(REVIEW ARTICLE)

Insomnia in patients with heart disease: A systematic review

Waguih William IsHak [1, 2, *], Mohadese Golsorkhi [1], Ariella Maghen [1], Laurel Tay [1], Salma Abdelmoteleb [1], Salma Ramadan [1], Samuel Korouri [1], Michele Hamilton [3] and Itai Danovitch [1]

[1] Department of Psychiatry and Behavioral Neurosciences, Cedars-Sinai Medical Center, Los Angeles, CA, USA.
[2] David Geffen School of Medicine at UCLA, Los Angeles, CA, USA.
[3] Smidt Heart Institute, Cedars-Sinai Medical Center, Los Angeles, CA, USA.

Abstract

Objective: The purpose of this paper is to review the literature on insomnia in patients with heart disease in order to answer the following questions: (a) What is the impact of insomnia on quality of life, morbidity, and mortality in patients with heart disease? (b) What is the impact of treatment interventions on insomnia in patients with heart disease?

Methods: Following the PRISMA guidelines, studies published from 1973 to 2023 that pertain to insomnia and heart disease were identified through the use of the PubMed and PsycINFO databases, using the keywords: 'cardiac' OR 'cardiovascular' OR 'heart' AND 'disease' AND 'insomnia'. Two authors independently conducted a focused analysis and reached a final consensus on 11 studies that met the specific selection criteria and passed the study quality checks.

Results: Management of insomnia in patients with heart disease involved combining different interventions, such as CBT-I with disease management or self-management programs, which demonstrated sustained improvements in sleep-related metrics in patients with heart disease and insomnia. While non-pharmacological approaches were the primary focus in most studies reviewed, medication-based interventions, such as zolpidem controlled-release, melatonin, and oxazepam, showed promising results.

Conclusion: The findings support the use of CBT-I as an effective non-pharmacological approach for managing insomnia in patients with heart disease. Future research should explore the long-term effects of interventions, optimal dosing and duration, and potential synergistic effects of combining different interventions.

Keywords: Insomnia; Heart Disease; Treatment; Interventions.

1. Introduction

Insomnia affects a large proportion of the general population worldwide with a significant negative impact on overall physical and mental health. Untreated insomnia is a public health burden with an estimated total cost of greater than $100 billion per year and approximately 400 million lost workdays per year due to absenteeism. The prevalence of insomnia in the general U.S. population is about 10-15%, and 33% among patients with medical conditions (Budhiraja, 2011). Insomnia is especially common among patients with heart disease, with a prevalence of 44% (Bankier, 2004, Taylor, 2007).

Insomnia is associated with poor outcomes in patients with heart disease. Research has found that insomnia is particularly associated with a subsequent risk of myocardial infarction (MI), stroke, and death in patients with heart disease in three recent meta-analyses of prospective studies (Cappuccio, 2011; Li, 2014; Sofi, 2017), making sleep

* Corresponding author: Waguih William IsHak.

disorders the 10th modifiable cardiovascular risk factor (Redline, 2011). Health related quality of life (HRQoL) is markedly decreased among patients with heart disease suffering from insomnia (IsHak, 2012). Insomnia is associated with fatigue, excessive daytime sleepiness, and functional decline even in patients with heart disease in a stable condition (Redeker, 2010). Poor sleep quality was found to be associated with depressive symptoms in patients with heart disease (Norra, 2012). Additionally, patients with heart disease comprise a population that is at risk and vulnerable to pandemics such as the COVID-19 pandemic. Hence, patients with heart disease experience an increased level of anxiety and fear which is compounding their insomnia symptoms. This issue also needs to be examined and reviewed in the literature during such a pandemic. Studies have consistently shown that difficulty initiating sleep, difficulty maintaining sleep and non-restorative sleep are associated with a risk of cardio-cerebral vascular events (He, 2017). It has been long known, in both the general population and patients with heart disease, that insomnia increases risk for MI and death (Daghlas, 2019). Short sleep duration was associated with a higher risk for stroke in a meta-analysis of 12 cohort studies and 6 cross-sectional studies (Ge, 2014). Evidence shows that hypnotics (such as zolpidem, trazodone, and benzodiazepines, among others) and cognitive behavioral therapy for Insomnia (CBT-I) improve outcomes (Li, 2014), however there are no head-to-head comparisons between both interventions in patients with heart disease suffering from insomnia (Redline, 2011; Sofi, 2014). CBT-I components include sleep restriction, stimulus control therapy, relaxation strategies, cognitive therapy, and sleep-hygiene education (Morin, 2006). Practice guidelines for the treatment of Insomnia show that CBT-I is a first-line treatment (Schutte-Rodin, 2008). Effect sizes for treatment using CBT-I are moderate to large (Edinger, 2001; Irwin, 2006; Wang, 2005) and studies have demonstrated its efficacy in the short-term and long term (Edinger, 2005; Edinger, 2001; Morin et al., 2006). Non-patients with heart disease with persistent insomnia revealed that CBT-I was similar in short term and superior in long term trials to hypnotics (Smith et al., 2002). Studies showed that patients with heart disease receiving CBT-I experienced significant improvements in insomnia symptoms (Rybarczyk, 2005; Rybarczyk, 2011; Redeker, 2017) with maintenance effects seen at one year follow-up (Rybarczyk 2011). The most recent study in 2020 showed that patients with heart disease who received CBT-I experienced an 8-point reduction in Insomnia Severity Index scores (Heenan, 2020); this change is both statistically and clinically significant (Phillips, 2007). Hypnotics include FDA-approved benzodiazepines and non-benzothiazine agents as well as off-label agents. Short/intermediate-acting benzodiazepines such as triazolam and temazepam are FDA-approved for insomnia and are generally preferred in patients with heart disease, however more cardiologists and primary care physicians tend to prescribe alprazolam and lorazepam for insomnia (Charney 2006). Prescribing trends show that benzodiazepines (BZDs; e.g., alprazolam) and non-BZD receptor agonists (e.g., zolpidem) increased from 1993 to 2010 (Kaufmann, 2016). Zolpidem, zaleplon, and eszopiclone (Z-drugs) are FDA approved for insomnia and have been shown to be effective in patients with heart disease in terms of sleep onset, total sleep time, and sleep quality (McCall, 2006). Zolpidem has been shown to improve sleep structure in patients with heart disease especially in heart failure (Gatti, 2016). There are a few trials of head-to-head comparisons between CBT-I and hypnotics for the treatment of Insomnia and none included comparing the above interventions in patients with heart disease. CBT-I may be administered online, by smartphone/tablet, and has a widely used application under a psychologist/health professional guidance, which has been shown to be as effective as in-person CBT (Reilly, 2019) but is much more feasible yet understudied in this patient population. The impact of treating insomnia in patients with heart disease on HRQoL/physical and mental health remains largely unknown. Examining and comparing the negative effects associated with insomnia such as sleep-related impairments (e.g., tiredness and trouble functioning), as well as myocardial infarctions, strokes, and mortality after treating insomnia in patients with heart disease may be particularly valuable to help identify methods to improve the care of this population.

