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Systematic review

Potential benefits of yoga in patients with heart failure: A meta-analysis of controlled trials

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ABSTRACT

Introduction: Heart failure (HF) is characterized by breathlessness and reduced exercise tolerance. In addition to drug treatment, guidelines recommend exercise training for HF patients. Since yoga combines breathing and physical exercises and apparently shows positive cardiovascular effects in healthy volunteers, the aim of this meta-analysis was to identify potential benefits of yoga in HF patients.

Methods: A systematic literature search in *Pubmed* and *Cochrane Central Register of Controlled Trials* was performed. Outcome measures in this meta-analysis were changes in maximum oxygen uptake (VO_2 peak), blood pressure, high sensitive C reactive protein (hs-CRP), 6-minutes walking distance (6-MWD), and quality of life (QoL).

Results: Five studies with 206 patients were included into the meta-analysis. Yoga therapy resulted in a significantly stronger decrease of hs-CRP compared to control with a mean difference (MD) of -0.39 mg/L [95% CI: -0.54, -0.24; n = 89]. In addition, oxygen uptake (VO_2 peak) was statistically significantly increased in the yoga group compared to control group (MD: 3.95 mL/kg/min [95% CI: 2.14, 5.77; n = 59]). The other outcomes, reduction in blood pressure, improvement in 6-MWD and QoL, did not show any statistically significant differences between yoga and control group.

Conclusion: In patients with heart failure, yoga indicated a positive effect and could be considered as complementary approach to drug treatment. However, larger randomized controlled trials with longer follow up periods and standardized endpoints are needed to provide definite conclusions.

1. Introduction

The clinical syndrome heart failure (HF) is caused by a structural and/or functional cardiac abnormality, which results in a reduced cardiac output and elevated intracardiac pressure. This leads to symptoms such as breathlessness, reduced exercise tolerance and ankle swelling. In addition, HF patients also show an increased mortality [1].

Severity of heart failure is often classified using the classification of the New York Heart Association (NYHA), ranging from NYHA I to NYHA IV, and describing the following symptoms during physical activity [2]:

- NYHA I: No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea (shortness of breath)
- NYHA II: Slight limitation of physical activity. Comfortable at rest.

Ordinary physical activity results in fatigue, palpitation, dyspnea (shortness of breath)
- NYHA III: Marked limitation of physical activity. Comfortable at rest. Less than ordinary activity causes fatigue, palpitation, or dyspnea
- NYHA IV: Unable to carry on any physical activity without discomfort. Symptoms of heart failure at rest. If any physical activity is undertaken, discomfort increases.

Several drug treatment options are recommended by the guidelines of the European Society of Cardiology (ESC) to reduce morbidity and mortality of patients with HF [1]. Beta-blockers, statins, ACE inhibitors, and sacubitril-valsartan have demonstrated a significant reduction in mortality and symptoms in randomized clinical trials in HF patients [3–7]. Nevertheless, in addition to drug treatment the ESC guidelines also propose exercise training for HF patients [1].

Yoga practices can consist of breathing exercises, physical exercises as well as postures and involves body, mind and soul. In healthy volunteers yoga significantly reduced heart rate as well as blood pressure and increased lung function [8]. Patients with diabetes reported that yoga practice was associated with stress reduction and improvement in sleep and diet [9]. A meta-analysis published by Gomes-Neto et al. in 2014 included two controlled trials and evaluated the effect of yoga in patients with heart failure. The study showed that yoga improved exercise capacity, measured by maximum oxygen uptake (VO_2 peak), and health related quality of life (QoL) [10].

The aim of this meta-analysis was to identify potential benefits of yoga in heart failure patients on VO_2 peak, improvement of QoL and 6-minutes walking distance (6-MWD) as well as reduction in blood pressure and high sensitive C reactive protein (hs-CRP), since elevated levels of hs-CRP are associated with an increased mortality in heart failure patients [11].

2. Methods

2.1. Criteria for inclusion into meta-analysis and search strategy

Before starting the systematic search, inclusion criteria were defined. To ensure that studies address similar clinical questions, they had to meet the following main criteria to be included into the meta-analysis: (i) any type of yoga as therapeutic intervention, (ii) patients with heart failure, classified with NYHA classification, (iii) a follow-up time of at least 4 weeks, and (iv) controlled study. Included studies could be exercise or non-exercise controlled, due to the following reasons, (a) to increase number of studies eligible for the meta-analysis, and (b) ESC guidelines recommend exercise and education to patients with heart failure [1] and therefore, patients treated with standard medical treatment, might already have a high activity level. Randomized as well as non-randomized studies were included into the meta-analysis. Additionally, studies were only eligible and included into the meta-analysis, if at least one of the following outcomes was measured, VO_2 peak, blood pressure, hs-CRP, 6-minutes walking distance, Minnesota living with heart failure questionnaire (MLHFQ) and/or Kansas City Cardiomyopathy Questionnaire (KCCQ). Studies investigating exercises similar to yoga or exercises in which yoga was only a part of a program were excluded from the study.

