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ORIGINAL ARTICLE

Non-pharmacological interventions for depression in patients with heart failure: a systematic review

Intervenciones no farmacológicas para la depresión en pacientes con falla cardíaca: una revisión sistemática

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Abstract

Background: *In advanced stages of heart failure, the prevalence of depression can exceed 50%, which is associated with a worse clinical state and increases medical care costs.* **Objective:** *To identify and synthesize the most effective non-pharmacological interventions for the treatment of depression in patients with heart failure.* **Method:** *Studies published up to September 2021 involving depression and heart failure were identified by reviewing the main databases. Two authors independently selected the literature.* **Results:** *Cognitive behavioral therapy and exercise were the most commonly used non-pharmacological interventions for depressive symptoms in patients with heart failure, with moderate to large effect sizes (Cohen's d between 0.5 and 3.4).* **Conclusion:** *In patients with heart failure, cognitive behavioral therapy and exercise were shown to be better than the usual care for depressive symptoms.*

Keywords: *Heart failure. Depression. Cognitive behavioral therapy. Exercise.*

Resumen

Introducción: *En fases avanzadas de la falla cardíaca, la prevalencia de la enfermedad depresiva puede superar el 50%, lo cual se asocia con un peor estado clínico, y hace que aumenten los costos en la atención médica.* **Objetivo:** *Identificar y sintetizar las intervenciones no farmacológicas más efectivas para el tratamiento de la depresión en pacientes con falla cardiaca.* **Método:** *Se hizo una pregunta estructurada y se realizó la búsqueda en las principales bases de datos hasta septiembre de 2021 con los términos que incluían depresión y falla cardíaca. Dos autoras realizaron la selección de la literatura encontrada y el análisis de los datos de forma independiente.* **Resultados:** *La terapia cognitivo-conductual y el ejercicio fueron las intervenciones no farmacológicas más usadas para tratar los síntomas depresivos en pacientes con falla cardiaca, con tamaños de efecto moderados a grandes (d de Cohen entre 0.5 y 3.4).* **Conclusión:** *En pacientes con falla cardiaca, la terapia cognitivo-conductual y el ejercicio demostraron ser mejores que el cuidado usual no farmacológico para tratar los síntomas depresivos.*

Palabras clave: *Falla cardíaca. Depresión. Terapia cognitiva-conductual. Ejercicio.*

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Introduction

Heart failure is defined by the presence of signs or symptoms suggestive of cardiac output deterioration and volume overload, and is caused by anatomical or functional heart disorders which affect ventricular filling or emptying, preventing it from meeting the organism's metabolic demands[1]. Its prevalence has increased and there are an estimated 23 million people diagnosed with this disease worldwide[2]. In 2012, the overall prevalence in Colombia was 2.3%[3].

Patients with heart failure may have a diminished quality of life due to the course of the disease and their mental health may be affected by other illnesses like depression[4]. Depression prolongs recovery, increases the number of days in the hospital and is associated with a worse prognosis, higher mortality rate and greater loss of work productivity[5-7]. It is also known that depressive symptoms may reach a prevalence of 25% in patients with heart failure[8]. In advanced heart failure stages, depression may exceed 50%[9], which is associated with a worse clinical state and increases medical care costs; therefore, interventions aimed at the mental component are a priority[10].

The treatment of depressive symptoms in these patients is an even greater challenge than in those without heart failure due to factors like polypharmacy, defined as taking three or more medications[11]. Potential drug interactions could produce the opposite effect to what is expected due to their side effects. Thus, patient-focused programs have implemented various non-pharmacological interventions aimed at the mental component[12,13]. The objective of this systematic review was to summarize the available evidence on the most effective non-pharmacological interventions for improving depressive symptoms in patients with heart failure.

Method

A systematic review of the literature published up to September 2021 was performed in PubMed, BIREME, Cochrane and PROSPERO, following the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) strategy guidelines[14]. The terms used for the search can be found in Table 1.

Randomized clinical trials (RCTs), patients with a diagnosis of heart failure and depression according to the DSM-V or other diagnostic tools, and articles including individual and/or group non-pharmacological interventions or programs aimed at treating depressive symptoms were included. The exclusion criteria were studies published in languages other than English or Spanish, as well as studies with pharmacological treatments as the intervention or comparator.