Insomnia has serious consequences in patients with heart disease; yet it often goes untreated or inadequately treated in this population (Manolis, 2020). Despite the evidence for CBT-I, barriers to access or implementation difficulties as well as continued use of hypnotics are still widespread (Sateia, 2017). Given the prevalence and impact of insomnia in patients with heart disease, there is a need to explore the impact of treatment interventions such as CBT-I and hypnotics in patients with heart disease.

This systematic review of literature on insomnia in patients with heart disease was performed to identify areas where future studies may elaborate upon by addressing the following questions: (a) What is the impact of insomnia on quality of life, morbidity, and mortality in patients with heart disease? (b) What is the impact of treatment interventions on insomnia in patients with heart disease?

2. Methods

2.1. Search strategy

We performed this systematic review in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Moher, 2009). A systematic literature search was conducted on articles in the PubMed and

PsycINFO databases that were published within the past 50 years, from September 1973 to September 2023, after setting exclusion and inclusion criteria using the keywords: 'cardiac' OR 'cardiovascular' OR 'cardiac' AND 'disease' AND insomnia.' Two authors independently conducted a focused analysis. We also conducted a manual search of reference lists for identified papers and previous reviews of insomnia in patients with heart disease.

2.2. Study Selection Criteria and Methodology

The following inclusion criteria were used: (a) articles published in English or had a published English translation; (b) articles published in a peer reviewed journal (with all articles in PubMed being published); (c) original studies in human adults (no reviews, no animal studies, age>=18); (d) original studies of any design that focused on describing or treating insomnia in patients with heart disease; (e) studies that used at least one insomnia assessment measure. Exclusion criteria included editorials, opinion pieces, and case reports. Two authors independently conducted a focused analysis then together reached a consensus on 11 studies that were able to meet the specific selection criteria. An additional independent reviewer examined the quality of each study by identifying its strengths and limitations using the criteria adapted from Lohr and Carey by the Agency for Healthcare Research and Quality (Lohr, 1999, West 2002). The reviewer assessed sample size, patient selection methods, bias, study groups comparison, blinding, intervention details, outcome measures, and statistical analysis plans. The findings from this study quality check method eventually led to the exclusion of studies that had significant limitations. The search method is displayed in a flow diagram in Figure 1.
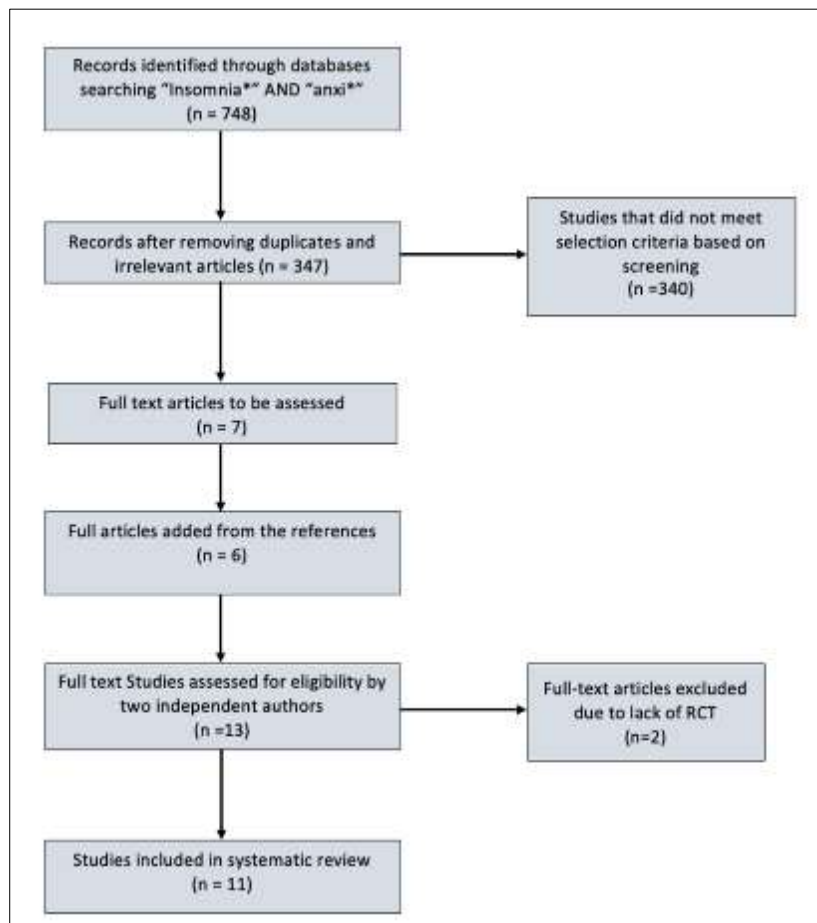

Figure 1 PRISMA flow diagram of search and study selection

2.3. Data Extraction and Yield

Key findings were derived from the full-text and table of the selected 16 studies. The study designs and findings were analyzed for quality and are detailed in the table provided.

3. Results

The findings from the reviewed studies are displayed in Table 1.

Table 1 Summary of findings from reviewed studies on insomnia in heart disease

	Author, Year, Location	Type of Study	Population and setting	Sample Size	Intervention /study group, frequency, and duration	Comparator / study group 2, frequency, and duration	Insomnia Primary Outcome? (If not, what is)	instrument used	Findings and significance	QUALITY CHECK
1.	Ryu, 2012, South Korea	Randomized clinical trial (RCT)	Diagnosis of CAD, admittance to CCU after PTCA	N=58 (29 each group)	Earplug delivered sleep-inducing music for 52 min + eye shield. Performed once starting at 10pm and questionnaires were collected at 7am the next morning.	No music, but earplugs and eye shield	Yes	Quantity of sleeping questionnaire concerning the total number of sleeping hours The modified Verranand Synder-Halpern (VSH) sleeping scale	Participants in the experimental group reported that the sleeping quantity and quality were significantly higher than control group (t= 3.181, p= 0.002, t= 5.269, p<0.001, respectively)	Double-blind RCT, quantity and quality of sleep measured pre- and post-intervention, significance levels reported, intention-to-treat analysis, appropriate statistical analysis were reported.
2.	Suna, 2014,	Multisite RCT	Symptomatic heart failure within six	N=106	DMP + twice-weekly supervised	Disease management	Yes	Pittsburgh Sleep Quality Index (PSQI)	PSQI global score improved	Double-blind RCT, quantity

