personer med kronisk obstruktiv lungsjukdom (KOL) eller hjärtsvikt.

**Metod:** Arbetets struktur utgår ifrån PRISMA:s checklista för litteraturstudier. Litteraturstudien innehåller olika typer av studier och publikationer som utforskar ocklusionsträning för ovanstående grupper. Urval skedde genom granskning av titlar och abstrakt, därefter granskning av full text samt kvalitets kontroll av båda författare.

**Resultat:** Arbetet inkluderade många olika typer av interventionsstudier. Av 11 inkluderande studier var samtliga original interventionsstudier. 8/11 behandlade hjärtsvikt. En stor majoritet av deltagare var män. Träningsmetoder som användes i interventionsstudier varierade från olika typer av benspark, benpress och cykling, allt med ocklusion av venöst återflöde av blod. Alla studier använde sig av olika träningsprotokoll. Rapporterade resultat visade på förbättringar gällande ökad funktionell träningskapacitet, muskelstyrka, minskad symptombörda och flertalet positiva fysiologiska förändringar för både personer med KOL och hjärtsvikt. Ett fåtal farhågor finns avseende säkerhet med metoden, men ingen studie rapporterade några allvarliga negativa händelser kopplat till ocklusionsträningen.

**Slutsats:** Med många rapporterade fördelar kan ocklusionsträning vara en alternativ träningsmetod för personer med KOL eller hjärtsvikt. Med få rapporterade negativa effekter verkar metoden säker för båda grupper. Trots detta hade samtliga studier små studiepopulationer, därav krävs det ytterligare studier med större populationer för att utvärdera ocklusionsträningens långsiktiga effekter, genomförbarhet och säkerhet för båda grupper. Bättre och fler studier som inkluderar kvinnor behövs även.
Introduction

Chronic obstructive pulmonary disease (COPD) and heart failure (HF) are two of the most common chronic conditions worldwide (1, 2). People with COPD and HF often become more sedentary (3, 4) and have a risk of secondary sarcopenia (5), especially in cases of more severe disease (6-8). Sarcopenia increases the risk of adverse events and is a prognostic factor for severity of disease and symptoms (7, 9).

For both groups exercise plays an important part when it comes to rehabilitation. This is due to a high prevalence of decreased muscle strength and endurance in peripheral skeletal muscles for both groups (10-12). For people with COPD or HF, exercise and physical activity; both aerobic and muscle strengthening, can help increase muscle strength and endurance, as well as increase physical capacity. It also increases health related quality of life as well as reduce the risk of hospitalisation and mortality (13, 14).

When performing aerobic exercise or physical activity the working muscles require oxygen. Through a complex interaction between various parts of the body, oxygenated blood is transported to the working muscle, so that the oxygen demand of the muscle can be met. The relative oxygen demand is based on intensity of work performed, muscle recruitment and muscle size. In cases with more severe HF or COPD, the ability to deliver enough oxygenated blood to the working muscles may be limited for both groups. This inability makes people with HF and COPD end up in anaerobic muscular effort faster, especially when performing exercise on higher relative intensity or with large muscle groups (15-17).

For people with HF, the difficulty to meet the required oxygen demand from the working skeletal muscles comes from a remoulded heart muscle tissue. The changes lead to reduced contractility which in turn leads to lower stroke volume and thus peripheral blood flow (16, 17).

People with COPD are limited due to structural changes in peripheral airways and lung tissue. The peripheral airways get tighter, while the emphysema; that is damages on the alveolar walls, leads to reduced gas exchange and reduced elastic rebound (18). In cases of more pronounced disease severity, both COPD and HF patients may encounter difficulties and constraints during more intense exercise. They can experience symptoms such as dyspnea or fatigue, stemming from their limited capacity to provide a sufficient supply of oxygen-enriched blood to the active skeletal musculature, therefore contributing to their exercise intolerance (11, 19, 20).

A goal when performing muscle-strengthening exercise for both people with COPD or HF is therefore to reduce the load on the cardiovascular or pulmonary systems by decreasing the relative intensity. By doing that, disease-related symptoms such as dyspnoea can be avoided. Methods used include training fewer or smaller muscles. This can be achieved by unilateral training or by focusing on small peripheral muscles (21, 22). By doing that, the total volume of working muscles decreases, which reduces the total oxygen demand and consumption. This decreases the load on the cardiovascular and pulmonary systems, thus reducing the risk that the limiting factor for muscle-strengthening exercise is those systems.

Another method of training that also could reduce the load on pulmonary and cardiovascular systems is Blood Flow Restriction Training (BFRT). It is a way of training that originates from a method called “KAATSU”. KAATSU is both a training method and a brand name. KAATSU means “additional pressure” in Japanese, and it was first introduced in 1966 by Yoshiaki Sato (23). The training method KAATSU is muscle strengthening training while limiting venous blood flow, which is the same as BFRT. Throughout this review KAATSU and blood flow restriction training will be used synonymously using the term BFRT.
BFRT involves placing an air pressure cuff or tourniquet proximal to the muscle belly. The cuff should exert enough pressure so that venous blood return is limited, without impeding the oxygen-rich arterial blood flow. This results in an accumulation of capillary blood with low oxygen tension. The aim is to simulate the metabolic environment with accumulated metabolites that occurs during high-load training, while keeping external load relatively low (24, 25).

The ability to regulate metabolites in the working muscle is the limiting factor for maintaining acid-base homeostasis inside the muscle. When enough metabolites gather, the pH of the muscle lowers which in turn simulate the release of growth hormone, consequently stimulating muscle hypertrophy (26). While the exact reason for the hypertrophy gains seen after a period of BFRT are not fully mapped, other factors for hypertrophy gains when performing BFRT include satellite cell activation, cell swelling, more myonuclei and a better stimulation of muscle protein synthesis (27-29).

The variability of exercise protocols when it comes to BFRT is large, but all exercise with vascular occlusion seems to fall within the term BFRT. Examples of BFRT varies from functional exercises such as walking (30, 31), to high as well as low intensity cycling for both upper and lower extremity (32-39). Furthermore, it could also include strength training of specific muscle groups (40), mostly revolving the knee joint, for example for osteoarthritis and ACL injuries (41).

The knowledge regarding effects and feasibility of BFRT for people with COPD or HF is limited. BFRT is a proposed method to muscle strengthening training in sarcopenia (42, 43), which is common for both people with COPD or HF (6-9). Therefore, BFRT should be evaluated as a possible treatment. When evaluating the effectiveness and tolerability, BFRT is deemed as more effective and tolerable compared to low-load training without occlusion in patients with sarcopenia (40).

The alternatives when it comes to muscle strengthening training and exercise for people with COPD and HF are many. Despite this, the compliance to exercise programmes remains low. This is due to both disease related reasons; like exacerbations, illness or death, and other more personal reasons such as lack of time, motivation, or cooperation. The cooperation aspect is described as patients unwilling to participate, difficulties with traveling or dropout due to the training program being too hard (44, 45). Low compliance and adherence create a conundrum of how clinicians can help increase adherence to exercise interventions. Having several different methods and modalities at your disposal as a clinician is one way of increasing adherence by being able to tailor the approach based on the individual. Therefore, adding further effective treatment methods is of clinical importance. BFRT could be a possible method to implement in clinical practice to perhaps increase compliance and adherence to exercise for some individuals.

