

# HEART FAILURE

Heart failure (HF) contributed to 1 in 8 of adult deaths in the United States in 2017. About 6.5 million American adults have been diagnosed with heart failure, which is a challenge to treat.

How do we best work with this difficult diagnosis? Regardless of where people are in terms of heart failure's progression, we want to build care around their Mission, Aspiration, and Purpose (MAP), truly engaging them in their care and developing a multifaceted Personal Health Plan (PHP).

While we want to optimally support Veterans wherever they may be with this diagnosis, the optimal—though not always possible—way is to prevent its development in the first place. Lifestyle and dietary measures promoting heart health are ideally woven in to a person's life before any problems even arise. This Whole Health tool explores how aspects of self-care such as Food and Drink, Power of the Mind, Moving the Body, Recharge, and other factors have an influence.

Professional care is also fundamental. Careful lifelong surveillance for and active treatment of hypertension, diabetes, obesity, and coronary artery disease (CAD) is essential. complementary and integrative health (CIH) approaches can play an important role as well. This clinical tool will briefly review conventional approaches to HF and then provide an overview of some of the most recent research surrounding self-care and CIH approaches that are helpful for clinicians to know.

## CONVENTIONAL MEDICINE WISDOM

Heart failure (HF) results when the heart's structure or function make it unable to fill with blood or eject blood as effectively as it normally would. People with heart failure have fluid retention (edema), shortness of breath, and fatigue, all of which may worsen over time. [1] Conventional medical therapy represents the centerpiece of treatment for people with symptomatic heart failure, with CIH approaches (discussed below) playing an adjunctive role. General treatment goals include:[2]

- Preventing progressive cardiovascular deterioration
- Minimizing symptoms and enhancing quality of life
- Increasing survival

Physiologic aims of treatment in the setting of significant left ventricular dysfunction (left ventricular ejection fraction [LVEF] less than 45%) are:

- Reducing preload and afterload
- Maintaining stable left ventricular function
- Limiting activation of the renin-angiotensin-aldosterone system
- Inhibiting release of neurohormonal factors

Pharmacotherapy is the mainstay for achieving these goals.[3] It is built around the use of beta blockers, angiotensin converting enzyme (ACE) inhibitors, angiotensin-2 receptor blockers (ARBs), and diuretics, among others. Digoxin and other digitalis glycosides are no longer used based on findings that they increased mortality.[4]

All of these considerations are valuable, *and* what else might be considered to augment prevention and management?

## **SELF-CARE**

This section highlights the importance of self-care approaches when it comes to preventing heart failure.[5,6] There are many options, and they are likely to be most effective when used in tandem.[7] The “[Heart Health](#)” Whole Health overview has a number of additional suggestions that are also relevant.”

## **SURROUNDINGS**

Trying to maintain good air quality is important with heart failure, just as it is for many cardiac concerns. Air pollution is linked to HF hospitalizations and mortality.[8]

In a preliminary study, repeated sauna treatment was shown to improve cardiac and endothelial function, as well as exercise tolerance in patients with HF. A recent meta-analysis concluded that the infrared sauna bath is associated with short-term improvements in cardiac function;[9] more research is needed regarding Finnish saunas, which have been found helpful for heart health in general.[10]

More information about surroundings for heart health in general (which should be applicable for people with HF) can be found in the Whole Health “[Heart Health](#)” overview.

## **PERSONAL DEVELOPMENT**

Personal Development includes anything that might help to foster personal growth. Patients with HF can potentially benefit from considering how elements like volunteerism, optimism, financial well-being, creativity, education, and employment fit into their Whole Health care. For more information, refer to the “Personal Development” chapter in the [Passport to Whole Health](#) and the “[Personal Development](#)” overview in the Whole Health Library.