	Australia		weeks of discharge	(intervention=54, control=52)	group exercise classes of one-hour duration. Duration: 12 weeks.	program (DMP): Duration: 12 weeks		Geriatric Depression Scale (GDS) Six-minutes' walk test BMI	significantly more in the ET group than the control group (−1.5±3.7 vs 0.4±3.8, p=0.03) Improved sleep quality correlated with improved exercise capacity and reduced depressive symptoms, but not with changes in body mass index or resting heartrate.	and quality of sleep and depression measured pre- and post-intervention, significance levels reported, intention-to-treat analysis, appropriate statistical analysis were reported.
3.	Wang, 2014, China	RCT (Experimental pretest and repeated posttest design)	Stable CHD, HF NYHA class II or III; Inpatient setting;	N=128 (Morning group=32, Night group=32, Morning-night group=32, Control group=32)	Standard sleep care + Nurse-led biofeedback-assisted relaxation 20 minutes. (Once daily for morning and night groups, twice a day for	Standard sleep care (included sleep hygiene education, room temperature adjustment, and noise and light control measures)	Yes	PSQI (Chinese version) SOL (sleep onset latency) TST (total sleep time) SE (sleep efficiency) Zung Self-Rating Anxiety Scale	Compared with the control group, the nurse-led biofeedback-assisted relaxation yielded a greater benefit for patients in the 3	Double-blind RCT, quantity and quality of sleep and anxiety measured pre- and post-intervention, significance levels reported,

| | | | | | morning/night group) Duration: 6 days | | | Sleep Medication (the dosage expressed in milligrams of sleep medication) | intervention groups. There were statistical differences among the groups: patients in the night group (FSOL= 33.15, P<.001; FTST= 17.99, P<0.001; FSE= 10.26, P= 0.002; FPSQI= 27.38, P<0.001; FSAS= 54.39, P<0.001, respectively) and in the morning-night group (FSOL= 33.62, P<0.001; FTST= 34.13, P<0.001; FSE= 24.04, P<0.001; FPSQI= 31.26, P<0.001; FSAS= | intention-to-treat analysis, appropriate statistical analysis were reported. |

										73.93, P<0.001, respectively) had slightly shorter sleep latency, experienced fewer awakenings, reported higher sleep quality, and used significantly fewer sleep medications than the morning group did(F= 32.97, P<0.001)	
4	Redeker, 2015, United States	RCT		Stable HF NYHA Class I-III	N= 48 (Treatment=29, control=19)	CBT-I in 4 biweekly 1-h sessions Duration: 8 weeks	HF self-management education	Yes	The Pittsburgh Sleep Quality Index The Insomnia Severity Index (ISI) The Multidimensional Assessment of Fatigue Index (MAF) The Epworth Sleepiness Scale (ESS)	BT-I was feasible and acceptable and had a statistically significant effect on insomnia and fatigue. A moderate-large effect of CBT-I on insomnia severity (p = 0.03)	Double-blind RCT, quantity and quality of sleep as well as depression measured pre- and post-intervention, significance levels reported, effect sizes

								The Center for Epidemiological Studies Depression Scale (CESD) State anxiety scale	A moderate CBT-I effects on actigraph-recorded sleep latency (p = 0.09) and duration (p = 0.15) A large improvement in fatigue (p = 0.04) No meaningful differences in sleepiness, depression, or anxiety at follow-up	reported, intention-to-treat analysis, appropriate statistical analysis were reported.
5	Gatti, 2016, Brazil	Randomized clinical cross-over trial	Heart failure (ischemic cardiomyopathy) and NYHA class I or II. Outpatient setting. Duration:1 week	N=15	12.5 mg zolpidem, controlled release (CR) for one week then a washout period for one week then crossed over to placebo.	Placebo	Yes	The Epworth Sleepiness Scale (ESS) The Pittsburgh Sleep Quality Index (PSQI) Dyspnea scales The Modified Medical Research Council (MMRC) scale.	Zolpidem CR improved sleep structure in patients with heart failure, did not change apnea hypopnea index, but slightly decreased lowest oxygen saturation.	Randomized Cross-over trial, quantity and quality of sleep measured pre- and post-intervention, significance levels reported, appropriate statistical analysis

										A 16% increase in total sleep time with the use of zolpidem CR and an increase in stage 3 NREM sleep. The apnea hypopnea index (AHI) did not change with zolpidem CR. A slight but significant decrease was observed in lowest oxygen saturation compared with baseline and placebo conditions (83.60 ± 5.51; 84.43 ± 3.80; 80.71 ± 5.18, P = 0.002).	were reported.
6	Santos, 2018, Brazil	RCT	Heart failure, Outpatient setting	N=32 (8 in each group)	Phototherapy group (40 minutes of	General guidance regarding their heart	Yes		PSQI The Minnesota Living with	All groups experienced improved quality of	Double-blind RCT, relatively smaller

				sun exposure daily) Sleep hygiene measures (received instructions regarding habits that improve sleep) Combination of phototherapy and sleep hygiene measure. Duration: 12 weeks	disease and the use of medications prescribed by their physicians		Heart Failure Questionnaire (MLHFQ The Dutch Fatigue Scale (DUFS) The Dutch Exertion Fatigue Scale (DEFS) The Baecke Habitual Physical Activity Questionnaire Center for Epidemiological Studies – Depression (CES-D)	sleep and health-related quality of life at the end of the intervention (week 12) and at follow-up (week 24), though differences were not statistically significant (p between 0.22 and0.40).	sample size, quantity and quality of sleep as well as health-related quality of life measured pre- and post-interventio n, significance levels reported, intention-to-treat analysis, appropriat e statistical analysis were reported.
7	Ghaeli, 2018, Iran	RCT	STEMI managed with primary PCI	N=40 (Melatonin=20, oxazepam=20)	3 mg of melatonin or 10 mg of oxazepam for one week after STEMI	N/A	Yes	Groningen Sleep Quality Score (GSQS) The Hamilton Anxiety Rating Scale (HAM-A)	Both oxazepam and melatonin significantly improved sleep quality of the patients (P=0.0001 for both groups)	Double-blind RCT, quality of sleep and anxiety measured pre- and post-interventio n, significance levels reported,

| | | | | | | | | | Both melatonin and oxazepam proved to be significantly effective in lowering anxiety levels (P= 0.0001 and P= 0.0015, respectively). When the final HAM-A scores were compared between the groups, they were significantly lower in the melatonin group (P= 0.019) | intention-to-treat analysis, appropriate statistical analysis were reported. |
| 8 | Javaheri, 2019, United States | RCT | CHD | N=29 (intervention=15, control=14) | General sleep education+ Web-based cognitive behavioral therapy for insomnia (CBT-I) Duration: 6 weeks | General sleep education | Yes | ISI PHQ8 Epworth Sleepiness Score (ESS) Duke Health Profile | There was a 6.2 ± 5.3-point reduction in ISI scores in the intervention arm and a 3.3 ± 5.1 reduction in the control arm (p-value= 0.1). | Double-blind RCT, quantity and quality of sleep as well as depression measured pre- and post-intervention, significance levels |