Two investigators (DCT, AMP) independently selected the studies by title and abstract and performed the full-text evaluation of the selected studies. A third investigator (LHL) resolved selection conflicts.

The main outcome was the difference between groups on the depression scale at the end of the interventions. Due to the diversity of measurement instruments used in the studies, the differences were compared using Cohen's d effect size, calculated from the means and standard deviations of the scores in the studies which provided this information. For interpretation, they were classified as: less than 0.2, no effect; from 0.2 to 0.5, small effect; from 0.5 to 0.8, moderate effect; and more than 0.8, large effect[15].

The risk of bias assessment was performed using the Cochrane tool for randomized clinical trials (ROB 2).

Results

In the search, 388 articles were found for title and abstract review. After applying the exclusion criteria, 314 were eliminated, 74 underwent full-text review and 9 were selected for the synthesis (Fig. 1). Four instruments were used in the studies; the most commonly used was PHQ-9 (n = 6), followed by BDI-II (n = 3).

Instruments used to measure depression

Hospital anxiety and depression scale (HADS)

This consists of depression and anxiety sub-scales, with seven items in each. A probable diagnosis of anxiety or depression is defined as having more than 10 points on the sub-scales[16].

Patient health questionnaire (PHQ-9)

This consists of nine items and evaluates the presence of depressive symptoms. The scale goes from 0 to 27; 0 to 4 means no illness, 5 to 9 mild illness, 10 to 19 moderate illness, and more than 20, severe depression[17].

Beck depression inventory-II (BDI-II)

This self-report has 21 items. Scores range from 0 to 63: 0-13, minimal depression; 14-19, mild depression; 20-28, moderate depression and 29-63, severe depression[18].

Table 1. Search strategy in the databases

PubMed
("heart failure"[MeSH Terms] OR "heart failure"[Title/Abstract] OR "cardiac failure"[Title/Abstract] OR "myocardial failure"[Title/Abstract] OR "ventricular dysfunction" [Title/Abstract] OR "decompensated heart"[Title/Abstract] OR "heart decompensation"[Title/Abstract]) AND ("depressive disorder"[MeSH Terms] OR "depression"[MeSH Terms] OR "depress*"[Title/Abstract] OR "melancholia"[Title/Abstract]) AND ("exercise therapy"[MeSH Terms] OR "exercise" [MeSH Terms] OR "exercise training"[Title/Abstract] OR "exercise-based rehabilitation"[Title/Abstract] OR "cardiac rehabilitation"[Title/Abstract] OR "exercise therap*" [Title/Abstract] OR "psychotherapy"[MeSH Terms] OR "psychotherap*"[Title/Abstract] OR "Mindfulness" [Title/Abstract] OR "relaxation therapy"[MeSH Terms] OR "Relaxation"[Title/Abstract] OR "non pharmacolog*" [Title/Abstract] OR "non pharmacolog*"[Title/Abstract] OR "NFIs"[Title/Abstract] OR "Logotherapy"[Title/Abstract] OR "psychosocial"[Title/Abstract] OR "psychoanalytic" [Title/Abstract] OR "cognitive"[Title/Abstract] OR ("telemedicine"[MeSH Terms] OR "telemedicine"[Title/Abstract] OR "telehealth"[Title/Abstract] OR "tele-health"[Title/Abstract] OR "Mobile Health"[Title/Abstract] OR "mhealth"[Title/Abstract] OR "m-health"[Title/Abstract] OR "telecare"[Title/Abstract] OR "tele-care"[Title/Abstract] OR "teleconsult*"[Title/Abstract] OR "tele consult*"[Title/Abstract] OR "telecounsel*"[Title/Abstract] OR "tele counsel*"[Title/Abstract] OR "eHealth"[Title/Abstract] OR "e-Health"[Title/Abstract] OR "remote consult*" [Title/Abstract] OR "telerehabilitation"[Title/Abstract] OR "tele-rehabilitation"[Title/Abstract] OR "virtual appointment"[Title/Abstract]))
Cochrane
Reviews matching "heart failure" in Title Abstract Keyword AND depression in Title Abstract Keyword - (Word variations have been searched) AND ("non-pharmacologic" in Title Abstract Keyword - (Word variations have been searched)- ("psychotherapies" in Title Abstract Keyword - (Word variations have been searched)
BIREME-LILACS
("heart failure") AND ("depression") AND (db:("LILACS" OR "IBECS" OR "BDENF" OR "BINACIS" OR "CUMED" OR "LIPECS" OR "HomeoIndex" OR "colecionaSUS"))

Hamilton depression rating scale (HDRS)

This has 17 items, with scores from 0 to 52 points, as follows: 0 to 7 no depression, 8 to 16 mild depression, 17 to 23 moderate and more than 24, severe depression[19].