Based on the inclusion criteria systematic searches in *PubMed* and *Cochrane Central Register of Controlled Trials* were performed in January 2019, and a refined search in April 2019 using the following key words: [*yoga* AND *heart failure*] OR [*Yoga* AND *heart insufficiency*] OR [*Yoga* AND *cardiac failure*] OR [*Yoga* AND *cardiac insufficiency*]. Furthermore, the reference lists of included studies were screened for additional trials eligible for inclusion into the meta-analysis. Apart form this, no other searches were performed. The search was restricted to published studies in the English language.

After identification of records by systematic search, the following steps were performed: (1) removal of duplicates, (2) screening of title and abstracts for eligibility, and (3) assessment of remaining records for inclusion into the meta-analysis by screening the full text articles.

If the same study outcomes were reported in conference abstracts or dissertations and full text publications, only the full text publications were included into the meta-analysis to avoid double counting.

2.2. Data extraction

Data was extracted from text, tables and/or figures by using a standard extraction procedure. If necessary for data extraction from figures, the Plot Digitizer software (version 2.6.8) [12] was used. All data were collected at the start of the study and included the following information: 1. first author, 2. year of publication, 3. number of subjects, 4. proportion of female and male patients, 5. mean age of subjects, 6. severity of heart failure by NYHA class, and 8. duration of follow-up.

Outcomes used for meta-analysis were defined before starting the literature search and the following outcomes were extracted from included studies: 1. VO_2 peak, 2. blood pressure, 3. hs-CRP, 4. 6-minutes walking distance, and 5. quality of life (QoL) MLHFQ and/or KCCQ.

MLHFQ is a disease-specific questionnaire for patients with HF. The questionnaire provides a total score with a range of 0 (best) to 105 (worst), and a decrease in total score corresponds to an improvement in QoL [13,14]. KCCQ is another disease-specific questionnaire for HF patients. This questionnaire provides a 0–100 scale where higher scores indicate more favorable states and therefore, increases in KCCQ overall score correlate with an improvement in QoL [15].

2.3. Assessment of study quality

Risk of bias was evaluated using the criteria of the Cochrane Collaboration assessment tool [16]: 1. random sequence generation, 2. allocation concealment, 3. blinding of participants and researchers, 4. blinding of outcome assessment, 5. incomplete outcome data, 6. selective reporting, and 7. other biases. Each category was judged using three risk levels: low risk, high risk and unclear risk. To evaluate "random sequence generation" and "allocation concealment", included studies were screened for the necessary informations. In addition, baseline characteristics of patients were screened for obvious randomization errors. Category "incomplete outcome data" was rated low if outcome data were provided for all included patients or reasons for lost-to-follow up were disclosed. For evaluation of "selective reporting" reported outcomes in result section of included studies was compared to protocols published previously (e.g. on clinicaltrials.gov) and/or the defined assessments in method section of the respective studies. If data for all pre-specified outcome assessments were reported in the results section, bias in this category was rated low. Assessment for "other bias" could include, but was not limited to no information on drug treatment compliance, specific comorbidities which might have an impact on HF or symptoms similar to HF, or findings which might lead to a conflict of interest.

In addition, to the evaluation of risk of bias based on the above mentioned steps, funnel plots were planned for each outcome to evaluate risk of publication bias. Funnel plots indicate an absence of bias, when effect estimates of included studies resemble symmetrically around the overall effect estimate [17].

2.4. Statistical analysis

For analysis of the parameters VO_2 peak, blood pressure, hs-CRP and 6-min walking distance, the mean changes from baseline and associated standard deviations (SDs) were used to calculate pooled estimates of the mean differences (MD) and corresponding 95% confidence intervals (CI) between yoga and control group.

Effects on QoL were analyzed by taking mean changes from baseline as well as associated SDs of MLFHQ or KCCQ from included studies. MLFHQ score was then reversed, that improvements in QoL were defined as positive changes to allow pooling of both scores KCCQ and MLFHQ. Afterwards, the standardized mean difference (SMD) of the pooled data and the corresponding 95% CI were calculated. In addition, both QoL scores were analyzed separately by calculating mean difference between yoga and control group. Except of the previous analysis no further analysis conducted.