									When comparing changes in ISI and PHQ8 between the two arms there were no statistically significant differences. There were no appreciable changes in the Duke Health profile metrics.	reported, intention-to-treat analysis, appropriate statistical analysis were reported.
9	Redeker, 2020, United States	RCT	Stable HF NYHA Class II-IV	N=51 (intervention=30 and control=21)	Four one-hour of bi-weekly group-based CBT-I Duration: 8 weeks	Heart failure self-management education	Yes	PSQI ISI Respironics Minimitter Actiwatch AW-64 The Multi-dimensional Assessment of Fatigue Index The Epworth Sleepiness Scale The Center for Epidemiological Studies Depression Scale	CBT-I had no effects on the biomarkers, but there were statistically significant negative cross-sectional correlations between the ratio of day/night urinary free cortisol and sleep disturbance, anxiety,	Double-blind RCT, quantity and quality of sleep, depression, pain, urine biomarkers, were measured pre- and post-intervention, significance levels reported, intention-to-treat analysis,

								Medical Outcomes Study SF-36v2 Physical Function Scale TheSF36v2 Bodily Pain scale. Dysfunctional Beliefs and Attitudes about Sleep Scale The Sleep Disturbance Questionnaire Urinary norepinephrine, epinephrine, cortisol, melatonin sulfate, and creatinine	fatigue, depression, and negative sleep cognitions.	appropriate statistical analysis were reported.
10	Siebmanns, 2021, Sweden	RCT	CVD	N=48 (24 each)	Nurse-led internet based CBT-I. Duration: 9 weeks	Internet-based self-study program Duration: 9 weeks	Yes	ISI Short Form Health Survey (SF-12) for quality of life Adherence to CBT-I.	The analysis of ISI showed a moderate, significant treatment effect of the CBT-I compared to the control group (−2.9 between-group mean difference, 95% CI −4.9 to −0.9,	Double-blind RCT, quantity and quality of sleep as well as health-related quality of life measured pre- and post-intervention, significance levels

| | | | | | | | | | p=0.004) at 9weeks

The improvement in ISI score in the I-CBTI group at the post-treatment follow-up was maintained at the 6-month follow-up (11.64 vs. 11.03, p=0.943). However, the between-group effect at 6months was not significant.

The mean score for SF-12 PCS improved in the I-CBTI group (40.46 at baseline versus 44.52 at the 6-month follow-up) and control group | reported, intention-to-treat analysis, appropriate statistical analysis were reported. |

								(39.71 at baseline vs. 40.44 at the 6-month follow-up), but between-group difference did not differ significantly (3.5 between-group mean difference, 95% CI −1.2 to 8.2, p=0.137) The adherent group showed a significant decrease in median ISI score from baseline to post-treatment (9weeks) (15 vs. 9, z=−3.082, p=0.002) but this was not found in the nonadherent group (15.5 vs. 16,	

									z=−0.577, p=0.564)	
11	Redeker, 2022, United States	RCT	Stable CHF NYHA class II or III	N=175 (intervention=91, control=84)	HF self-management education + Bi-weekly CBT-I Duration: 8 weeks	HF self-management education	Yes	ISI PSQI PROMIS Sleep questionnaire to evaluate sleep quality. The Sleep Disturbance Questionnaire (SDQ) Wrist actigraphy (Respironics Minimitter Actiwatch-2 or Actiwatch Spectrum Plus) Six-Minute Walk Test	CBT-I had sustained effects on ISI (P=0.0002), PSQI (P<0.0001), PROMIS (P<0.0001), SDQ (P=0.0005)	Double-blind RCT, relatively larger sample size, quantity and quality of sleep as well as health-related quality of life measured pre- and post-intervention, significance levels reported, intention-to-treat analysis, appropriate statistical analysis were reported.

3.1. What are the most commonly utilized measures for insomnia in patients with heart disease?

Insomnia among individuals with heart disease is assessed using various measures providing comprehensive insights into its presence and impact. The most utilized sleep measures in the 11 reviewed studies, where several studies used more than one measure, include: Pittsburgh Sleep Quality Index (PSQI) in six studies, Insomnia Severity Index (ISI) in five studies, Epworth Sleepiness Score (ESS) in five studies, Sleep Disturbance Questionnaire (SDQ) in two studies, and the Multidimensional Assessment of Fatigue Index (MAF) in one study. The Pittsburgh Sleep Quality Index (PSQI) is a widely employed questionnaire that evaluates overall sleep quality and disturbances over a one-month period. It covers aspects such as sleep latency, duration, efficiency, sleep disturbances, use of sleep medication, daytime dysfunction, and subjective sleep quality (Buysse, 1989). The Insomnia Severity Index (ISI) is a widely used self-report questionnaire designed to measure the severity of insomnia symptoms and their impact on an individual's daily functioning. It is a practical tool measuring the severity and perceived distress associated with insomnia. The ISI evaluates the individual's perception of sleep difficulties, including trouble falling asleep, staying asleep, and early morning awakening. (Bastien, 2001). The Verran and Snyder-Halpern (VSH) Sleep Scale is also utilized to assess various dimensions of sleep, including quality, quantity, and disturbances. This scale provides an assessment of sleep patterns and disturbances by collecting information about sleep initiation, maintenance, and quality (Snyder-Halpern 1987). Other measures used in assessing insomnia in patients with heart disease include the Groningen Sleep Quality Score (GSQS), sleep onset latency (SOL), total sleep time (TST), sleep efficiency (SE), and the Sleep Disturbance Questionnaire (SDQ).

3.2. What are the interventions used to treat insomnia in patients with heart disease and what is the impact of each treatment intervention?

The interventions used in patients with heart disease that aim to improve sleep quality and address insomnia symptoms include various approaches such as CBT-I based interventions in five studies (Redeker, 2015; Javaheri, 2019; Redeker, 2020; Siebmanns, 2021; Redeker, 2022) medication-based interventions in two studies: zolpidem, controlled release (CR) (Gatti, 2016), and melatonin or oxazepam (Ghaeli, 2018). The remaining trials used earplug delivered sleep-inducing music and eye shields (Ryu, 2012); disease management program (DMP) and supervised group exercise classes (Suna, 2014); standard sleep care and nurse-led biofeedback-assisted relaxation (Wang, 2014); combination of a phototherapy group and sleep hygiene measures (Santos, 2018).