The limited knowledge and lack of randomized clinical trials to evaluate BFRT for people with COPD or HF led to the making of a scoping review. The aim of this scoping review was to map the existing knowledge, effects, safety, and feasibility of BFRT for people with COPD or HF.
Methods
This scoping review was structured according to PRISMA's checklist for scoping reviews (46).

Firstly, we identified which databases would be eligible to find relevant articles in. This was done in conversation with both tutors and a university librarian. The authors got help with how the construction of the search query and adjust it to the different databases. Then inclusion and exclusion criteria were formulated and defined during the primary screening process. Some clarification on the criteria was done in the later screening process. The search was first conducted in September 2023 and were regularly searched until November 2023 in case of any updates. One article was published in full text in December 2023 and was included in full text. The selection process and the screening process is presented in figure 1, PRISMA's flow diagram, where the first selection process was from title and abstract. The second stage was to read the full text. If a full text was not available on the database, the online University library was used to inquire the full text. One study was included where full text was available on the university library and not the database.

Information sources
Information sources in the scoping review was limited to databases and reference lists of included sources.

List of databases used:
- PubMed
- Web of science
- J-Stage

Conference abstracts were included.
The latest search was conducted 2023-11-20.

Search
The following full search was developed by both authors in collaboration with a university librarian. The query is an example taken from a search conducted on the PubMed database and can be directly pasted into a search query box:

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No limits in timeline or filters were used.
Eligibility criteria
For this review, only studies that were peer reviewed original articles of an experimental design were included. Included articles needed to consist of established data variables and needed to be in accordance with the objective of this study.

Inclusion:
Any peer reviewed study with any design and any type of publication that somehow explore the effects of BFRT for human subjects with COPD or HF was included if they were in or translated to English. Studies that examined effects of BFRT for people with cardiovascular diseases (CVD) was included if people with HF were part of the study population. Any year of publication was eligible.

Exclusion:
Non-peer reviewed publications. BFRT for other populations than COPD or HF was excluded from the result. Articles that were deemed to be scientific editorials, scientific ideas, expert letters, opinion papers or animal studies were not considered for data extraction, however they could be part of the discussion.

Data charting process
The sources collected were summarized and sorted by disease, protocol, outcome measures, safety and feasability. All articles were screened based on title and abstract by both authors. Selected articles were read and analyzed by both authors. The data synthesis was done separately at first and then by both authors. An article was eligible when read and reviewed by both authors, relevant to any major objective of this study, included at least one of the data items and fit the criteria for eligibility.

A charting process related to effects of BFRT for COPD or HF subjects was performed.

Critical appraisal of individual sources of evidence
Sources of evidence were checked for peer-review by both authors using Ulrichsweb (47), before being included in this scoping review. For the articles not found on Ulrichsweb we searched peer review policies of the journals the articles were published in. This was the only methods for critical appraisal. All included articles were peer reviewed.

Synthesis of results
The data from each study was first summarized in a separate document before a more complete composite summary of all included studies.
Results
Selection of sources of evidence
The first stage in selection of sources was identification of databases and via other methods. This step consisted of search queries on each of them on each database and removal of duplicates. The search on both databases and via other sources resulted in 86 articles after 19 duplicates were removed. Number of sources from each database and other methods can be seen in figure 1.

The second stage consisted of screening, first based on title and abstract. After screening of title and abstract 70 irrelevant articles were removed which resulted in 16 remaining articles. These articles were then screened for full text, also followed by removal of irrelevant articles. This resulted in 11 articles sought for retrieval for this scoping review. 8 of them were towards HF and 3 towards COPD. Reason for exclusion and available text can be seen under “screening” in figure 1.
### Characteristics of sources of evidence

The characteristics of included studies are shown below in table 1.