If mean changes from baseline were not available, numbers were calculated using mean at the end and beginning of the included study. If necessary the associated SDs were calculated according to the Cochrane Handbook [17].

This meta-analysis was performed using the Cochrane Collaboration software Review Manager 5.3 [18]. For all analysis a random effects model was chosen, due to the variability of the intervention yoga and potential factors of heterogeneity influencing the final outcome, such as size of study populations, mean age of study population and study

duration.

Heterogeneity among included studies was statistically assessed by calculating the I^2. Based on Higgins and Thompson an I^2 between 25% and 50% indicates a moderate and $I^2 > 50\%$ a high heterogeneity, respectively [19]. Therefore, low and high levels of heterogeneity were considered as $I^2 \leq 50\%$ and $I^2 > 50\%$, respectively. A p-value of ≤ 0.05 was considered statistically significant. In addition, heterogeneity between included studies was also manually explored by comparing the following parameters: differences in mean age of patients, in NYHA class and time of follow-up.

3. Results

3.1. Literature screening and characteristics of included studies

The first systematic literature search in January 2019 identified 155 records of which 111 were duplicates. The refined search in April 2019 identified 67 records with 13 duplicates. After duplicate removal, title / abstract screening as well as screening for inclusion criteria seven full-text articles reporting on five controlled trials were identified by both searches, respectively. Six of these articles with a total of 206 patients were included into the meta-analysis [20–25]. Krishna et al. reported on their trial in three full-text articles [22,23,26], of which two were included into the meta-analysis. The third article [26] was used for the risk of bias assessment but not included into the final meta-analysis, due to reporting on outcomes not predefined for analysis in this study. The full screening process is shown in Fig. 1.

The included studies showed slight heterogeneity, due to the following reasons. In one study included into the meta-analysis the yoga group was compared to another exercise group performing hydrotherapy. All other studies compared yoga group to non-exercise groups (Table 1). The study populations differed, with youngest patients aged around 50 years in Krishna et al. [22,23] and oldest patients in Donesky et al. (2017) with an average age of 73 years in the yoga group [24]. In

addition, Krishna et al. included patients with the mildest forms of HF with NYHA I and NYHA II, whereas all other studies also included patients with NYHA III. Two studies Krishna et al. (2014a/b) and Hägglund et al. (2017) ran for 12 weeks, whereas the other three studies only had follow-up times of 8 (to 10) weeks. In one study, patient suffered besides HF also from COPD [24], another disease with symptoms such as dyspnea and strong impact on QoL. Main characteristics of included studies are listed in Table 1.

3.2. Risk of bias assessment of included studies

One study included in the meta-analysis indicated a high risk of bias due to missing of a randomization process [24]. In two other studies a randomization was performed, but further information were not disclosed in the publications, which resulted in an unclear bias in terms of "random sequence generation "and "allocation concealment "[20,21]. Due to the nature of the studies, a blinding was not applicable and therefore all studies show a high risk of bias in these criteria. In three of the five studies patients received drug treatment but there were no information provided on the compliance to these drug treatments, which led to an unclear risk in terms of "other bias "[20,22,23,25,26]. The study by Pullen et al. (2010) was rated with a high risk for "other bias", due to no information on compliance to drug treatments and due to the fact that the follow-up time was not clearly defined with 8 to 10 weeks [21]. Donesky et al. (2017) was also rated with high risk in "other bias", due to missing information on potential drug treatments and the reason that all patients suffered besides HF from COPD [24]. An overview of the risk of bias assessment is presented in Table 2.

Funnel plots were planned to estimate publication bias for each assessed outcome. But due to the very limited number of five studies eligible for this meta-analysis, funnel plots were inappropriate to estimate publication bias.

3.3. Effect of yoga on 6-min walking distance and quality of life

Compared to control group, yoga therapy improved 6-minutes walking distance statistically non-significant by (MD) 72.15 m [95% CI: -60.82, 205.12; n = 137] (Fig. 2A). QoL as pooled analysis of changes by KCCQ and MLFHQ (Fig. 2B) did not show any statistically significant improvement by yoga vs. control with a SMD of 1.05 [95% CI: -0.72, 2.82; n = 196]). A separate analysis of both QoL scores showed a MD of 15.97 [95% CI: 2.88, 29.06; n = 151; I^2 = 81%] for MLFHQ, favoring yoga, whereas KCCQ favored control with a MD of -2.44 [95% CI: -10.82, 5.93; n = 45; I^2 = 0%].