3.2.1. Cognitive Behavioral Therapy for Insomnia

Several studies have demonstrated the favorable impact of Cognitive Behavioral Therapy for Insomnia (CBT-I) in treating patients with heart disease. In one study, a clinical psychologist who is an expert in sleep medicine, conducted CBT-I sessions biweekly over an eight-week period. These sessions followed standard methods and included components such as sleep hygiene education. Another study implemented a six-week educational program called Go! To Sleep (GTS), which used an interactive online platform. GTS incorporated various components of CBT-I, including stimulus control, sleep restriction therapy, sleep hygiene, cognitive therapy, and relaxation therapy. Each week of the program focused on specific topics, gradually introducing participants to the science of sleep, and implementing behavior changes (Redeker, 2015; Redeker, 2018; Redeker, 2022). Furthermore, a CBT-I program structured into nine modules was implemented in another study. These modules provide knowledge about cardiac disease and its impact on daily life. Participants learned about sleep measurement, the importance of sleep, and factors affecting sleep. Cognitive aspects were also addressed, helping participants identify and manage distressing thoughts and stress related to heart disease that can affect sleep. The program concluded with an evaluation of the knowledge gained and plans for maintaining changes to improve sleep (Siebmanns, 2021).

Impact: CBT-I had a moderate to large effect on reducing insomnia severity in 29 patients diagnosed with HF, with a statistically significant p-value of 0.03. The average decrease in insomnia severity was over seven points in the CBT-I group, surpassing the six-point threshold indicative of clinical improvement and enhanced daytime functionality. The mean ISI score at the follow-up stage suggested that most patients in the CBT-I group experienced remission from insomnia. Specifically, 76% of the CBT-I group showed improvements across one or more levels of insomnia severity. This contrasts with the control group, where only 41% showed improvement (p = 0.17). The impact on self-reported sleep quality, SL, and SE were minor to moderate. CBT-I also showed moderate effects on actigraph-recorded sleep onset delay (p = 0.09) and duration (p = 0.15). A significant enhancement in fatigue was noted (p=0.04), along with a slight improvement in physical functionality, but there were no substantial differences in sleepiness, depression, or anxiety during the follow-up (Redeker, 2015). Another research effort aimed to demonstrate the impact of CBT-I on the circadian rhythm (via measuring urinary melatonin sulfate). An elevated median day/night ratio of melatonin was noted in the CBT-I group both before and after the intervention. However, CBT-I did not seem to have a noticeable impact on this biomarker (Redeker, 2018). The study aimed to assess the impact of web-based CBT-I (wCBT-I) on insomnia symptoms in patients with CHD. A total of 24 participants were randomized into two groups: one receiving wCBT-I and

general sleep education, and the other receiving general sleep education alone as a wait-list control. After a six-week intervention period, the results showed that the intervention demonstrated a notable reduction in ISI scores by 6.2 ± 5.3 points (p = 0.0005), indicating an improvement in insomnia symptoms. In the control group, there was also a reduction of 3.3 ± 5.1 points in ISI scores (p = 0.03). However, when comparing the changes in ISI between the two groups, no statistically significant differences were observed (p = 0.1). Within the treatment arm, SL decreased by 6.0 ± 8.0 minutes (p = 0.006) and SE increased by 3.2 ± 5.3% (p = 0.02). These findings suggest that wCBT-I can effectively reduce insomnia symptoms in patients with CHD and improve sleep parameters (Javaheri, 2020). In another parallel randomized controlled trial (RCT), a total of 48 patients with the diagnosis of CVD were randomly assigned to either the I-CBTI or the control group. The ISI was used to assess the perceived severity of insomnia symptoms. The nine-week I-CBTI program, consisting of nine modules with support from a registered nurse, was compared to a self-study program in the control group, which included three modules from the I-CBTI intervention without support. The intention-to-treat analysis showed a significant treatment effect of I-CBTI compared to the control group at nine weeks (-2.9 between-group mean difference, p = 0.004). The improvement in ISI score observed in the I-CBTI group was sustained at the six-month follow-up (11.64 vs. 11.03, p = 0.943). However, the between-group effect at six months was not statistically significant (-2.1 between-group mean difference, p = 0.111). These findings suggest that the treatment intervention of I-CBTI had a moderate, significant short-term impact on reducing insomnia symptoms in patients with heart disease, although the long-term effects were not statistically significant (Siebmanns, 2021). Another study examined the impact of CBT-I (Healthy Sleep: HS group) and HF self-management (Healthy Hearts: HH group), on insomnia symptoms in 175 patients with HF. The results showed statistically significant improvements in insomnia severity in intervention group at 3 months, 6 months, and 12 months compared to baseline. The HS group demonstrated a larger and sustained improvement in insomnia severity, with a decrease of more than six points on the ISI at 6 and 12 months. The percentage of participants with clinical levels of insomnia severity (ISI >15) significantly decreased in the HS group compared to the HH group. Furthermore, a greater proportion of participants in the HS group achieved remission (ISI >7) at one year compared to the HH group. The improvements in insomnia symptoms were supported by statistically significant effects on specific aspects such as difficulty falling asleep, worry/distress about sleep, and interference of sleep with daily functioning. The findings suggest that CBT-I has a more significant impact on reducing insomnia symptoms in patients with heart disease compared to HF self-management (Redeker 2022).

3.2.2. Medication therapy

Medication trials in patients with heart disease included one trial using 12.5mg zolpidem, controlled release (CR) for one week followed by a washout period for one week then crossed over to placebo (Gatti, 2016), and a second trials using 3mg of melatonin or 10mg of oxazepam for one week after STEMI (Ghaeli, 2018).

Impact: A double-blind, randomized, placebo-controlled crossover trial studied the acute effects of zolpidem CR, a non-benzodiazepine GABA-A receptor agonist, on insomnia in 15 patients with HF and reduced ejection fraction. Patients underwent baseline polysomnography, received 12.5 mg zolpidem CR or a placebo, and had their sleep assessed again with further polysomnography. The results suggested that zolpidem CR increased total sleep time (TST) and N3 non-rapid eye movement (non-REM) sleep compared to the placebo and baseline. Zolpidem CR was found to extend the TST by an average of 16% compared to placebo, with a noticeable trend towards improved sleep efficiency (P = 0.06). A significant increase in the N3 non-REM stage was observed, indicating a potential improvement in sleep patterns (p = 0.015). This could be beneficial for heart failure patients as the N3 stage is characterized by reduced cardiac demand. However, REM sleep did not significantly change with zolpidem CR use. The results indicate that zolpidem CR may positively impact sleep architecture in HF patients, presenting a potential treatment intervention for insomnia in this population (Gatti, 2016). Another clinical trial evaluated the efficacy of melatonin (3 mg) and oxazepam (10 mg) in improving sleep quality and reducing anxiety in 40 patients diagnosed with STEMI and treated with primary PCI. Patients' sleep quality was assessed using the GSQS. Both melatonin and oxazepam significantly improved sleep quality compared to baseline values (P = 0.0001 for both). The average GSQS scores demonstrated a statistically significant difference between the melatonin and oxazepam groups, with the melatonin group showing lower scores, indicating a more favorable effect of this medication on sleep quality. Consequently, melatonin could serve as a beneficial alternative for heart disease patients suffering from insomnia, especially those who have contraindications to benzodiazepines or experience significant adverse effects from these drugs (Ghaeli, 2018).