## **FOOD & DRINK**

A 2018 review looked at research focused on the Mediterranean, DASH (Dietary Approaches to Stop Hypertension), Paleolithic, and vegetarian diets for HF prevention and treatment.[11] Based on available evidence, researchers concluded that the Mediterranean and DASH diets are likely to have a protective effect on incidence and the worsening of function. Another review done the same year found that low-protein and low-carb diets also show promise in terms of functional capacity, noting that more studies are needed.[12]

In the MEDIT-AHF Study, the Mediterranean Diet did not affect long-term mortality after an episode of acute heart failure, but it was linked to lower rates of rehospitalization.[13]

People with heart failure have active catabolism, and they process adenosine triphosphate (ATP) and micronutrients rapidly. There have been calls to explore how combinations of various nutrients, including L-carnitine, taurine, thiamine, and coenzyme Q-10, can have potential benefits.[14] The role of decreasing some dietary components has also been on the research radar; for example, a 2018 review concluded that evidence remains inconclusive regarding reducing sodium intake for people with HF.[15]

The effect the microbiome—the organisms that live in the gut—has on heart failure is another area of active study. Several newly discovered pathways have been linked to the production of compounds that can influence its development and progression.[16]

Of course, as with all cardiovascular concerns, tobacco cessation and judicious consumption of alcohol should also be given consideration. Review the Whole Health [“DASH Diet”](#) tool.

## **RECHARGE**

As for anyone with any chronic condition (and, really, everyone), getting good sleep is vital, especially for those with HF.[17] People with HF have a high likelihood of sleep problems. A 2016 study of 1,011 people with HF found that half of them had a diagnosis of insomnia; those who did were found, during a mean follow up period of 801 days, to have significantly more coronary events.[18] In fact, insomnia was an independent predictor of them. Managing sleep-disordered breathing (e.g., due to sleep apnea) can also decrease the progression/severity of heart failure.[19] HF can be associated with changes in a person’s overall energy level; explore how they can optimize using—and recharging—their reserves.

## **FAMILY, FRIENDS, & CO-WORKERS**

As with other chronic health concerns, social connections play an important role for people with HF in maintaining health and well-being. It seems to have a positive relationship on heart-failure self-care behaviors, and it is linked to a better likelihood that people will be able to follow through with their treatment plans.[20] Heart failure can limit connections with others; keep this in mind when developing PHPs. Cardiac rehabilitation programs can be an important opportunity for Veterans to connect with each other, as can shared medical appointments or various well-being classes. Telemedicine can be a powerful tool for helping Veterans avoid social isolation.[21]

## **SPIRIT & SOUL**

As is noted in the [“Spirit & Soul”](#) Whole Health overview, regular participation in spiritual practices may help promote optimal overall health. Of course, once HF is present, many patients struggle with their spirituality, adding to an already stressful situation.

Appropriate attention to the spiritual needs of a person with HF may help them with coping, as well as finding peace with their circumstances.[22]

## **POWER OF THE MIND**

Attention to mood can be of critical importance, as negative emotional states may induce autonomic imbalance by promoting sympathetic overdrive and parasympathetic withdrawal. People with heart failure commonly have depression and anxiety, which are linked to poorer physical outcomes.[23] Depression is an independent risk factor for HF as well. Screening for these concerns, in and of itself, is important to keep in mind. The Whole Health “[Depression](#)” overview contains additional information. Psychosocial stress in general also plays an important role.

A 2018 review identified 24 trials focused on “Mind-Body Interventions” and their effects on HF. The conclusion was that several of these demonstrate “small-to-moderate positive effects” on subjective and objective outcomes.[24] The selected studies included 7 focused on tai chi and 4 on yoga (briefly discussed in the Moving the Body section in this tool) as well as relaxation, meditation, biofeedback, and stress management. Pilates, acupuncture, and reflexology—though not commonly considered mind-body interventions by many—were also featured. Another 2016 review concluded that cognitive behavioral approaches (it included relaxation, Guided Imagery, and meditation in this group) show promise for HF, and more studies will be helpful.[25] Specifically, the studies noted that symptom-related quality of life improved with meditation and Guided Imagery.

Breathing exercises have been found to improve exercise, functional performance, and various physiologic measures related to heart failure and can be considered.[19] To learn more about this option, check out the “[Breathing](#)” Whole Health tool. A small inpatient study found that brief Cognitive Therapy (CT) by nurses could improve short-term event-free survival.[26]

## **MOVING THE BODY**

Regular aerobic exercise helps prevent HF, and it is helpful for people who already have HF as well.[27] A 2019 Cochrane review found no link between exercise-based cardiac rehabilitation and short-term mortality; however, it did note improvements in numbers of hospital admissions and health-related quality of life.[28] Specifically, inspiratory muscle training has been found helpful.[29] Having HF is not in and of itself a contraindication to participation in fitness activities. Regular exercise also improves depressive symptoms in people with HF, as it does in most people.