For both assessed outcomes, 6-minutes walking distance and pooled QoL heterogeneity among included studies was considered significantly high with I^2 = 95% (p < 0.00001) and I^2 = 96% (p < 0.00001), respectively.

3.4. Effect of yoga on blood pressure, inflammatory marker hs-CRP and oxygen uptake

Yoga and control group indicated comparable effects on reduction of systolic and diastolic blood pressure (Fig. 3A/B) with MDs of -3.09 mmHg [95% CI: -11.48, 5.29; n = 122] and -3.98 mmHg [-16.70, 8.75; n = 122), respectively. For both outcomes the heterogeneity between included studies was high with I^2 = 63% (p = 0.1) for systolic and I^2 = 95% (p < 0.0001) for diastolic blood pressure reduction.

The inflammatory marker hs-CRP (Fig. 3C) decreased statistically significant by yoga therapy compared to control group with a mean difference between both groups of -0.39 mg/L [95% CI: -0.54, -0.24; n = 89]). Important to mention here, for the extraction of hs-CRP data from Pullen et al. 2008 the Plot Digitizer software was used.

The analysis of VO_2 peak data, indicated that yoga was more effective for this outcome with a 3.95 mL/kg/min [95% CI: 2.14, 5.77; n = 59] higher improvement versus control (Fig. 3D).
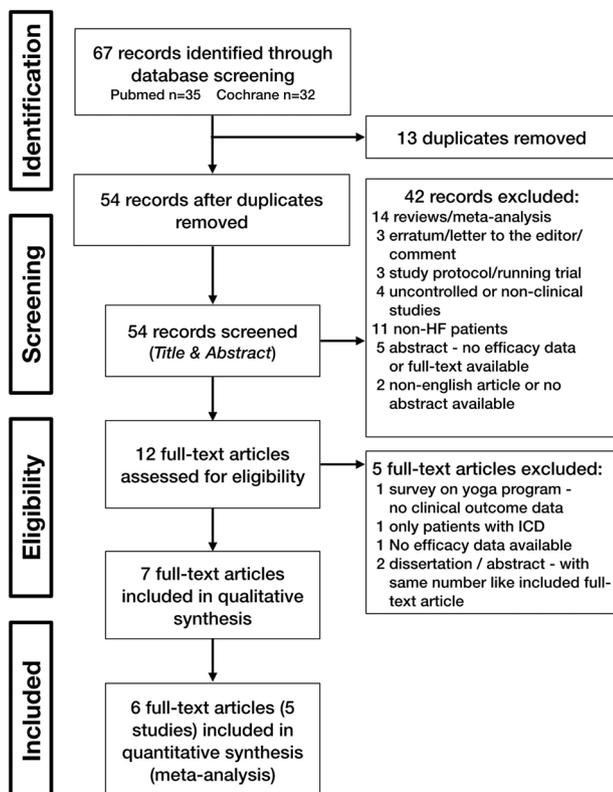

Fig. 1. Systematic literature screening process. ICD, implantable cardioverter defibrillator.

Table 1
Characteristics of studies included into the meta-analysis.

Study	Comparison	N (% women)	Mean age ± SD (years)	NYHA class	Medical treatment (nYG / nCG)	Time of follow-up (weeks)
Pullen et al. 2008	Yoga (two sessions/week) plus standard medical treatment vs. standard medical treatment	YG: 9 (77.8%) CG: 10 (30.0%)	YG: 52.1 ± 3.3 CG: 50.5 ± 12.8	I-III	• ACE-I: 6 / 8 • ALB: 4 / 6 • ARB: 0 /2 • β-Blocker: 8 / 10 • Statins: 5 / 5	8
Pullen et al. 2010	Yoga (two sessions/week) plus standard medical treatment vs. standard medical treatment	YG: 21 (52%) CG: 19 (31.6%)	YG: 55.8 ± 7.6 CG: 52.5 ± 12.7	I-III	• ACE-I: 13 / 17 • ALB: 7 / 8 • ARB: 4 /2 • β-Blocker: 20 / 19 • Statins: 15 / 12	8 (to 10)
Krishna et al. 2014a/b/c*	Yoga (six sessions/week) plus standard medical treatment vs. standard medical treatment	YG: 44 (27.3%) CG: 48 (33.3%)	YG: 49.34 ± 5.70 CG: 50.14 ± 4.54	I-II	• ACE-I & ARB: 8 / 4 • Antidiabetics: 10 / 12 • β-Blocker: 34 / 38 • Diuretics: 4 / 3 • Oral antiplatelet agents: 13 / 15 • Statins: 30 / 32	12
Donesky et al. 2017	Tele-Yoga (two sessions/week) vs. educational program (leaflet plus weekly phone call)	YG: 7 (57.1%) CG: 8 (75.0%)	YG: 73.0 ± 14.3 CG: 70.5 ± 2.7	II-III**	not listed	8
Hägglund et al. 2017	Yoga (two sessions/week) plus medical treatment vs. hydrotherapy training (two sessions/week) plus medical treatment	YG: 20 (25.0%) CG: 20 (45.0%)	YG: 64.1 ± 9.4 CG: 65.7 ± 8.5	I-III	• ACE-I: 18 / 18 • ALB: 5 / 7 • ARB: 4 /2 • β-Blocker: 19 / 20 • Diuretics: 15 / 19 • Statins: 7 / 10 • Wafarin: 7 / 9	12