<table>
<thead>
<tr>
<th>Author [study design]</th>
<th>Subject characteristics</th>
<th>Intervention characteristics</th>
<th>Intervention program design</th>
<th>Blood flow restriction method</th>
<th>Outcome results</th>
<th>Adverse events</th>
</tr>
</thead>
</table>
| Groennebaek et al., (2019) (48) [RCT] | **Disease:** CHF  
**Mean age (±SD):** 64±8  
**Sex (T – M/F):** 36-34/2 | IG: Bilateral leg extension with BFR. CG: no exercise | 4 sets to failure. 30 second rest with cuffs on. 3x per week for 6 weeks | 14 cm cuffs inflated to 50% of individual arterial occlusion | IG: 6MWT↑, MIS↑, QOL↑, MF↑ | None |
| Tanaka and Takarada, (2018) (49) [RCT] | **Disease:** CHF  
**Mean age (±SD):** 60.7±11.1  
**Sex (T – M/F):** 30 – 30/0 | Cycle ergometer AT, at 40-70% peak VO₂. IG: with BFR, CG: without BFR | 5-minute warmup + 15 minutes 3x per week for 6 months | Cuff placed on proximal part of thigh. Mean pressure of 208.7±7.4 mmHg | IG: peak VO₂/watt↑, serum BNP↓, exercise capacity↑, aerobic threshold↑ | None |
| Kohlbrenner et al., (2021) (50) [Single subject case report] | **Disease:** COPD  
**Mean age (±SD):** 60  
**Sex (T – M/F):** 1 -1/0 | Bilateral seated leg press & knee extension + complementary cycling | 4 sets (1st set 30 repetitions, then 3×15 rep.). 45° rest with cuffs on. 2x per week for 6 weeks followed by a 6 week period of high load strength training at 3×8-12 reps 2 times per week | 11 cm cuffs proximal thigh. 70% AOP. | SB↓, LLS↑ (Knee extensor 520%, knee flexor 95%), FEC (6MWT)↑, 1STS↑ | None |
| Ishizaka et al., (2019) (51) [Pilot study] | **Disease:** CVD including HF  
**Mean age (±SD):** 48±14  
**Sex (T – M/F):** 7 –6/1 (*) | Bilateral seated leg extension | Quasi-experimental design | Cuff width: 60 mm, Pressure: 180 mmHg | -Similar respiratory and circulatory responses among controls and intervention group | None |
<p>| Kohlbrenner et al., (2023) (52)  | <strong>Disease:</strong> COPD  | <strong>Mean age (±SD):</strong> 63±9  | <strong>Sex (T – M/F):</strong> 30 – 17/13  | <strong>IG:</strong> LL-BFR-ST  | <strong>CG:</strong> HL-ST  | <strong>Leg muscle strength training</strong>  | <strong>24 sessions in total, 2x/week for 12 weeks</strong>  | <strong>IG:</strong> 30% of 1RM  | <strong>CG:</strong> 70% of 1RM  | <strong>IG: 70% occlusion</strong>  | <strong>IG: PA↑. No significant strength difference between IG and CG</strong>  | <strong>Improvements in both groups in isometric strength, estimated dynamic strength, 6MWT, 1STS, SB.</strong>  | None  |
| Johnson et al., 2021 (53) [Case comparison] | <strong>Disease:</strong> HF  | <strong>Mean age (±SD):</strong> 56.5±14.5  | <strong>Sex (T – M/F):</strong> 2 - 1/1  | <strong>Supine alternating straight leg raises</strong>  | <strong>1 session:</strong> 5 sets, 15 repetition alternating SLR with BFR, 5min rest no cuffs  | <strong>60% LOP for both S-HF and LS-HF.</strong>  | None  |
| Gempel et al., 2021 (54) [Case report] | <strong>Disease:</strong> HF  | <strong>Mean age (±SD):</strong> 42  | <strong>Sex (T – M/F):</strong> 1 – 0/1  | <strong>Supine alternating straight leg raises</strong>  | <strong>3 sets x 30 repetitions, 5 min rest with deflated cuffs between sets, 2x/week for 3 weeks</strong>  | <strong>60% LOP</strong>  | **No changes in SV, nor CI, SMS knee extension ↑ (50%), SMS hip extension↑ (12.5% &amp; 13%), slight increase in LVEF%, GI-issues ****  |
| Lau C. W. et al., (2023) (55) [Single-blinded RCT] | <strong>Disease:</strong> COPD (AE COPD)  | <strong>Mean age (±SD):</strong> 74.9 ±11.9  | <strong>Sex (T – M/F):</strong> 45 - 43/2  | <strong>Supine single limb unilateral isotonic knee extension</strong>  | <strong>Both IG and CG also received a standardized pulmonary rehabilitation protocol</strong>  | <strong>4 sets; set 1: 30 repetitions, set 2-4: 15 repetitions or to failure (≥15 repetitions). 30 second rest between sets. Execution speed: 1-2 seconds/repetition. 5-6 unilateral sessions / week for 2 week. Eligibility was ≥10 sessions. Both IG &amp; CG used 15-30% of estimated 1RM, but only IG had BFR</strong>  | <strong>80% LOP, for maximum of 10 minutes</strong>  | <strong>MVIC↑ (IG: 20N, CG: 6N), SB↓</strong>  | **Significantly more “acute medical events” in IG compared to CG (acute exacerbations, hospital acquired infections, accidental fall and insomnia) ****  |
| Kothonidis et al., (2020) (56) [Crossover study] | <strong>Disease:</strong> CHF  | <strong>Mean age (±SD):</strong> 55.6 ±12.2  | <strong>Sex (T – M/F):</strong> 9 - 7/2  | <strong>Cycling @ 65% of VO2 max. Participants performed both with and without BFR at the same intensity</strong>  | <strong>20 min cycling with BFR, and 20 min without</strong>  | <strong>Occlusion pressure proportional to thigh circumference</strong>  | <strong>Acute response to exercise: with BFR: Mean VO2 ↑, HR ↑, fatigue ↑, dyspnea ↑; all compared to control (acute response without BFR). No difference in SBP and DBP between groups</strong>  | None  |</p>
<table>
<thead>
<tr>
<th>Study</th>
<th>Disease:</th>
<th>Unilateral plantar flexion</th>
<th>Occulsion pressure: 130% of systolic blood pressure for all sets with BFR.</th>
<th>RE with BFR at 20% 1RM had comparable effects to RE without BFR at 60% 1RM in healthy subjects</th>
<th>None</th>
</tr>
</thead>
<tbody>
<tr>
<td>Takahashi et al., (2010) (57) [Research study]</td>
<td><strong>DHF</strong></td>
<td>2 min (30 rep/min), 1x40% 1RM, 1x50% 1RM, 1x60% 1RM without BFR.  2 min (30 rep/min), 1x20% 1RM, 1x30% 1RM, 1x40% 1RM with BFR.</td>
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<tr>
<td>Ishizaka et al., (2022) (58) [Block-randomized cross-sectional experimental study]</td>
<td><strong>CVD inclu</strong>d HF</td>
<td>Block randomization 3x15 at 20% 1RM with or without BFR followed by the other. 30 seconds rest between sets. 5 min rest between blocks. Lifting tempo was 1 second concentric and one second eccentric.</td>
<td>Start mmHg, elevated to 200 mmHg, 5cm cuffs.</td>
<td>Similar respiratory and circulatory responses, dyspnea, and knee extensor effort when performing BFRT for healthy subjects and cardiovascular rehabilitation patients</td>
<td>None</td>
</tr>
</tbody>
</table>

**RCT** - Randomized control trial, **CHF** - Chronic/congestive heart failure, **±SD** - ±Standard deviation, **T** - Total subjects, **M/F** - Male/Female, **IG** - Intervention group, **BFR** - Blood flow restriction, **CG** - Control group, **6MWT** - 6 Minute walk test, **MIS** - Maximum isometric strength, **QOL** - Quality of life, **MF** - Mitochondrial function, **AT** - Aerobic training, **VO2** - Volume of oxygen, **BNP** - Brain natriuretic peptide, **COPD** - Chronic obstructive pulmonary disease, **AOP** - Arterial occlusion pressure, **SB** - Symptom burden, **LLS** - Lower limb strength, **FEC** - Functional exercise capacity, **1STS** - one minute sit to stand, **CVD** - Cardiovascular disease, **HF** - Heart failure, **LL-BFR-ST** - Low load blood flow restriction strength training, **HL-ST** - High load strength training, **1RM** - One rep max, **PA** - Physical activity, **LOP** - Limb occlusion pressure, **S-HF** - Severe heart failure, **LS-HF** - Less severe heart failure, **CV** - Cardiac performance, **SV** - Stroke volume, **CI** - Cardiac index, **SMS** - Skeletal muscle strength, **BFEV** - Left ventricular ejection fraction, **GI issues** - Gastrointestinal issues, **AE COPD** - Acute exacerbation chronic obstructive pulmonary disease, **MVIC** - Maximum voluntary isometric contraction, **HR** - Heart rate, **SBP** - Systolic blood pressure, **DBP** - Diastolic blood pressure, **RE** - Resistance exercise

* Only the number in the parenthesis had HF and their data is only relevant to objective, but specific data could not be extracted, despite author contact

**authors only address these as minor adverse events or non-serious adverse event

**Table 1 – Summary of included studies**
Chronic obstructive pulmonary disease studies

Three studies looked at BFRT with COPD (50, 52, 55), with one of them being COPD subjects with a recent acute exacerbation (AE COPD) (55). One was a single subject mixed protocol case report (50), one were randomized controlled trials (RCT) (55) and one a randomized pilot study (52). The RCT by Lau et al. compared BFRT to low load strength training (LL-ST) (55) and the randomized pilot study by Kohlbrenner et al. compared BFRT to high load strength training (HL-ST) (52). In total there were 76 people studied, where 36 completed a BFRT program and of those 9 were female (25%). The case study was a woman (50) and the subsequent pilot study had 7/15 female participants in the IG (52), but the study by Lau et al. study only had 1/20 female participants in their IG group (55).