Interventions

Two interventions were found most often, cognitive behavioral therapy (CBT) and exercise. The intervention time in the studies was three to 12 months.

Cognitive behavioral therapy

Cognitive behavioral therapy focuses on the relationship between thoughts and behavior, to understand the cognitive and behavioral processes and improve negative behaviors[20]. It has been effective for treating depression and is an adjunct intervention to the rest of the therapies[21]. Five studies on CBT were found[12,22-25]. The first[23], with 74 patients with heart failure, New York Heart Association (NYHA) functional class II and III and major depression, compared exercise (n = 20), CBT (n = 19) or a combination of the two (n = 18) with the usual care (n = 17). The exercise only group received 12 weekly home visits to monitor and adapt the exercise prescription. The patients assigned to CBT received several one-hour sessions at home. The combined exercise and CBT interventions were administered simultaneously or separately, according to the patients' tolerance. The usual care consisted of providing basic recommendations about caring for their health. Both groups were evaluated with the HDRS at 4, 8, 12 and 24 weeks. They reported that those who received a combination of CBT and exercise had lower HDRS scores at 12 and 24 weeks[23]. Another study[22] with 41 hospitalized patients with depressive symptoms and NYHA III/IV heart failure randomly assigned these patients to 30-minute CBT sessions. They also received a notebook with instructions to take home and five to ten-minute weekly telephone calls after discharge. They were compared with the usual care, consisting of written instructions on the emotional consequences of living with heart failure, and 40 to 60 minutes of counseling about their illness. Depressive symptoms were measured one week and three months later, finding that, although the BDI-II scores improved in both groups, the differences between the groups were not significant[22]. In the third study,[12] 158 heart failure patients with NYHA functional class I, II and III and depression were included and received on-site 60-minute CBT sessions led by experienced therapists and 20 to 30-minute telephone interventions to prevent relapse, 6 to 12 months after randomization. The control group received education about heart failure provided by a