YG: Yoga group; CG Control group; SD: Standard deviation; NYHA: New York Heart Association; ACE-I: ACE inhibitor; ALB: Aldosterone blocker; ARB: Angiotensin II receptor blocker *Krishna et al. 2014c only used for information on medical treatment; **Patients had comorbidity COPD with FEV1 values of 1.2 ± 0.5 liters (YG) and 1.3 ± 0.8 liters (CG).

4. Discussion

Patients with heart failure suffer from different symptoms such as breathlessness, fatigue and reduced exercise tolerance [1]. In addition, the ESC-HF pilot study showed a 17% 12-month all-cause mortality rate for hospitalized heart failure patients with reduced ejection fraction [27]. Besides drug treatment, guidelines recommend properly designed exercise training for heart failure patients [1].

Yoga has shown to positively effect cardiovascular outcomes and risk as well as QoL in healthy volunteers and patients with chronic disease [8,9,28–32]. A previously published systematic review and meta-analysis indicated that yoga can favorably modifying risk factors for cardiovascular disease and metabolic syndromes, such as reductions in blood pressure, low- and high-density lipoprotein cholesterol, triglycerides and body mass index [33].

Compared to the meta-analysis by Gomes-Neto et al. [10], which evaluated changes in VO₂ peak and QOL by including two studies, the present meta-analysis also evaluated the effect of yoga on 6-MWD, blood pressure and hs-CRP in heart failure patients, respectively. In addition, a total of five controlled trials were included into this meta-analysis.

In addition to already published evidence, this study shows that yoga might have a positive effect in patients with HF on reduction of inflammatory marker hs-CRP and increase of maximum oxygen uptake measured by VO₂ peak.

Yoga statistically significant reduced hs-CRP level by -0.39 mg/L compared to control in this study. A review by Sarvottam and Yadav reported that yoga-based lifestyle intervention reduced the hs-CRP level in obese and postmenopausal women [34]. In contrast, a systematic review on mind-body therapies in women at risk for cardio-metabolic diseases did not identify a significant reduction in hs-CRP level compared to control group [35]. Two other studies with healthy or elderly participants, revealed a statistically significant reduction of hs-CRP by yoga from baseline value [36,37], but in contrast to this meta-analysis the reduction was not statistically significant compared to control group [36,37]. Nevertheless, the reduction of hs-CRP in this meta-analysis by yoga supports the assumption that practicing yoga decreases this inflammatory marker.

Table 2
Risk of bias assessment of studies included into the meta-analysis.

Study	Random sequence generation	Allocation concealment	Blinding of participants and researchers	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Pullen et al. 2008	unclear	unclear	high	high	low	low	unclear
Pullen et al. 2010	unclear	unclear	high	high	low	low	high
Krishna et al. 2014a/b/c*	low	low	high	high	low	low	unclear
Donesky et al. 2017**	high	high	high	high	low	low	high
Hägglund et al. 2017	low	low	high	high	low	low	unclear