All included studies had complementary rehabilitation protocols in addition to the BFRT. The BFRT protocol in all studies were 4 sets consisting of 30 repetitions for set 1 and 15 repetitions for the remaining 3 sets with a predetermined repetition speed. The study by Lau et al. looking at AE COPD patients were older (74.9 ±11.9 ) than in the two studies by Kohlbrenner et al. (62 and 63±9). Higher occlusion pressure was also used by Lau et al. than in the studies by Kohlbrenner et al. (80% / 70%). Similar external load was used for all subjects conducting BFRT (15-30% / 30%) (50, 52, 55). The case study by Kohlbrenner et al. had a combined study protocol consisting of 6 weeks of BFRT and 6 weeks of strength training at 70% of estimated 1RM at 3 sets of 8-12 repetitions, so called high load strength training (HL-ST). All measures were after the combined 12-week period (50). The subsequent study by Kohlbrenner et al. then compared the first 6-week period to the second 6-week period against one another over a period of 12 weeks. They also modified the time on the stationary bike at a 7/10 on the modified Borg scale for dyspnea from 30 minutes to 20 minutes and added 4x90 minutes of educational and behavioral program for all subjects. (52)

In the study done by Lau et al. it was a notable dropout rate in both groups, with more dropouts in the BFRT group (40% / 20%). One person in the control group dropped out because of unpredicted early discharge and 2 subjects dropped out in the BFRT group also due to unpredicted early discharge. 3 more subjects in the BFRT group dropped out because of infection contact precautions and 2 defaulted training, one due to pain related to occlusion pressure and one due to an asymptomatic bradycardia related to the underlying complete heart block with conservative treatment. That means only 1/8 of the dropouts in the BFRT was directly related to BFRT, that being pain from the cuff pressure (55).

There were significantly more acute medical events in the BFRT group in the study by Lau et al. such as acute exacerbations or hospital acquired infections. Three additional medical events were reported (fall with knee injury, insomnia, and limited walking because of low back pain) (55). Despite of this, no Lau et al. reported no significant adverse events (55), and the two Kohlbrenner studies reporting no adverse events at all (50, 52).
Heart failure studies
Eight studies were identified in total with five being available for full text (48, 49, 51, 56, 58) and three only having an available abstract (53, 54, 57). Three studies specified the subjects as having HF and three as the subjects having CHF and two studies had data about cardiovascular patients with one study having one (51) and another study having two (58) subjects having HF of included participants. Despite initiative to contact the author of these studies, isolated data on these patients could not be extracted.

5/8 of included studies looked at acute effects of BFRT (51, 53, 56-58). These studies cannot be included in table 2. These studies do however provide an insight into the acute effects and therefore the safety and feasibility of BFRT for HF subjects. All those studies had different protocols and measures and methodological approaches. In the acutely measured studies similar respiratory, circulatory and symptom specific measures seem to be similar between healthy subjects and subjects with CVD including HF (51, 58), but seem to be slightly elevated when compared non-BFRT at the same intensity (51, 56, 58). Cardiac performance, defined as left ventricular ejection fraction, stroke volume and cardiac index is also increased for one subject with severe HF and diminished for a subject with less severe (53). 3/8 studies looked at non-acute effects, there being two randomized controlled trials (48, 49) and one case study (54). More about these can be seen in table 2. Out of data collected there were a total of 20 subjects that were investigated for acute effects and four were female (20%). In the studies that looked at non acute effects there were a total of 67 subjects and 3 were female. Out of those 67, only 28 completed a BFRT program and three were female (11%).

Two of the studies mainly focused on BFRT cycling at similar intensities (40-70% of peak VO2 (49) vs 65% of VO2 (56)). One measured BFRT cycling at a specific intensity vs non BFRT cycling at the same intensity and the training response over a 6-month period (49) and the other measured acute responses to BFRT cycling (56). Although more disease specific symptoms such as dyspnoea and heart rate were acutely elevated (56), it seems to be safe and feasible and yield positive results as seen in table 1 in a 6-month period (49).

Six studies had some form of resistance or strength-based intervention. Two of these were built on one another (53, 54) and one participant continued the BFRT protocol into a program (54) after the initial session (53). Two of these six studies looked at non-acute effects and one of them were available for full text (48). Both showed specific increases in strength (48, 54).

Three of the included studies had direct limitations in data extraction. One studies did not include number of participants, mean age, nor gender distribution (57). Two articles had summarized data on CVD patients including HF, but not specifically data on the HF subjects despite initiative to contact the author (51, 58).

No adverse events were reported, but the study by Gempel et al. was cut short due to gastrointestinal issues with the subject, which seemed to worsen with BFRT. They also reported some rare premature ventricular contractions during the sessions (54). No significant or serious adverse event was reported in any study.
Summarized outcome measures of effects

In total there were 3 studies for COPD (50, 52, 55) and 3 for HF (48, 49, 54) that looked at non-acute effects. See table 2. Five out of eight included studies looked at acute effects of BFRT (51, 53, 56-58). All studies that investigated acute responses were for HF and are not included in table 2.

Table 2 – Summarized long-term/non-acute effects of BFRT for both COPD and HF from intervention studies

<table>
<thead>
<tr>
<th>Specific changes in strength</th>
<th>Functional/aerobic changes</th>
<th>Physiological/metabolic changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isometric strength ↑ (48, 50, 52, 54, 55)</td>
<td>Functional exercise capacity (six-minute walking test↑ (48, 50, 52), 1 min sit to stand ↑ (50, 52))</td>
<td>% of left ventricular ejection fraction ↑ (54)</td>
</tr>
<tr>
<td>Estimated maximum dynamic strength ↑ (50, 52)</td>
<td>Exercise capacity ↑ (Peak VO2/watt ↑ &amp; Aerobic threshold ↑ (49))</td>
<td>Mitochondrial function ↑ (48)</td>
</tr>
<tr>
<td>Dynamic strength (three rep max test) ↑ (48)</td>
<td>Quality of life ↑ (48)</td>
<td>Brain natriuretic peptide ↓ (49)</td>
</tr>
<tr>
<td>Strength endurance ↑ (48)</td>
<td>Symptom burden ↓ (COPD assessment test score ↓ (50, 52, 55))</td>
<td></td>
</tr>
<tr>
<td>Physical activity ↑ (52)</td>
<td></td>
<td></td>
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BFRT - Blood flow restriction training, COPD - chronic obstructive pulmonary disease, HF - heart failure, VO2 - Volume of oxygen

Specific changes in strength

COPD

All three studies included measurements and improvements in one or several measures of strength (50, 52, 55). Both Kohlbrenner studies primarily measured isometric strength, but also evaluated estimated maximum dynamic strength (50, 52). Kohlbrenner 2021 found that after 12 weeks of progression from low load BFRT to HL-ST they found a 433 and 521% increase in knee extensor strength and 184 and 95% increase in knee flexor strength for each respective leg (50). In the subsequent 2023 study also done by Kohlbrenner et al. both groups found positive changes in knee extensor isometric strength with both the BFRT group and the HL-ST group having 50% of participants exceeding minimal clinical important difference (MCID). No significant between group difference were shown. Similarly, no between-group differences was seen for either leg in knee flexor strength with both groups showing slight increases (52). Additionally, Lau et al. found increases in maximum voluntary isometric contraction for both the BFRT group and the control group. Median increase was 20N with an interquartile range of 3 - 38N and the control group had a median increase of 12N with an interquartile range of -9 – 30. The between group difference was statistically insignificant, but the within-group difference (changes from baseline to last measurement) in both groups were significant.