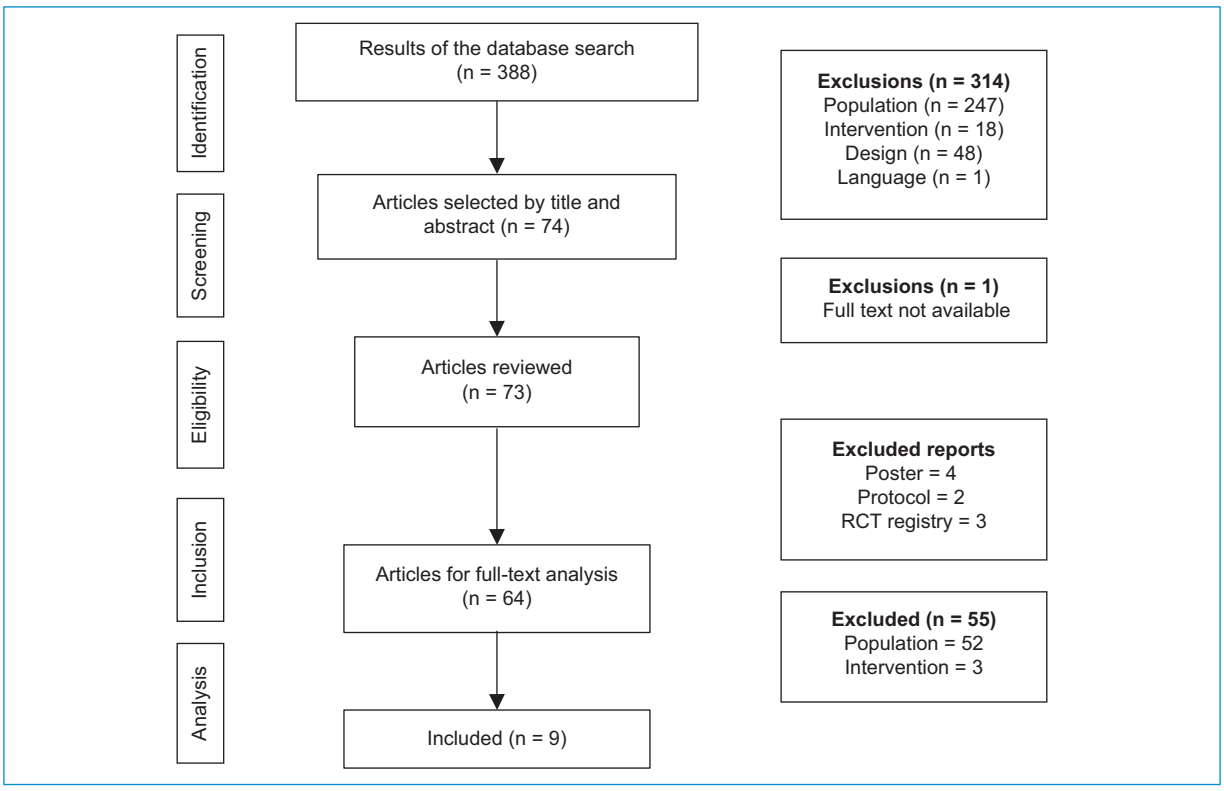

Figure 1. Flow chart.

cardiac rehabilitation nurse. All received educational materials on self-care. After six months, they found that the BDI-II scores were lower in the CBT group than in the control group[12]. Another study[25] with 50 patients with heart failure and mild depressive symptoms randomized to CBT (n = 25) or a virtual discussion forum (n = 25) measured depressive symptoms at the beginning and after nine weeks of intervention. The CBT included seven modules, with reading and homework to complete. The control group participated in several sessions of a virtual discussion forum on different topics. A mental health nurse specialist with experience in caring for patients with heart failure, supervised by a clinical psychologist and a cardiologist, answered questions from participants in both groups. No significant differences were found in the PHQ-9 scores between the groups after the interventions[25]. Finally, a study of 233 patients with heart failure and depressive symptoms compared six weekly CBT sessions and two telephone sessions over four months with the usual care which included general recommendations on how to deal with depression and anxiety. They found that CBT improved depressive symptoms and the effects persisted at eight and twelve months[24].

Exercise

Exercise was also one of the most common interventions[13,17,18,26]. In the first[13] of three studies published by the same authors in 2019, 46 patients with systolic heart failure were randomized to mild to moderate aerobic exercise plus standard medical treatment or to standard medical treatment with no exercise intervention. Both groups showed a significant reduction in depressive symptoms after 12 weeks, with significant differences in PHQ-9 favoring the exercise group after six and 12 weeks. The second study[17] included 69 patients with heart failure and mild to moderate depression, randomly classified into three groups: low to moderately intense exercise, moderately intense exercise and no exercise. All of the patients in the exercise groups were supervised and received feedback to adjust the exercise intensity prescription. The group without exercise was advised to maintain their usual activity. They concluded that there was a significant reduction in depression in all three groups, with a greater difference in both exercise programs. Finally, the third study[26] included 46 patients with heart failure and depression, randomized to