3.2.3. Earplug delivered sleep-inducing music + eye shield

This intervention involves listening to sleep-inducing music through earplugs and wearing an eye shield to promote sleep. In the experimental group, participants assigned to the intervention for treating insomnia in patients with heart disease listened to sleep-inducing music while in the Cardiac Care Unit (CCU). The music consisted of a combination of nature sounds and delta wave control music. The participants received the music through earphones from 10:00 PM to 10:53 PM. If a subject fell asleep during the music, the earphones were intentionally kept on until 5 AM the next morning

to avoid disturbing their sleep. Additionally, an eye bandage was applied at 10 PM and removed at 5 AM. Participants completed questionnaires regarding the quantity and quality of their sleep at 7 AM on the same day. This intervention aimed to promote better sleep-in patients with heart disease using specially designed sleep-inducing music and ensuring uninterrupted rest during the night (Ryu, 2012).

Impact: The study conducted on playing sleep inducing music in 29 patients admitted to the cardiac care unit (CCU) post percutaneous transluminal coronary angiography (PTCA) has shown to have a significant positive impact on both the quantity and quality of sleep ($p = 0.002$ and $p < 0.001$ respectively). This intervention addresses insomnia in this population by increasing the total sleep time, as measured in minutes from the time of falling asleep to awakening, with adjustments made for waking periods in the night. It also enhances the quality of sleep, as assessed by the modified VSH sleeping scale. These findings suggest that sleep-inducing music could be a beneficial, non-pharmacological treatment strategy for mitigating insomnia in heart disease patients, thereby potentially improving their overall health outcomes and quality of life (Ryu, 2012).

3.2.4. Disease management program + supervised group exercise

Participants received a comprehensive Disease Management Program (DMP) education on HF physiology, medications, and management, as well as information on the role of exercise in HF. Additionally they participated in twice-weekly hospital-based supervised group exercise classes for approximately one hour over the course of 12 weeks. These exercise classes were designed based on evidence-based recommendations for HF and included a warm-up period, aerobics, resistance exercises (concentric and eccentric), balance exercises, and stretching. The workouts were tailored to the capabilities of each participant and followed the FITT (frequency, intensity, time, type) guidelines for exercise prescription and progression (Suna, 2015).

Impact: A 12-week DMP with an additional structured ET program is reported to have a substantial positive impact on sleep quality in 54 patients diagnosed with symptomatic HF. Using the PSQI, participants in the intervention group showed significantly improved global sleep quality, notably in components related to sleep quality and sleep disturbances ($p=0.03$). Although the mean difference in PSQI scores between the groups was less than the minimal clinically significant difference (three points), categorial analysis revealed that those in the intervention group were more likely to experience a clinically meaningful improvement and less likely to experience a notable deterioration in sleep quality ($p=0.016$). Notably, the greater improvement in sleep disturbances was largely driven by reduced difficulty in breathing at night. The study also identified a correlation between improvements in global sleep quality and improvements in both geriatric depression score ($p<0.001$) and exercise performance ($p=0.04$), implying a potential interconnected influence. Therefore, the introduction of a structured exercise program as part of a DMP can improve sleep quality, reduce sleep disturbances, and thus may be a potent strategy to address insomnia in HF patients (Suna, 2015).

3.2.5. Standard sleep care + Nurse-led biofeedback-assisted relaxation

Standard sleep care consists of sleep hygiene, adjusting room temperature, and implementing measures to control noise and light levels. The relaxation program utilized guided imagery and involved a voice recording from a relaxation audio book. The program was stored on a mini-MP3 player and featured a soothing female voice accompanied by soft background music. Participants listened to the 20-minute program using earphones in their quiet rooms, which consisted of two consecutive phases. During the initial five minutes, subjects observed peripheral skin temperature displays on a biofeedback device, providing feedback on physiological activity related to sympathetic tone fluctuations. The objective was to enable participants to learn control over maladaptive stress responses by modulating their sympathetic tone using the biofeedback device. Subsequently, for the following 15 minutes, subjects continued to listen to relaxation program without monitoring the temperature (Wang, 2014).

Impact: Nurse-led biofeedback-assisted relaxation training can significantly improve sleep quality for patients with stable CHD, particularly for those experiencing sleep disturbances. However, the effect of the treatment appears to be contingent upon the timing of the training sessions. The training involved listening to a guided imagery relaxation program while observing peripheral skin temperature as a measure of sympathetic tone through a biofeedback device. The training was implemented on different schedules across three intervention groups (32 patients in each group): in the morning, at night, and both in the morning and at night. Post-intervention sleep-related indicators, including SOL, TST, SE, sleep quality (measured by the PSQI), and levels of anxiety (measured by the SAS), all demonstrated statistically significant improvements in the three intervention groups ($F_{SOL} = 9.41$, $P<0.001$; $F_{TST} = 3.47$, $P = 0.017$; $F_{SE} = 5.05$, $P = 0.002$; $F_{PSQI} = 3.91$, $P = 0.009$; $F_{SAS} = 9.02$, $P<0.001$). However, the night group and the morning-night group showed greater improvements in their sleep quality than the morning group, suggesting that the timing of the intervention could impact its effectiveness ($P<0.05$) (Wang, 2014).

3.2.6. Phototherapy and sleep hygiene measures

Engaging in 40 minutes of sun exposure daily during the first half of the morning and sleep hygiene measures receiving detailed instructions on various habits that promote better sleep. These instructions included guidelines such as only going to bed when feeling sleepy, getting out of bed if not asleep within 20 minutes, incorporating relaxation activities before bedtime, maintaining a regular sleep schedule, avoiding activities like reading or watching TV in bed, refraining from consuming heavy meals close to bedtime, avoiding intense exercise within six hours before sleep, abstaining from consuming stimulating substances like coffee, tea, or alcohol within four to six hours before bedtime, and refraining from smoking for at least four to six hours before sleep. These sleep hygiene measures aimed to optimize participants' sleep habits and create an environment conducive to better sleep quality (Santos, 2018).

Impact: A study implemented non-pharmacological treatment options for 32 individuals with HF, dividing them into four groups: control group, phototherapy group (PT), a sleep hygiene measures group (SHM), and a combined phototherapy and sleep hygiene group (PT+SHM). The control group received general advice about heart disease and medication use, while the PT group was instructed to have daily sun exposure. The SHM group received guidance about practices that enhance sleep quality, and the PT+SHM group received instructions from both the phototherapy and sleep hygiene protocols. Sleep quality and health-related quality of life were evaluated as primary outcomes at baseline, 4, 8, 12, and 24 weeks using the PSQI. Most individuals experienced improved sleep in the 4th week of therapy in all groups. All intervention groups showed improved sleep quality and health-related quality of life at the end of the 12-week intervention period and at the 24-week follow-up, though differences between the groups were not statistically significant, indicating that all interventions had a positive impact on insomnia in HF patients (Santos, 2018).