Furthermore, both Kohlbrenner studies evaluated estimated dynamic strength changes for people with COPD. Both studies had an increase in estimated one rep max (1RM) by completing reps at a lower weight and then calculating an estimated 1RM. Changes in estimated 1 RM for leg extension was 12.4 kg (243% increase from baseline) (50) and a mean of 9.5 kg (27% increase from baseline) (52). Changes in estimated 1 RM for leg press was 37.1 kg (82% increase from baseline) (50) and a mean of 26.1 kg (30 % increase from baseline) (52). No statistical between-group difference was seen for the HL-ST and the BFRT in terms of dynamic strength (52).
HF
Several strength measurements were used in the assessment by Groennebaek et al. Maximal isometric strength improved in the BFRT group by 29.7 Nm compared to the no exercise CG, and 24.6 Nm compared to the remote ischemic conditioning (RIC) group. Within the BFRT group there was 22.1 Nm improvement. Dynamic strength (measured by a three-repetition maximum) improved in the BFRT group 8.2 kg compared to the no exercise CG, and 6.8kg compared to the RIC group. Within the BFRT group there was a 8.8kg improvement. Strength endurance, measured by completed reps increased for the BFRT 5.8 repetitions compared to the no exercise CG, as well as the RIC group. Within the BFRT group there was a 4.6 repetition improvement (48). Furthermore, Gempel et al. found an increase in maximum isometric strength in both knee extensors and hip flexors (54).

Functional / Aerobic changes

COPD
All included studies for people with COPD found a decrease in symptom burden measured by the COPD assessment test (CAT) (50, 52, 55). Changes was -6 (50), -1(±7), with 3/10 moving past the MCID (52) and -7 (55). Both the Kohlbrenner studies evaluated six-minute walking test (6MWT) and one minute sit to stand (1STS) and used them as a collective measurement for functional exercise capacity. The case study by Kohlbrenner et al. showed a 44m meter increase in the 6MWT and a 14-repetition change in the 1STS, with both results yielding changes above the MCID of 30m and three repetitions respectively (50). The 2023 RCT showed smaller improvements with relatively low mean changes of five meters and one repetition post intervention in the BFRT group. There were no between group difference for the BFRT group and the HL-ST group, but subjects from the BFRT group managed to increase the above the MCID more in both the 6MWT (60% in the BFRT group / 36% in the HL-ST group) and for the 1STS the (50% in the BFRT group / 29% in the HL-ST group). Similarly, the change in physical activity did not show any between group difference, but only the BFRT group showed within-group improvements beyond the MCID (52).

HF
Groennebaek was the only HF study to measure improvements in the 6MWT. They found a 39.0m improvement in the BFRT group compared to CG with no exercise. They also found a 31.3 improvement compared to remote ischemic group and the BFRT group. Lastly, they found a 35.9m within-group improvement in the BFRT group. They also found improvements in self-reported disease related quality of life in the BFRT group. With a 5.4 point increase compared to the no exercise CG and 7.0 compared to RIC-group. The within group improvement for the BFRT-group was 6.3 points (48).

Tanaka and Takarada found an increase in peak VO$_2$/W (mL/kg/min) increased in the BFRT group (16.3±3.6 → 22.1±3.7). There was also an increase in the CG, but lesser and not statistically significant. Aerobic threshold also increased to a statistically significant level in the BFRT group, but not the CG group (49).
**Physiological / Metabolic changes**

**COPD**

No specific measures were used in any of the COPD studies for physiological or metabolic changes post intervention.

**HF**

Tanaka and Takarada had several metabolic parameters, a change from baseline was the brain natriuretic peptide value for the BFRT group \(148.1 \pm 118.7 \rightarrow 75.3 \pm 70.6\) in 6 months. The value for the CG was lesser and not statistically significant. There was also a significant inverse correlation between changes in BNP levels and exercise capacity in the BFR group compared to the CG. The other statistically significant measure was a small change in C-reactive protein concentration \(49\).

Groennebaek et al. found significant between group differences in increases in RNA synthesis rate and mitochondrial respiratory function \(48\).

**Syntheses of results**

The results included a broad array of study designs, such as RCTs \(48, 49, 55\), pilot studies \(51, 52\), case reports \(50, 53, 54\) and other intervention-based studies \(57, 58\). Eight out of eleven of included studies focused on HF, with the remaining 3 \(27\%\) focused on COPD. A majority of subjects were male for the data that was available.

One study had more dropouts and more acute medical events in the BFR-group and one study there was a participant unable to complete strength training with BFR at 20% intensity. No further issues regarding feasibility were reported.

No serious adverse events were reported in any of the included studies, however the study by Lau et al. had more acute medical events in the BFR group compared to the CG group and one patient with previous gastrointestinal problems seemed to get exacerbated gastrointestinal problems in accordance with BFRT.

Results obtained from intervention studies show promising effects of BFRT in terms of physiological adaptations such as increased muscle strength, quality of life and physical exercise capacity. This was shown among studies in 6-minute walking test \(48, 50, 52\) and 1-minute sit to stand \(50, 52\).

Regarding the characteristics among intervention studies, there was a variety of methods and protocols used. Leg extensions, seated leg press, supine SLR, plantar flexion and cycling were some of the interventions used.

There were a lot of different measurements done to evaluate BFRTs effects.
Discussion

Based on the results presented in this review, blood flow restriction training indicates positive effects in several different measures in both subjects with HF and COPD. Positive effects seem to be the case regardless of intervention methodology. The methodology of intervention and methodology of measurements were vast. The evaluation used were outcome measures for changes in strength, functional/aerobic changes, and physiological/metabolic changes. Among the recorded effects were increases in muscle strength, functional exercise capacity, and several aerobic measures.

Specific changes in strength

COPD

All studies on people with COPD found positive effects regarding muscle strength. The results from the intervention group (IG) in Kohlbrenner et al (2023) (52) study is proportional to the results seen among healthy individuals following a similar training protocol (60). High load resistance training (HL-RT) and low load blood flow restriction strength training (LL-BFR-ST) both seems to generate equal strength gains among healthy individuals and people with COPD. In the study with healthy individuals the cuff pressure seems to be a key factor in hypertrophy gains (60). Kohlbrenner et al also showed large improvements in leg strength in their case study from 2021 (50). Although BFRT could be the reason to those highly increased results (more than 500% increases in strength), the large improvements could also be due to the patient having a very low baseline starting strength. Despite the study showing great results, the fact that it was done on a single subject makes it hard to draw any conclusions on larger populations from it. , Another study that indicated good effects of BFRT was Lau et al (55) who showed that the increase in maximum voluntary isometric contraction (MVIC) were more than 3 times as high in the IG compared to the CG. Although this study had a limited number of participants, it does corroborate the results seen in the single subject study done by kohlbrenner et al (50). .