Table 2. Score differences between study groups

Author	Scale	Time	n	Intervention	Control group	Difference between groups	p
Gary 2010[23]	HDRS	6 months	56	Exercise	Usual care	–0.1	0.26
Dekker 2012[22]	BDI-II	3 months	41	CBT	Usual care	–0.8	0.129
Freedland 2015[12]	BDI-II	6 months	158	CBT	Usual care	–4.43 (95% CI: –7.68; –1.18)	0.008
		12 months	158	CBT	Usual care	–4.82 (95% CI: –8.14; – 1.49)	0.005
	HDRS	6 months	158	CBT	Usual care	–3.95 (95% CI: –5.81; –2.08)	< 0.001
Lundgren 2016[25]	PHQ-9	9 weeks	7	CBT	Virtual discussion forum	–1.2	0.21
Cully 2017[24]	PHQ-9	8 months	228	CBT	Usual care	–3.20	< 0.001
		12 months	224	CBT	Usual care	–2.67	0.011
Blumenthal 2012[18]	BDI-II	3 months	653	Aerobic exercise	Usual care	–1.31 (95% CI: –2.54; –0.09)	0.04
		12 months	653	Aerobic exercise	Usual care	–1.56 (95% CI: –2.84; –0.27)	0.02
Abdelbasset 2019[13]	PHQ-9	6 weeks	46	Exercise	No exercise	–3.891	< 0.001
		12 weeks	46	Exercise	No exercise	–4.89	< 0.001
Abdelbasset 2019[26]	PHQ-9	6 weeks	57	MICAE	No exercise	–3.82	< 0.001
		12 weeks	57	MICAE	No exercise	–5.42	< 0.001
Abdelbasset 2019[17]	PHQ-9	6 weeks	69	LMIEP MICEP	No exercise	LMIEP –3.91 MICEP –3.82	< 0.001 < 0.001
		12 weeks	69	LMIEP MICEP	No exercise	LMIEP –4.89 MICEP –5.42	< 0.001 < 0.001

CBT: cognitive behavioral therapy; PHQ9: Patient Health Questionnaire-9; BDI-II: Beck Depression Inventory-II; HDRS: Hamilton Depression Rating Scale; 95% CI: 95% confidence interval; MICAE: moderate-intensity continuous aerobic exercise; LMIEP: low to moderate-intensity exercise program; MICEP: moderate-intensity continuous exercise program.

continuous, moderately intense aerobic exercise three times a week for 12 weeks, or to receive recommendations including being active, relaxing and setting simple goals for 12 weeks. Both groups had a significant reduction in their levels of depression, with a greater reduction in the intervention group[26]. Finally, a study of 653 patients with heart failure and depression according to the BDI-II, randomly assigned them to 90 minutes per week of supervised aerobic exercise for three months, followed by at least 120 minutes per week of exercise at home for nine months, or to an education program and evaluation by cardiology. No significant differences were reported between the groups[18].

Usual non-pharmacological care

In the included studies, the usual non-pharmacological care refers to receiving information, written instructions or educational materials on the illness. No studies were included comparing the use of antidepressants, which in many cases is recognized as the usual care for depression.

Table 2 shows the score differences between groups for each study.

Effect sizes

Effect sizes were calculated for seven studies[12,13,17,22-25] which had available information. Some studies evaluated more than one intervention or had different follow up times, and therefore several effect sizes could be calculated (Table 3).

Quality of the studies

All nine articles included had some risk of bias (Fig. 2).

Table 3. Average scores after the intervention and effect sizes (Cohen's d)

Author/Year	Intervention	Scale	Time	n intervention	n control	Post-intervention (SD)	Post-control (SD)	Cohen's d (Post)
Abdelbasset[17]	MICEP	PHQ-9	12 weeks	23	23	3.12 (1.18)	8.54 (2.14)	3.14
Abdelbasset[13]	LMIEP	PHQ-9	12 weeks	23	23	3.65 (1.21)	11.65 (3.28)	2.81
Abdelbasset[17]	MICEP	PHQ-9	6 weeks	23	23	7.83 (3.22)	8.54 (2.14)	1.18
Abdelbasset[13]	LMIEP	PHQ-9	6 weeks	23	23	7.74 (3.26)	11.65 (3.28)	1.20
Freedland 2015[12]	CBT	HDRS	6 months	79	79	12.1 (6.0)	8.2 (5.9)	0.66
Cully 2017[24]	CBT	PHQ-9	4 months	132	101	10.3 (5.1)	13.3 (5.8)	0.55
Cully 2017[24]	CBT	PHQ-9	8 months	128	100	10.3 (5.5)	13.5 (6.0)	0.55
Cully 2017[24]	CBT	PHQ-9	12 months	125	99	10.6 (5.1)	13.2 (6.4)	0.45
Dekker 2012[22]	CBT	BDI-II	3 months	20	21	9.3 (1.6)	10.1 (1.7)	0.49
Freedland 2015[12]	CBT	BDI-II	6 months	79	79	17.3 (10.7)	12.8 (10.6)	0.42
Lundgren 2016[25]	CBT	PHQ-9	9 weeks	25	25	8.6 (4.6)	9.8 (4.3)	0.27
Gary 2010[23]	CBT + Exercise	HDRS	6 months	15	14	6.1 (5.1)	8.2 (5.4)	0.40
Gary 2010[23]	CBT	HDRS	6 months	16	14	7.1 (4.9)	8.2 (5.4)	0.21
Gary 2010[23]	Exercise	HDRS	6 months	17	14	8.3 (5.2)	8.2 (5.4)	0.02