* Krishna et al. 2014c only used for risk of bias assessment, since this publication disclosed the most information on the randomization procedure.
** Trial registration number NCT02078739; retrievable under www.clinicaltrials.gov.
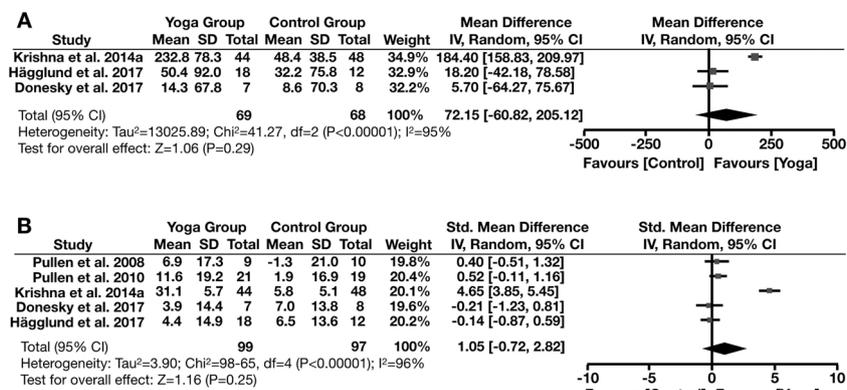
Fig. 2. Analysis of mean change in (A) 6-minutes walking distance [meter] presented as mean difference and (B) QoL (pooled analysis of KCCQ and MLHFQ) presented in standardized mean difference between yoga Group and control Group.

The importance of hs-CRP was described by Kalogeropoulos et al., who concluded from their study with 794 acute heart failure patients, that elevated levels of hs-CRP were associated with a higher mortality [11]. To be mentioned here is that the baseline hs-CRP levels of the included studies and the pooled decrease of -0.39 mg/L in this meta-analysis (Fig. 3C) were relatively small compared to the levels measured by Kalogeropoulos et al. [11]. In addition to that, the above discussed results from other studies, clearly point out that more trials are needed to finally estimated the effect of yoga on hs-CRP and in particular the potential effect on hs-CRP associated mortality in patients with HF.

How physical activities such as yoga reduce hs-CRP levels is not yet fully understood, but the following mechanism might be involved: decreased cytokine production by adipose tissue, improved endothelial function, an increased insulin sensitivity and antioxidant effects [38,39]. Known until now is, that production of hs-CRP is stimulated by interleukin 6 (IL-6) and to a smaller extent by IL-1 and tumor necrosis factor alpha (TNF-alpha). Individuals with obesity, insulin resistance and/or activated endothelial cells show an increased production of IL-6 and TNF-alpha [38]. Therefore it is hypothesized, that yoga, like other exercises, decreases hs-CRP levels by a reduced production of IL-6 and TNF-alpha resulting from an improvement of adipose tissue, endothelial function and insulin sensitivity.

The meta-analysis of the VO_2 peak assessment, an indicator for exercise tolerance, shows an increase of 3.95 mL/kg/min [95% CI: 2.14, 5.77] by yoga compared to control. Gomes-Neto et al. calculated a comparable, but slightly different increase of 3.87 [1.95, 5.80] in VO_2 peak in their meta-analysis, although the exactly same two studies were used for both analysis. A reason for the slight difference between the previous work [10] and this meta-analysis might be that it seems like Gomes-Neto et al. used in their meta-analysis for SDs of the mean changes from baseline, the SDs of the 8 weeks assessment from Pullen et al. 2008 [10,22]. In this meta-analysis the SDs associated to the mean change were calculated based on the Cochrane Handbook [17].
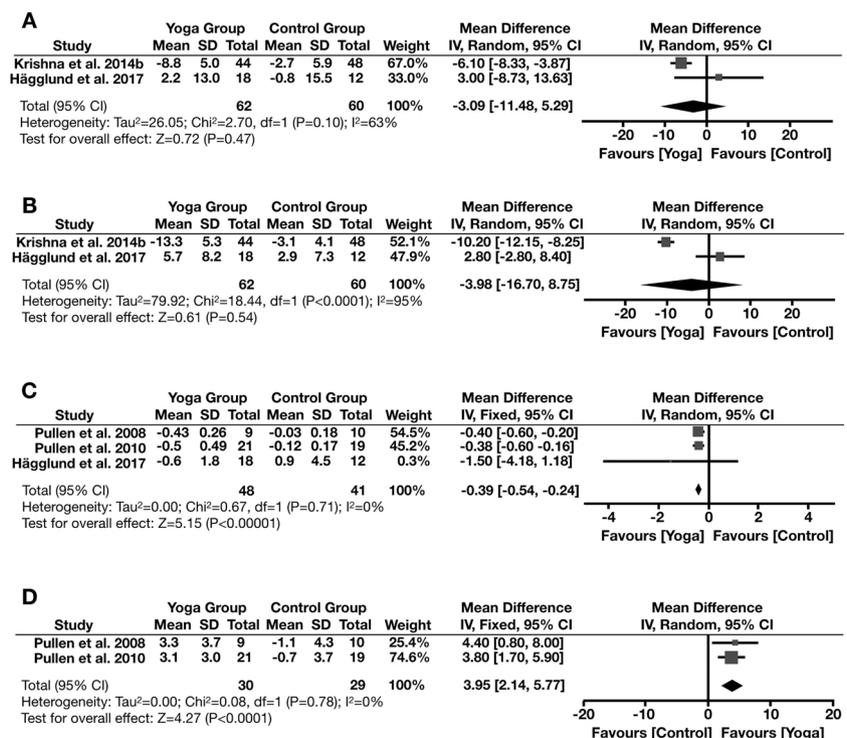