HF

Of the two studies that looked at changes in strength, both found increases in several measures (48, 54). Although no hard conclusions can be drawn because of the small sample size, with one case study and only having an abstract available (54) and the other having 36 people that got divided into three groups, meaning only twelve completed a BFRT program (48). The fact remains that out of the total 13 people who completed and got evaluated for strength, all of them showed improvements in strength. And for those who got compared to the remote ischemic conditioning-group and the no exercise group, the improvements were far better, showing a promise for strength increases in HF subjects after a period of BFRT.

Functional / aerobic changes and physiological /metabolic changes

COPD

Lau et al found positive improvements in the short physical performance battery score (SPPB), and the COPD assessment test (CAT) with the IG showing slightly larger increases (55). Kohlbrenner also used the CAT as a measurement of symptom burden and found positive effects (50, 52). Kohlbrenner et al. also investigated quality of life and found no between group difference, but there were subjects improving beyond the MCID in both groups (52).

Kohlbrenner et. al found an increase in functional exercise capacity (50) and increased physical activity (52) for subjects with COPD. Alongside this they also found increases in the 6MWT and 1STS in both studies (50, 52). were seen in the case study by Kohlbrenner et al., with an improvement of 44m in the 6-MWT for a subject with COPD compared to before start of intervention (50). However, Lau et al. did not see an increase in group who did BFRT, but rather only found an increase in their CG. Although the authors do attribute this to the larger number of acute medical events (acute exacerbations, hospital acquired infections,
accidental fall, and acquired insomnia) in the IG compared to the CG (55). The previous raised concerns mainly focus on direct risks (61, 62) and not secondary risks, such as increased risk for falls or decreased autoimmune function. Secondary risks are not reported in the large Japanese survey for over 12,000 individuals who has undergone KAATSU training (63) but could perhaps be an unexplored safety and feasibility concern in the rehabilitative use of BFRT.

No specific measures were used in any of the COPD studies for physiological or metabolic changes post intervention.

HF
For functional and aerobic measurements Tanaka and Takarada showed improved exercise capacity, indicated by changes in peak VO$_2$/watt and aerobic threshold compared to other HF controls (49). Further, Groennebaek et. al had a 39m more increase in six-minute walking test (6-MWT) than the CG for subjects with HF. (48). Similar changes were seen in the COPD studies, despite different disease and methodological approach.

Tanaka and Takarada also found a decrease in brain neurotic peptide (BNP), especially for the IG. High BNP levels indicate the heart’s inability to pump efficiently enough, making it a marker for disease severity in HF. They also found an inverse relation with BNP levels and exercise capacity, meaning high BNP indicates a low exercise capacity and lower BNP indicates a higher exercise capacity. The IG had a higher aerobic threshold and exercise capacity, as well as lower BNP. This suggest that aerobic training with blood flow restriction (AT-BFR) can be more beneficial than aerobic training without BFR at the same relative intensity (40-70% of peak VO$_2$/watt) for increasing tolerance, capacity and reducing disease specific markers for subjects with HF (49).

Kothonidis et al. also investigated cycling at approximately the same relative intensity (65% of VO$_2$ peak) as Tanaka and Takarada did. Instead, Kothonidis et al. measured acute responses and found that when the same relative intensity is being held with and without BFR, the training with BFR produces more of mean VO$_2$, more fatigue and dyspnea and a higher heart rate. However, the intervention is still deemed to be feasible and safe. These two findings by Kothonidis et al. and Tanaka and Takarada suggests is that if you are able to train at a higher internal objective intensity (higher heart rate, dyspnea and other internal objective markers for high intensity as demonstrated by Kothonidis et al.) and a higher subjective intensity (for example using a RPE-scale) while keeping the external objective intensity (for example what Watt you cycle on) the same, it could yield very beneficial results (as demonstrated by Tanaka and Takarada), while still being feasible and safe (56). Simply put, if the exercise is deemed tougher or harder and creates more fatigue-like symptoms but is still safe, feasible, tolerable, and maintainable, then it will yield more beneficial results. This, however, creates a responsibility and demand for competence and perhaps surveillance by clinicians to be able to manage the correct training load and intensity for these possibly frail patients. It is unclear of if and how trained the clinicians prescribing BFRT or KAATSU is, or if the training is supervised.

Further, Groennebaek et al. found improvements in mitochondrial respiratory function and RNA synthesis rate (48) and Tanaka and Takarada showed an increase C-reactive protein concentration (49) and Gempel et al. found a slight increase in % of left ventricular ejection fraction (54).
Specific findings related to feasibility and safety

Lau et al. noticed a difference in the IG compared to the CG in terms of acute medical events such as acute exacerbations or hospital acquired infections. Three additional medical events were reported (fall with knee injury, insomnia, and limited walking because of low back pain). They also had several other dropouts, mostly in the IG. One person in the CG dropped out because of unpredicted early discharge and 2 subjects dropped out in the IG also due to unpredicted early discharge. 3 more subjects in the IG dropped out because of infection contact precautions and 2 defaulted training, one due to pain related to occlusion pressure and one due to an asymptomatic bradycardia related to the underlying complete heart block with conservative treatment (55). Since this study looked at COPD subjects after an acute exacerbation period, and it is a very fragile group and might be even more sensitive to training overall. Therefore, it may not be optimal to participate in a training methodology that is pushing the limit of capacity for these individuals. Usually, after an acute exacerbation you would be quite restrictive of when to do strenuous physical work, depending on the specific region or country’s guidelines of care.

However, it is effective to use neuromuscular electrostimulation (NMES) to prevent further muscle dysfunction after an acute exacerbation (64). There have also been studies looking at NMES and BFRT showing promising muscle-building results in healthy individuals (65, 66). Furthermore, NMES does increase type-I muscle fibers (64), which is inherently low in subjects with COPD (67) and in HF (68). Additionally, BFRT strains and builds more type-I muscle fibers compared to high load strength training (69) which might be a good exercise adaptation for these groups since there inherent fiber type shift (67, 68). Similar thoughts were raised by Thiebaud et al. were they hypothesized the benefits of BFRT for COPD subjects (59).

When it comes to reported negative effects, there were no negative physiological adaptations in muscle strength/size or exercise capacity as a result of BFRT. However, one study reported gastrointestinal issues after BFRT. Although these issues were amplified when performing BFRT, it is not reported if it were specifically linked to BFRT, or just training in general. The patient had gastrointestinal problems prior to BFRT intervention, so BFRT was not the root of the issues, but the issues seemed exacerbate with BFRT (54).

Risks and possible contraindications

With the minor events reported for AE-COPD subjects being more acute medical events as seen in the study by Lau et al. (55) and for HF the GI-issues seen in the case study by Gempel et al. (54) the question remains as to why. The acute medical events is a multifactorial issue and hard to attribute to one factor. The GI issues could possibly be connected to a previously raised concern about BFRT for primarily subjects with CVD, including HF. This is the exercise pressor reflex (EPR) (16, 17). Much less is discussed when it comes to COPD. Further highlighted concerns about the EPR and BFRT for groups of interest can be read in other sources (61, 62).