SD: standard deviation; LMIEP: low to moderate-intensity exercise program; MICEP: moderate-intensity continuous exercise program; CBT: cognitive-behavioral therapy; PHQ9: Patient Health Questionnaire-9; BDI-II: Beck Depression Inventory-II; HDRS: Hamilton Depression Rating Scale.
Cohen's d categories: less than 0.2, null effect; between 0.2 and 0.5, small effect; between 0.5 and 0.8, medium effect and greater than 0.8, large effect.

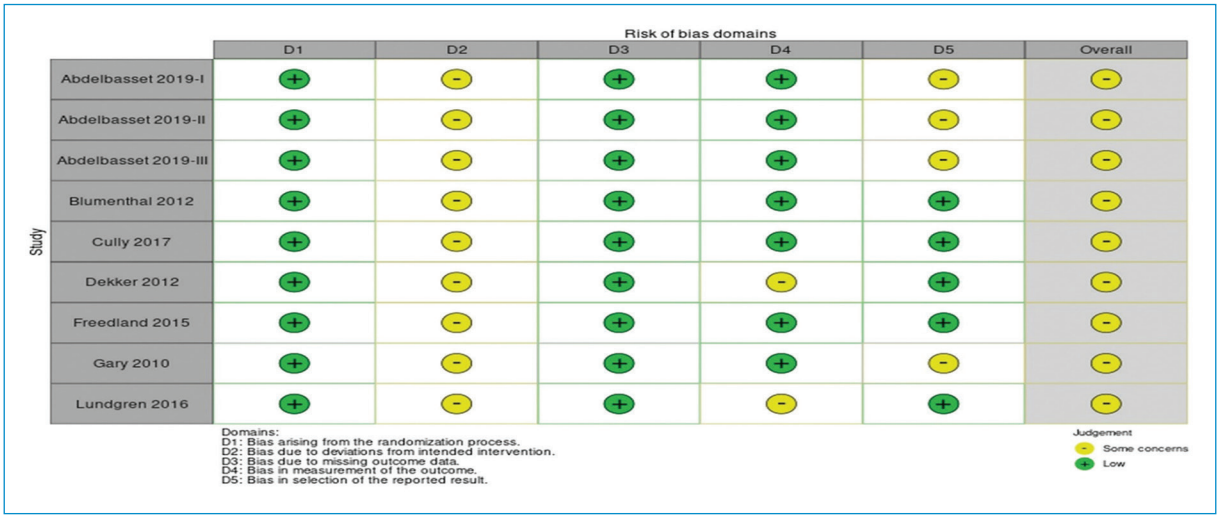

Figure 2. Evaluation of the quality of the evidence using the ROB 2.0 instrument.

Discussion

Heart failure is often associated with depression, which leads to a deterioration in quality of life and a higher risk of death[27]. Several studies have reported that patients with heart failure and more acute physical symptoms experience more severe depression, and that patients with depression and heart failure report lower mental and physical health scores[28,29]. The most important results of this study showed differences in the depression scores in favor of exercise intervention compared with the control groups. Two studies were

found showing mild to moderate effectiveness of exercise, with moderate exercise for 12 weeks showing the greatest effectiveness on depression measured with the PHQ-9[13]. On the other hand, CBT showed more contradictory results as, of the five CBT studies, three[12,23,24] reported differences in the depression scores for the intervention groups compared with the control, and two[22,25] found no statistically significant differences.

None of the studies included in this review blinded the participants, which is hard due to the type of interventions. And in only some of the studies were those who evaluated the outcomes masked, which could lead to bias. The literature has reported a lack of good quality studies evaluating the effectiveness of the interventions[30]. The systematic review performed by Wolts et al. in 2012[30] only found one RCT with a CBT intervention and concluded that there was insufficient proof of its effects.