Fig. 3. Analysis of mean changes in (A) Systolic Blood Pressure [mmHg], (B) Diastolic Blood Pressure [mmHg], (C) hs-CRP [mg/L] and (D) VO_2 peak [mL/kg/min] in yoga group compared with control group.

The positive effect of yoga on the improvement in exercise tolerance is supported by a systematic review and meta-analysis with studies in patients with coronary heart disease performing exercise-based cardiac rehabilitation. This meta-analysis included yoga and tai-chi and showed a significant improvement in total time exercise and maximum exercise tolerance compared to control group [40].

To be mentioned here is that the effect of yoga on VO_2 peak measured in this meta-analysis might be more meaningful for the prognosis of HF patients than hs-CRP levels, by showing a pooled increase of almost 4 mL/kg/min (Fig. 3D). Already moderate increases of VO_2 peak by 6% can lead to a lower risk of 5%, 4%, 8%, and 7% of time to all-cause mortality or all-cause hospitalization, time to cardiovascular mortality or cardiovascular hospitalization, cardiovascular mortality or heart failure hospitalization, and all-cause mortality, respectively [41].

Interestingly, other studies investigating the increase of VO_2 peak by yoga in healthy adult women and 7–9 year old school children showed increases of up to 3.3 mL/kg/min [42,43], which is comparable to the effects seen in this study. In this meta-analysis included study of Pullen et al. (2010) [21] measured an increase of VO_2 peak of 20% (+3.11 mL/kg/min) within 8 weeks of yoga therapy. They discussed that yoga postures, breathing exercise and meditation might attenuate sympathetic activation and could lead to a decrease of ventricular filling pressure, which improves exercise tolerance [21].

The pooled analysis of quality of life did not indicate a statistically significant benefit of yoga vs. control. Nevertheless, the meta-analysis of MLFHQ alone, including three studies [20–22], showed a change of 15.97 points. This improvement by yoga can be assumed as clinically relevant, since a change in MLFHQ score of 5 points can be considered as a clinically improved difference in score [44,45]. Gomes-Neto et al. measured a comparable effect with a change in MLFHQ of 12.46 points by only including the two studies of Pullen et al. [20,21].

In contrast to the MLFHQ, the QoL score KCCQ was non-significantly favoring control over yoga therapy in this meta-analysis. Reasons might be that in the MLFHQ analysis the population was 3.5 times larger than the one available for the KCCQ analysis, which could have an influence on the results. In addition, one study within the KCCQ analysis compared yoga to hydrotherapy and patients in the control (hydrotherapy) group used more medical drug treatments against HF than patients in the yoga group (4.2 drugs vs. 3.6 drugs) [25], which could have had an effect on the quality of life and other outcome measurements. The second study included into the meta-analysis of changes in KCCQ involved patients with both COPD and heart failure [24], which also might have influenced the final outcome.

Improvement in 6-minutes walking distance (Fig. 2A) and reduction in systolic and diastolic blood pressure (Fig. 3A/B) favored yoga therapy without achieving statistical significance. Former studies have shown, that in dependance of other risk factors such as age, baseline blood pressure, and comorbidities, yoga practice had a positive effect on lowering blood pressure in patients with and without HF [23,32,46,47]. In addition, a Cochrane review identified eight studies investigating the effect of yoga for primary prevention of cardiovascular disease and measured diastolic blood pressure reduction of -2,90 [-4,52, -1,28] mmHg [48], which is slightly lower compared to the effect measured in this meta-analysis (-3.98 mmHg [-16.70, 8.75]). The effect size of yoga on systolic blood pressure was not estimated in the Cochrane review [48].

Even though this meta-analysis and the previously discussed studies indicate a positive effect of yoga on blood pressure reduction larger trials with longer follow-up times than 8–12 weeks are needed to conclude if yoga has a positive effect on blood pressure. Ideally, studies should not solely focus on blood pressure reduction, but also on the prevention of cardiovascular events.