The EPR can be summarized as a mechanism that regulates autonomic responses in the cardiovascular system. It enhances sympathetic output and reduces parasympathetic activity during and immediately after physical activity. The EPR serves as a reflex to respond to exercise through the mechanically sensitive mechano-reflex and metabo-sensitive metabo-reflex by raising blood flow, cardiac output, ventilation, HR, and blood pressure (70). However, due to limited ability to increase ventilation (18) and cardiac output (62) for people with COPD or HF the EPR response is unique for both groups. It can even be viewed as tonically active in subjects that have a limited ability to deliver oxygenated blood to active muscle tissue, because the mechano-reflex raises sympathetic activity (SA) and subsequently blood pressure and mechanoreceptors is hypersensitized in conditions with limited perfusion (61, 62). It is also noteworthy that HF subjects have an increase in baseline of SA and a decrease in baseline of parasympathetic activity, directly linked with mortality rate (71).
Dynamic exercise primarily triggers the EPR, which in turn increases SA and elevations in mean arterial pressure (MAP). For healthy individuals MAP is primarily driven by CO; i.e. tachycardia, enhanced ventricular contractility and stroke volume (72-76). The more intense exercise, the less CO increases are, and the MAP is instead driven by increases in total peripheral resistance, leading to an even more exaggerated SA (77). This mechanism is also true for subjects that cannot drive CO due to their disease (such as HF subjects). This leads to exaggerated SA and increase systemic vascular resistance (SVR). Persisted SA exacerbates ventricular dysfunction, leading to increased cardiovascular and overall mortality risk (62).

Furthermore, increased blood pressure response to metaboreflex activity driven by SVR seen in HF subjects leads to increased excitatory signals from group III and IV afferents (the afferents that signal the EPR), and has a sympatho-excitation response, impairing femoral blood flow, probably contributing to their exercise intolerance (62). These concerns were not discussed in any studies included for analysis in this review.

It is possible that both the exacerbated GI issues seen by Gempel et al. could be linked to an overactive sympathetic activity and therefore exacerbating the issues. This was neither investigated nor discussed in the available paper abstract.

The papers in this review that looked at acute effects of BFRT found markers that indicate higher sympathetic nerve activity. However, the risk is having a prolonged sympathetic activity with the underlying mortality (71) and prognostic risk (78), especially seen in HF, future studies should monitor sympathetic and parasympathetic nerve activity not only during but after and changes over time as well. The need to further evaluate if the increase seen from BFRT is prolonged or subsides and might even be a beneficial part of the regulating the homeostasis of the autonomic nervous system is an integral part of finding out the benefit or risk of BFRT for especially HF subjects.

Pain and discomfort

Training with arterial occlusion might seem like a painful or unpleasant way of training due to the increased pressure that occurs. Despite this, only one study reported any pain related to the cuffs when performing BFRT. It was reported by Lau et al that one individual defaulted BFRT due to pain related to the cuff inflation (55). The discomfort or pain when performing BFRT could be a factor that makes people avoid the method. But with only one person out of the total 181 people in all studies reporting pain or discomfort, the method appears tolerable. Studies with larger populations are needed to fully examine this risk.

There is also a recent systematic review looking at pain sensitivity and BFRT. They found that BFRT can induce hypoalgesia, both locally and remotely, thereby raising the pain threshold. They found that a variable to pain-sensitivity and BFRT is pressure, with a higher pressure resulting in a greater exercise-induced hypoalgesia. They also found that exercise to failure both with and without BFR had a similar pain desensitizing effect (79).

In the large national Japanese survey where 12 642 people have reportedly received KAATSU training, including people with cardiac diseases, respiratory diseases, hypertension, neuromuscular diseases, obesity, cerebrovascular diseases, orthopedic diseases and elderly. It was shown the relative very low prevalence of adverse effects in general. Some reported side effects were subcutaneous hemorrhageand numbness. They also reported other side effects with very rare prevalence, there among pain being reported by a total of 10 people out of 12 642 (63).

The subcutaneous hemorrhages were more prevalent in the upper extremities more so than the lower extremities and tended to pass with time and not impede the continuation of the intervention plan. It is however rather likely that some levels of pain were associated with the subcutaneous hemorrhages, although not reported, nor evaluated in terms of intensity of pain or characteristics of pain in this survey. Subcutaneous hemorrhages might be more prevalent if the subjects use antithrombotic medications.
Thrombotic risks
Exercise affects hemostasis, the maintenance of balance between coagulation and fibrinolysis. Regular exercise enhances fibrinolysis, but intense exercise may increase coagulation, leading to a potential risk of venous thrombosis. This can in turn lead to microvascular occlusion, muscle damage and cell necrosis (80).

Through a survey, Nakajima et al. showed a 0.06% incidence of venous thrombosis when completing BFRT in Asian facilities (63), lower than for the general Asian population (81).

Further, it seems as though BFRT does not elicit an increased risk of thrombosis and DVT, as shown in cardiac surgery patients (82), patients with stable ischemic heart disease (83) and healthy individuals (84). However, no studies with HF or COPD subjects have looked at markers for thrombosis.

Other considerations
Lau et al. showed a difference in sessions completed in the CG compared to the IG within 10-12 sessions with the CG completing more sessions in total, most likely due to more complications and acute medical events in the IG. They also measured acceptance and found a non-significant positive acceptance rate of 75% in the IG rating “like” or “very like” and 60% in the CG “like” or “very like”, with the CG trending more toward “like”, and the IG group trending more towards “very like” (55). Whilst being rated as slightly more enjoyable, the IG had lower attendance rate.

In a study discussing the feasibility of BFRT in COPD subjects Pereira-Neto et al., made the conclusion that BFRT might elicit lower adherence rate. Although they concluded that the perspectives were positive for the possible effects achieved by BFRT for all groups (people with COPD and health professionals). The authors also stated that a lot of concerns regarding safety screening needs to be further researched before clinical application (85).

As presented by Patterson et al. a structured and systematically prescribed protocol for BFRT that is strength or resistance based and a protocol for one that is aerobic based is essential to both prevent adverse events and to manage possible unwanted reactions or outcomes (86). One study did report negative effects in the form of symptom burden during BFRT (56). In the study they reported an increase in HR, fatigue and dyspnoea compared to controls. This could indicate that BFRT was the reason for those negative symptoms, but in the study both the IG and controls performed cycling at the same intensities. With BFRT being a method used to enable a lower intensity than regular training, the symptoms are most likely due to BFRT being performed at a too high external intensity, with “too high” meaning the intensity could have been lowered to achieve the same physiological results from the exercise. BFRT does not need to be performed on intensities higher than 40% of 1RM to have equal effects as that to regular training on 70% of 1RM (87). This is also supported by Takahashi et al (2010) who concluded that RE with BFR at 20% or 1RM gives equal effects as RE without BFR at 60% of 1RM (57).