Regarding the effect size calculation, only half of the studies included in this review provided the required information, and, of the 14 values calculated, four indicated a large effect size, three a moderate effect size, six a small effect size, and one a null effect size. The study by Thombs et al.[31] found a small effect size for CBT and a lack of statistically significant results for interpersonal psychotherapy. For their part, Jeyanantham et al.[32] reported a difference in the depression score in favor of CBT, with a moderate effect size.

Various studies have shown that exercise provides multiple benefits for outcomes like hospitalization rates and mortality reduction[33,34]. They also recognize that psychosocial interventions, pharmacological treatment and exercise are useful and that, beyond usual care, CBT along with an educational program in patients with heart failure and depression can reduce depression, anxiety and symptoms of fatigue, improving social and mental function as well as the quality of life[18]. In 2020, Ishak et al.[35] observed six interventions: antidepressants, collaborative care, psychotherapy, exercise, education and other non-pharmacological interventions and, although the patients showed improvement in depression, the evidence was contradictory for exercise and education.

In this review, we found that exercise is the intervention with the greatest impact on improving depressive symptoms in patients with heart failure, unlike the systematic review of observational studies performed by Jeyanatham et al.[32] which concluded that CBT is more effective than the usual care, but that larger RCTs are needed to evaluate the clinical effects.

It is important to mention that there may be differences in the findings due to some studies only including patients with mild or moderate depression, as the difference in the change of scores for these levels of depression, as a measure of the effect of the interventions, could be smaller. Other aspects to consider are the barriers caused by the diversity of the instruments, criteria and methodologies employed for diagnosing this group of patients, as well as the non-pharmacological interventions used[36], which do not allow for comparisons or meta-analysis.

The American Heart Association (AHA) has published recommendations for depressive symptom screening in patients with cardiovascular disease, which state that the diagnosis of depression should be based on the DSM-V criteria, in addition to using tools specifically validated in patients with heart disease[37,38]. The difficulty with these tools and their cut-off points is that they may not be appropriate for patients with cardiovascular disease, as some of the heart disease symptoms may overlap or be confused with depressive symptoms[39]. Most of the instruments that evaluate depressive symptoms in patients with heart failure are based on scales which are self-administered by the patients or filled out by the medical staff and do not include all the criteria for the clinical diagnosis of depression[40]. However, several studies have evaluated the psychometric performance of these scales in patients with heart failure[12,41-44] and have found them to perform adequately in depression screening. One study reported 94% sensitivity and 85% specificity for HADS, with a cut-off of 7 points[42]. Another study reported 70% sensitivity and 92% specificity for the PHQ-9, with a cut-off of 10[43]. In addition, another study comparing the scales concluded that HADS-D, PHQ-9 and BDI-II perform similarly, with high specificity for identifying possible cases of depression in both ambulatory and hospitalized patients with heart failure, and that HADS-D appears to have an advantage over the others as a screening tool, due to its higher sensitivity[44].

Strengths and limitations

A positive aspect of this study is that only randomized clinical trials were included, and the PRISMA recommendations were followed. The limitations include the variety of instruments used to measure the depressive symptoms and interventions, which made it impossible

to conduct a meta-analysis. In none of the studies were the patients blinded to their assignment, and in only a few were the evaluators blinded. No studies were included comparing the non-pharmacological interventions with pharmacotherapy, which in many cases is the first-line treatment for people with depression. Furthermore, three of the four studies which evaluated exercise were by the same authors and included the same participants, varying only in exercise intensity.

Practice implications

Depression can lead to significant changes in quality of life, especially in patients with heart failure, and therefore measures are needed to prevent or treat it[45]. Healthcare providers should be able to implement both pharmacological and non-pharmacological therapies to prevent and treat the symptoms of depression and improve the care and quality of life of patients with heart failure[46].

Conclusions

Exercise proved to be better than the usual non-pharmacological care for patients with heart failure and depressive symptoms. Regarding CBT, contradictory differences were found in the results. More studies are needed to evaluate non-pharmacological interventions, using different types of interventions, durations and intensity, singly or accompanied by pharmacological treatment.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical disclosures

Human and animal protection. The authors declare that no experiments were conducted on human beings or animals for this study.

Data confidentiality. The authors declare that no patient data appears in this article.

Right to privacy and informed consent. The authors declare that no patient data appears in this article.

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