A recently published review by Pullen et al. (2018) discussed the physiological mechanisms by which yoga improves cardiovascular disease related-outcomes. The authors wrote that yoga might lead to musculoskeletal and vagal nerve stimulation and reduction of perceived stress. These three mechanism might promote parasympathetic activation and the release of stimulating factors, finally resulting in positive effects on heart rate, blood pressure and inflammatory cytokines [49]. These assumptions by Pullen et al. (2018) might explain the underlying physiological mechanism of the potential benefits of yoga in heart failure patients found in this study.

To be mentioned here is that the study of Krishna et al. showed stronger effects by yoga on the assessed outcomes than the other studies included into the meta-analysis. Factors influencing the stronger response to yoga might be that Krishna et al. included younger as well as less severe heart failure (NYHA I-II) patients [22,23]. Especially the severity of heart failure can have a strong impact, since patients with NYHA I-II have no to slight limitations of physical activities, whereas all other studies than Krishna et al. included also patients with NYHA III, showing a marked limitation of physical activity [2,20–26].

As shown in Table 1 patients in included studies received specific medications against heart failure such as beta-blockers and ACE inhibitors. ESC guidelines recommend these medications, because it is well known that they reduce mortality as well as morbidity and improve symptoms and exercise capacity [1]. Since both, yoga and control groups, received medications in most studies, one can expect that the medications should not have affected the final outcomes of this meta-analysis. Nevertheless, the medication compliance rates within the included studies are not known and slight differences in medication compliance between yoga and control group might already have an impact on assessed outcomes. A recommendation could be that future studies investigating the effect of yoga in heart failure should always report (i) the compliance to yoga sessions as well as (ii) the compliance to specific medications against heart failure to be able to better estimated the impact of each intervention.

This meta-analysis has several limitations.

First, the systematic searches, selection and appraisal of studies, evaluation of bias of included studies, data extraction, and the meta-analysis itself were performed by only a single person. In addition, the search was restricted to studies published in English language.

Second, the literature search was limited to two databases and screening of reference lists of included studies, which might have led to a non-identification of studies actually eligible for inclusion into this meta-analysis. A more extensive search approach or the input of an information specialist might have identified more studies on yoga in patients with heart failure. The literature search can be considered as a major limitation.

Third, statistical heterogeneity of the following outcome measures, 6-minutes walking distance, QoL and reduction in diastolic blood pressure was statistically significant.

Fourth, the follow-up times of included studies were short with 8–12 weeks. To confirm the findings of this meta-analysis, longer trials are needed.

Fifth, a publication bias among included studies can not be ruled out, since funnel plots were not eligible for bias estimation. Nevertheless, based on the estimates in this meta-analysis a slight bias might only be visible for Krishna et al., especially for QoL, due to the above discussed reasons.

Sixth, number of studies and patients included into the meta-analysis and particular included into the individual analyses of each outcome were low. Unfortunately, there was no assessment common in all included studies. A recommendation for future research evaluating the effect of yoga in heart failure patients or any other cardiovascular disease should be, to define standardized assessments, which could be mandatory in all studies. This would allow a higher comparability between studies and could increase the number of studies and patients for future meta-analysis. In addition, the definition of assessments that are also used in trials to evaluate the effect of drug treatments, might even allow stronger conclusions of the complementary effect of yoga on conventional drug treatments in patients with heart failure.

5. Conclusion

Despite all mentioned limitations and to the best of my knowledge, this meta-analysis is the first pooled analysis of five studies investigating the effect of yoga in heart failure patients and therefore, might give more indications on the potential benefits of yoga in heart failure.

The analysis indicates that, in patients with heart failure yoga can have a positive and improving effect on reduction of hs-CRP level and increase of VO_2 peak. The combination of physical exercises, postures and especially breathing techniques could be an optimal activity for patients with the main symptom dyspnea and limitations in physical activity. Nevertheless, yoga should only be seen as a complementary therapy of well established drug treatments investigated in clinical trials. To better quantify the effect of yoga in patients with heart failure and to give recommendations, e. g. in guidelines, more data are needed. In particular, more studies with standardized endpoints of high importance for heart failure patients and the treating physicians should be performed. These would comprise endpoints such as cardiovascular events (stroke, myocardial infarction) and mortality as it is the usual procedure in most HF trials with drug treatments. To increase the quality of these studies, they should be designed as randomized, controlled trials comparing yoga with non-exercise but also other exercises with known benefits in heart failure, to get more and clear evidence if yoga could become an important part of a holistic treatment concept for heart failure patients.

Author`s contributions

LM was the only author of this study and planned the meta-analysis, conducted the literature search, performed the analysis as well as data evaluation and prepared the manuscript.

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Declaration of competing interest

The authors has no conflict of interest.

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