Gender homogeneity
Due to the limited number of women included in intervention studies, the results from some studies cannot be generalized towards all COPD or HF subjects. This is something that future studies needs to take in consideration when conducting interventions with BFRT for both people with COPD and HF. This is important if we want to get a full understanding of how BFRT affects everyone with COPD or HF, not only half of the population. Tanaka and Takarada was the only authors to explain why only men were included in their study. Their explanation was that aerobic exercise training was proven useful to lower cardiovascular mortality among men, but not women, therefore they only included men in their study (49). The remaining studies did not provide an explanation as to why most or only men were included.
**Standardization of blood flow restriction training**

When it comes to how vascular occlusion was achieved in the different studies, there was no form of standardization or protocol followed. Many of the included intervention studies had different cuffs, used different pressures, and had different rest periods. The cuffs used varied from 6 cm (51) wide to 14 cm (48), while some did not report the width of the cuff. Notably, related to cuff size, Madarame et al. When determining the pressure to use there were a lot of different strategies. Many studies used a percentage of limb occlusion pressure (48, 50, 53, 55), while some used a percentage of systolic blood pressure (49, 57). One study used cuff width proportional to thigh circumference (56). This was the only study that used this method and there was no explanation as to why.

The rest periods and intervention intensities also varied a lot between studies. These differences in standardization could lead to results that do not fully represent the effects of BFRT, when placing, width and pressure of the cuff play a meaningful role on the effect of BFRT (60).

When evaluating the method BFRT, a standardization of variables would be optimal, so that every intervention study followed similar protocols. An example could be to set a specific percentage width of the cuff relative to the subject’s circumference of the specific body part, and an occlusion pressure relative to the subject’s both systolic and diastolic blood pressure. Regarding cuff pressure for BFRT, it is suggested that the optimal pressure should be between 50-80% of AOP (88). It would also be important to take the vasodilatory response to exercise into account when determining what cuff pressure should be used. This would make sure that the occlusion method does not affect the result in different ways between studies.

Another standardization that varied between studies was the resting periods. There was variation in both time in rest between sets and regarding the cuff; if it stayed inflated or not during rest. This could also possibly be a variable affecting the result of BFRT. The intensity at which BFRT was performed could also have a big impact on whether it is a feasible method or not. If performed on an external intensity that’s too high, the effects could be that the person can’t perform the exercise, or that the symptoms become too much, resulting in cancelled intervention.

As mentioned regarding the method used by Kothonidis et al. (56), the results suggest higher symptom burden in the IG than CG, but this is due to BFRT being performed at the same external intensity. If BFRT should be performed correctly, it should be done at a minimum of 30% of 1RM for best result and minimal symptom burden. Arpan et al report that BFRT at less than 30% of 1RM does not produce better results than control groups (57, 88).

In summary, future studies should focus on having a standardized protocol that takes current evidence regarding pressure, cuff width and intensity into consideration.

**Reviews**

When conducting the search on databases, there were three reviews found that had looked at BFRT for people with various cardiovascular diseases (48, 49). With the subject BFRT for people with cardiovascular diseases being so limited, these reviews all had one or more of the studies included in this scoping review for their result regarding BFRT for people with HF specifically. The three reviews had somewhat different objectives, with one looking more specifically at safety (89), and the other 2 on effects of BFRT (48, 51). All results for HF in the reviews were from three studies that were also included in this scoping review (90). Therefore, the results for people with HF in the reviews align with the results seen in this article. The reviews also concluded that more studies are needed to further map the effects, safety and feasibility of BFRT for people with various CVD, including HF. No reviews regarding BFRT for people with COPD were found.
Method discussion
The reason for this scoping review was to map the existing knowledge when it comes to BFRT for people with COPD or HF. A scoping review design were chosen instead of a systematic review due to the subject being relatively unexplored and had a lack of high quality RCT studies. Due to the limit in RCT studies the use of a scoping review enabled collection of all sorts of intervention study designs. This could potentially lower the credibility of the results found but was necessary to be able to conduct a collection of existing knowledge. At the beginning of writing, the PRISMA structure for scoping reviews was strictly followed, which was changed later in the work process to give better structure for the review. Some headlines included in PRISMA's structure were abundant when making this review and were therefore removed in later stages of writing.

The search query included many different descriptions and synonyms for both HF, COPD and BFRT which gave a lot of room for articles to be included. The use of MESH terms also minimized the risk of relevant articles being missed, although established MESH terms for BFRT is lacking. Inclusion and exclusion criteria were clearly stated to make screening process easier. The clear inclusion- and exclusion criteria could have led to interesting articles being ruled out due to not matching one or a few of the criteria. The search was done on three databases, which generated a total of 86 articles. With the search only being done on three databases there is a risk of relevant articles being left out. One database (J-stage) could potentially be a red flag when it comes to reliability. J-STAGE is a platform for scholarly publications in Japan. It is developed and managed by the Japan Science and Technology Agency with the aim to spread research from Japan to the rest of the world. With this in mind, the database was used due to it having many relevant sources of evidence that were peer reviewed. The screening process were done based on both title and abstract to make sure relevant articles were included and excluded. The second stage included screening of full text, which were done by both authors to ensure proper understanding and relevance of each article.

Limitations
With BFRT being a relatively un-explored way of training, especially for non-healthy individuals, one limitation when making this scoping review was that the number of sources regarding BFRT for people with COPD or HF were very limited. Especially for people with COPD. One study regarding BFRT for people with COPD were excluded due to the article only being available in German (91). There is also a possibility that we missed some articles in Japanese when searching on J-stage.

The lack of MESH terms for BFRT made it more difficult to make sure every source including BFRT for people with COPD or HF was found.
Limited conclusions can be drawn towards women and towards COPD due to a small percentage of women were included and only a handful of studies were toward COPD, with 2/3 being from the same author.

Another limitation was that some intervention studies among the sources of evidence only had meeting abstract available (52, 56, 57), or limited text (53, 54). This gave limited information about those specific studies which could have led to some crucial information being left out. The low number of participants in the studies also prevents any firm conclusions.

Further limitations of included articles is that one article did not disclose number of participants and gender distribution (57) and the author was not reachable by mail. Another author was also contacted by mail to find out more about the specific individuals with HF and their specific data and what order they did the block randomization in both studies, (51, 58) but no answer was received.
Conclusions
The charted results from the included studies indicate promising outcomes for BFRT as a potential rehabilitation method for individuals with COPD or HF. With many reported improvements such as functional exercise capacity, muscle strength, exercise tolerance, quality of life, reduced symptom burden, and several positive physiological changes for both people with COPD and HF indicate that BFRT might be an alternative rehabilitation method for muscle strengthening training for people with COPD and HF. BFRT seems to be safe and effective, despite a vast methodology between studies. No studies showed worse effects of BFRT compared to control groups, which indicates that BFRT might be equal, and in some cases more effective than other forms of training (49, 52). However, strong conclusions cannot be made due to the low number of study participants.

Although the results look promising, the need for further research to evaluate its safety, feasibility, and long-term effects remains evident for both groups. This conclusion is also supported by the included reviews. Future studies require a more standardized exercise protocol and characteristics consistent with current level of evidence, as well as larger groups and more included women.
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