4. Discussion

Cognitive Behavioral Therapy for Insomnia (CBT-I) demonstrated effectiveness in reducing insomnia severity and fatigue. A nurse-led CBT-I showed a significant treatment effect compared to the control group. Web-based CBT-I, when combined with general sleep education, resulted in improved insomnia severity scores. CBT-I combined with heart failure self-management had sustained effects on insomnia severity, sleep quality, health-related quality of life, and sleep disturbance. Zolpidem CR improved sleep structure and increased total sleep time in heart failure patients. Phototherapy combined with sleep hygiene measures led to improved sleep quality and health-related quality of life. Both melatonin and oxazepam were effective in improving sleep quality and reducing anxiety levels. The use of earplugs and sleep-inducing music resulted in significantly higher sleep quantity and quality compared to a control group. Participants involved in a Disease Management Program showed a significant improvement in their sleep quality compared to the control group. Nurse-led biofeedback-assisted relaxation yielded greater benefits for patients in the intervention groups compared to the control group.

In summary, various interventions showed positive treatment effects on insomnia and related outcomes in patients with heart disease, although the specific results varied across the studies.

This systematic review of randomized clinical trials investigating interventions for insomnia in patients with heart disease provides valuable insight into the management of sleep-related issues in this population. These findings shed light on several key aspects that can help enhance our understanding and inform clinical practice.

The utilization of standardized measures, such as the PSQI, ISI, ESS, SDQ, and MAF, across the studies ensures consistent and reliable assessment of sleep quality, insomnia severity, daytime sleepiness, sleep disturbances, and fatigue levels. These measures are essential tools for evaluating the effectiveness of interventions and monitoring changes in sleep-related outcomes.

CBT-I emerged as a prominent intervention in the reviewed studies, demonstrating positive effects on various sleep-related outcomes. The findings support the use of CBT-I as an effective non-pharmacological approach for managing insomnia in patients with heart disease. Its inclusion in clinical practice guidelines and routine care for this population may lead to improved sleep quality and overall well-being.

While non-pharmacological approaches were the primary focus in most studies, medication-based interventions, such as zolpidem controlled-release, melatonin, and oxazepam, showed promising results in improving sleep outcomes. These findings suggest that carefully selected medications may have a role in the management of insomnia in patients with heart disease, particularly when integrated with a comprehensive treatment approach.

5. Conclusions and future directions

Combining different interventions, such as CBT-I with disease management or self-management programs, demonstrated sustained improvements in sleep-related metrics. This highlights the potential benefits of a multimodal treatment approach that addresses various aspects of sleep hygiene, behavioral modifications, and self-management strategies in patients with heart disease and insomnia.

While the reviewed studies provide valuable insight, several areas warrant further investigation. Future research should explore the long-term effects of interventions, optimal dosing and duration, and potential synergistic effects of combining different interventions. Additionally, the relationship between sleep and physiological markers in patients with heart disease requires further exploration to better understand the underlying mechanisms and potential treatment targets.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

[1]   Bankier B, Januzzi JL, Littman AB. The high prevalence of multiple psychiatric disorders in stable outpatients with coronary heart disease. Psychosom Med 2004;66:645-50.

[2]   Taylor DJ, Mallory LJ, Lichstein KL, Durrence HH, Riedel BW, Bush AJ. Comorbidity of chronic insomnia with medical problems. Sleep 2007;30:213-8.

[3]   Bastien CH, Vallières A, Morin CM. Validation of the Insomnia Severity Index as an outcome measure for insomnia research. Sleep medicine. 2001;2(4):297-307.

[4]   Budhiraja R, Roth T, Hudgel DW, Budhiraja P, Drake CL. Prevalence and polysomnographic correlates of insomnia comorbid with medical disorders. Sleep2011;34:859-67.

[5]   Buysse DJ, Reynolds III CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry research. 1989;28(2):193-213.

[6]   Cappuccio FP, Cooper D, D'Elia L, Strazzullo P, Miller MA. Sleep duration predicts cardiovascular outcomes: a systematic review and meta-analysis of prospective studies. Eur Heart J 2011;32:1484-92.

[7]   Charney DSMS, Harris RA. Hypnotics and sedatives. In: Brunton LL, Lazo JS, Parker KL (eds) Goodman and Gilman's the pharmacological basis of therapeutics. McGraw-Hill, Inc, New York, NY, pp 401–427, 2006.

[8]   Daghlas I, Dashti HS, Lane J, Aragam KG, Rutter MK, Saxena R, Vetter C. Sleep Duration and Myocardial Infarction. J Am Coll Cardiol. 2019 Sep 10;74(10):1304-1314.

[9]   Edinger, JD, Means, MK. Cognitive-behavioral therapy for primary insomnia. Clinical Psychology Review, 2005;25(5), 539–558.

[10]   Edinger, JD Wohlgemuth WK, Radtke RA, Marsh GR, Quillian, RE. Cognitive behavioral therapy for treatment of chronic primary insomnia: A randomized controlled trial. JAMA, 2001;285(14), 1856–1864.

[11]   Gatti RC, Burke PR, Otuyama LJ, Almeida DR, Tufik S, Poyares D. Effects of zolpidem CR on sleep and nocturnal ventilation in patients with heart failure. Sleep. 2016;39(8):1501-5.

[12]   Ge B, Guo X. Short and long sleep durations are both associated with increased risk of stroke: a meta-analysis of observational studies. Int J Stroke. 2015 Feb;10(2):177-84.

[13]   Ghaeli P, Solduzian M, Vejdani S, Talasaz AH. Comparison of the effects of melatonin and oxazepam on anxiety levels and sleep quality in patients with ST-segment-elevation myocardial infarction following primary percutaneous coronary intervention: a randomized clinical trial. Annals of Pharmacotherapy. 2018;52(10):949-55.

[14]   He Q, Zhang P, Li G, Dai H, Shi J. The association between insomnia symptoms and risk of cardio-cerebral vascular events: A meta-analysis of prospective cohort studies. Eur J Prev Cardiol. 2017 Jul;24(10):1071-1082.

[15] Heenan A, Pipe A, Lemay K, Davidson JR, Tulloch H. Cognitive-Behavioral Therapy for Insomnia Tailored to Patients with Cardiovascular Disease: A Pre-Post Study. Behav Sleep Med. 2020 May-Jun;18(3):372-385.

[16] Irwin, MR, Cole, JC, Nicassio, PM. Comparative meta-analysis of behavioral interventions for insomnia and their efficacy in middle-aged adults and in older adults 55+ years of age. Health Psychology, 2006;25(1), 3–14.

[17] IsHak WW, Bagot K, Thomas S, Magakian N, Bedwani D, Larson D, Brownstein A, Zaky C. Quality of life in patients suffering from insomnia. Innov Clin Neurosci. 2012 Oct;9(10):13-26.

