



# Impact of Melatonin Supplementation on Heart Failure Patients: A Systematic Review of Randomized Controlled Trials

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## ABSTRACT

**Introduction:** Heart failure is characterized by the inability of heart to pump blood effectively, resulting in high mortality rates and physiological strain. Recent research has indicated that melatonin, produced by the pineal gland to regulate the sleep-wake cycle, shows promise in improving cardiovascular health. Its antioxidants and ability to enhance mitochondrial function could be valuable in treating heart failure. This systematic review sought to investigate the effects of melatonin supplementation on outcomes in heart failure patients through randomized controlled trials (RCTs).

**Search Strategy:** This study followed PRISMA guidelines and Cochrane systematic review principles. Scholarly databases, including PubMed, Scopus, and Web of Science, were searched without time limitations. Additionally, grey literature was explored using the Google Scholar search engine. Keywords such as "Heart Failure" and "Melatonin" and their synonyms were used. Inclusion criteria encompassed RCTs focusing on evaluating the effect of melatonin supplementation on patients with heart failure compared to control groups. Exclusion criteria included review articles, observational and quasi-experimental studies, letters to editors, and articles lacking primary data or clear method descriptions. Two authors independently performed screening and data extraction, and any disagreements were resolved through consensus involving a third author. The ROB2 critical appraisal tool was used to assess the quality of the included articles, and the final data were presented in an extraction table.

**Results:** A total of 582 articles were initially identified, with 144 duplicates and 362 irrelevant titles and abstracts removed. A full-text assessment was conducted on 73 articles, including three RCTs in the study. Significant differences between intervention and control groups were observed in several key outcomes, including enhanced quality of life (n = 2), improved fatigue status and appetite (n = 1), decreased delirium (n = 1), decreased hospitalization expenses (n = 2), reduced hospitalization time (n = 1), improved sleep after surgery (n = 1), improved nutritional status (n = 1), lowered serum levels of NT-proBNP (n = 1), improved left ventricular ejection fraction (n = 1), and improved mortality rate (n = 2). Additionally, the New York Heart Association class improved in one study, showing an increasing functional class of patients.

**Conclusion and Discussion:** The use of melatonin in patients with heart failure appears to be a promising approach to improving their condition. However, the effectiveness of these interventions varies, highlighting the importance of tailored approaches.

### Citation:

Sayar A, Iraj A, Movagharnia E, Manookian A. Impact of Melatonin Supplementation on Heart Failure Patients: A Systematic Review of Randomized Controlled Trials. *Iranian biomedical journal. Supplementary* (12-2024): 387.

**Keywords:** Heart failure, Melatonin, Systematic review