[18] Javaheri S, Reid M, Drerup M, Mehra R, Redline S. Reducing coronary heart disease risk through treatment of insomnia using web-based cognitive behavioral therapy for insomnia: a methodological approach. Behavioral sleep medicine. 2020;18(3):334-44.

[19] Kaufmann CN, Spira AP, Alexander GC, Rutkow L, Mojtabai R. Trends in prescribing of sedative-hypnotic medications in the USA: 1993-2010. Pharmacoepidemiol Drug Saf. 2016 Jun;25(6):637-45.

[20] Li M, Zhang XW, Hou WS, Tang ZY. Insomnia and risk of cardiovascular disease: a meta-analysis of cohort studies. Int J Cardiol 2014;176:1044-7.

[21] Lohr K, Carey T. Assessing "best evidence": issues in grading the quality of studies for systematic reviews. The Joint Commission Journal on Quality Improvement. 1999;25(9):470-9.

[22] Manolis TA, Manolis AA, Apostolopoulos EJ, Melita H, Manolis AS. Cardiovascular Complications of Sleep Disorders: A Better Night's Sleep for a Healthier Heart / From Bench to Bedside. Curr Vasc Pharmacol. 2021;19(2):210-232.

[23] McCall WV, Erman M, Krystal AD. A polysomnography study of eszopiclone in elderly patients with insomnia. Curr Med Res Opin 2006;22(9):1633–1642.

[24] Moher D, Liberati A, Tetzlaff J, Altman D, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Medicine. 2009;6(7):1-6.

[25] Morin CM, Belleville G, Bélanger L, Ivers H. The Insomnia Severity Index: psychometric indicators to detect insomnia cases and evaluate treatment response. Sleep. 2011 May 1;34(5):601-8.

[26] Norra C, Kummer J, Boecker M, Skobel E, Schauerte P, Wirtz M, Gauggel S, Forkmann T. Poor sleep quality is associated with depressive symptoms in patients with heart disease. Int J Behav Med. 2012 Dec;19(4):526-34. doi:10.1007/s12529-011-9205-2. PubMed PMID: 22125117.

[27] Phillips B, Mannino, DM. Do insomnia complaints cause hypertension or cardiovascular disease? Journal of Clinical Sleep Medicine. 2007;3(5), 489–494.

[28] Redeker NS, Conley S, Anderson G, Cline J, Andrews L, Mohsenin V, et al. Effects of cognitive behavioral therapy for insomnia on sleep, symptoms, stress, and autonomic function among patients with heart failure. Behavioral sleep medicine. 2018.

[29] Redeker NS, Jeon S, Andrews L, Cline J, Jacoby D, Mohsenin V. Feasibility and efficacy of a self-management intervention for insomnia in stable heart failure. Journal of Clinical Sleep Medicine. 2015;11(10):1109-19.

[30] Redeker NS, Yaggi HK, Jacoby D, Hollenbeak CS, Breazeale S, Conley S, et al. Cognitive behavioral therapy for insomnia has sustained effects on insomnia, fatigue, and function among people with chronic heart failure and insomnia: the HeartSleep Study. Sleep. 2022;45(1):zsab252.

[31] Redline S, Foody J. Sleep disturbances: time to join the top 10 potentially modifiable cardiovascular risk factors? Circulation 2011;124:2049-51.

[32] Rybarczyk B, Mack L, Harris JH, Stepanski, E. Testing two types of self-help CBT-I for insomnia in older adults with arthritis or coronary artery disease. Rehabilitation Psychology, 2011;56(4), 257–266.

[33] Rybarczyk B, Stepanski E, Fogg L, Lopez M, Barry P, Davis A. A placebo-controlled test of cognitive-behavioral therapy for comorbid insomnia in older adults. J Consult Clin Psychol, 2005;73(6), 1164–1174. 006X.73.6.1164

[34] Reilly ED, Robinson SA, Petrakis BA, Kuhn E, Pigeon WR, Wiener RS, McInnes DK, Quigley KS. Mobile App Use for Insomnia Self-Management: Pilot Findings on Sleep Outcomes in Veterans. Interact J Med Res. 2019 Jul 24;8(3):e12408. doi:10.2196/12408.

[35] Ryu MJ, Park JS, Park H. Effect of sleep-inducing music on sleep in persons with percutaneous transluminal coronary angiography in the cardiac care unit. Journal of clinical nursing. 2012;21(5-6):728-35.

[36]   Sateia MJ, Buysse DJ, Krystal AD, Neubauer DN, Heald JL. Clinical practice guideline for the pharmacologic treatment of chronic insomnia in adults: an American Academy of Sleep Medicine clinical practice guideline. J Clin Sleep Med. 2017;13(2):307–349.

[37]   Santos MAD, Conceição APD, Ferretti-Rebustini REL, Ciol MA, Heithkemper MM, Cruz DALMD. Non-pharmacological interventions for sleep and quality of life: a randomized pilot study. Rev Lat Am Enfermagem. 2018 Nov 14;26:e3079.

[38]   Schutte-Rodin S, Broch L, Buysse D, Dorsey C, Sateia M. Clinical guideline for the evaluation and management of chronic insomnia in adults. Journal of Clinical Sleep Medicine, 2008;4(5), 487–504.

[39]   Siebmanns S, Johansson P, Ulander M, Johansson L, Andersson G, Broström A. The effect of nurse-led Internet-based cognitive behavioural therapy for insomnia on patients with cardiovascular disease: A randomized controlled trial with 6-month follow-up. Nursing Open. 2021;8(4):1755-68.

[40]   Sofi F, Cesari F, Casini A, Macchi C, Abbate R, Gensini GF. Insomnia and risk of cardiovascular disease: a meta-analysis. Eur J Prev Cardiol 2014;21:57-64.

[41]   Smith   MT, Perlis ML, Park A, Smith MS, Pennington J, Giles DE,   Buysse DJ. Comparative   meta-analysis   of pharmacotherapy   and   behavior   therapy   for   persistent   insomnia. American   Journal   of   Psychiatry, 2002;159(1), 5–11.

[42]   Snyder-Halpern R, Verran JA. Instrumentation to describe subjective sleep characteristics in healthy subjects. Research in nursing & health. 1987;10(3):155-63.

[43]   Suna JM, Mudge A, Stewart I, Marquart L, O'Rourke P, Scott A. The effect of a supervised exercise training programme on sleep quality in recently discharged heart failure patients. European Journal of Cardiovascular Nursing. 2015;14(3):198-205.

[44]   Wang L-N, Tao H, Zhao Y, Zhou Y-Q, Jiang X-R. Optimal timing for initiation of biofeedback-assisted relaxation training in hospitalized coronary heart disease patients with sleep disturbances. Journal of Cardiovascular Nursing. 2014;29(4):367-76.

[45]   West S, King V, Carey T, McKoy K, Sutton S, Lux L. Systems to Rate the Strength Of Scientific Evidence. Agency for Healthcare Research and Quality; 2002. Report No.: 02-E016.