Tai chi has been shown to improve quality of life and mood in patients with HF.[30,31] In terms of yoga, a recent review found that there are not yet enough studies to allow firm conclusions to be drawn.[32]

## PROFESSIONAL CARE: COMPLEMENTARY APPROACHES

### ACUPUNCTURE

Acupuncture has been used for heart failure in China since the times of the Han Dynasty (206 BCE to 220 CE). A 2019 review of 32 trials noted methodological flaws but also concluded that in the trials thus far, intervention groups seem to have improvements in ejection fraction, cardiac output, 6-minute walk test, and brain-type natriuretic peptide (BNP) levels.[33] A 2016 meta-analysis concluded that data on acupuncture for HF is inconclusive, noting that in one acute study, acupuncture shortened ICU stays by 2.2 days in people with acute heart failure and reduced risk of readmission, without showing an effect on mortality.[34] Another study showed an improvement in left ventricular function (ejection fraction). A paucity of data exists, but there is some suggestion of improvement in exercise capacity as well. A recent article offers a detailed review of the underlying thinking about how acupuncture might have benefits specifically for people with HF, even going into specific acupoints and reviewing study findings related to them.[35]

### DIETARY SUPPLEMENTS

**Note:** Go to [Passport to Whole Health](#), Chapter 15, “Biologically Based Approaches: Dietary Supplements” for more information about how to determine whether or not a specific supplement is appropriate for a given individual. Supplements are not regulated with the same degree of oversight as medications, and it is important that clinicians keep this in mind. Products vary greatly in terms of accuracy of labeling, presence of adulterants, and the legitimacy of claims made by the manufacturer.

With the exception of omega-3 fatty acids, the supplements listed below are not part of the VA formulary, but it is likely that people will ask clinicians about them. Research surrounding HF supplements continues and many of them show promise.[36] A 2020 review found that the best evidence of benefit was for omega-3 fatty acids, with a trend toward benefit for coenzyme Q10.[37] A position paper released in 2020 by the International Lipid Expert Panel noted that intake of hawthorn, CoQ10, l-carnitine, d-ribose, carnosine, vitamin D, probiotic, omega-3s, and beet nitrates “might be associated with improvements in self-perceived quality of life and/or functional parameters...with minimal or no side effects.”[38] The benefits seem to be most helpful in earlier stages of heart failure. At this point, the authors agreed that supplements for HF are best considered as adjunctive approaches to evidence-based pharmacological management, noting that overall, their safety profiles are quite reassuring, according to recent reviews.

### OMEGA-3 POLYUNSATURATED FATTY ACIDS

Omega-3s may favorably affect structure and function of mitochondrial membranes.[39] Studies following people with chronic HF for up to nearly 4 years (and the main one was the GISSI-HF trial) found that 1 gm of omega-3s daily (which requires taking a few grams of fish oil to get that amount) was linked to significantly reduced time to death and time to

hospitalization.[40] The quality of the reviews was rated as moderate, and the strength of evidence supporting the use of omega-3 supplements was rated as weak.[37]

## **COENZYME Q10**

Coenzyme Q10 (CoQ10), also known as ubiquinone, is a naturally occurring, vitaminlike substance present in small amounts in most diets. It is produced within the body from tyrosine, partially through a common pathway shared with cholesterol synthesis. CoQ10 is found in most cellular membranes, but its highest concentrations are within the mitochondrial membranes of organs that have significant energy requirements, especially the heart.[41] It is involved in the electron transport chain (supporting the creation of ATP), and it is also a potent antioxidant. It inhibits LDL oxidation. It also seems to improve endothelial function, where it is intricately involved with the electron transport chain and energy production. Plasma and myocardial CoQ10 concentrations are lower in people with HF and associated with increasing severity of symptoms.[42]

Over the years, many trials of CoQ10 in the setting of HF have been published, but most have been of variable quality. However, the findings of the 2014 Q-SYMBIO randomized controlled trial, demonstrated that CoQ10 has multiple benefits for people with HF.[43] This two-year prospective trial, which involved 420 people, found that just 15% in the CoQ10 group had adverse CV events, as compared to 26% of those in the placebo group. Cardiovascular mortality, all-cause mortality, and hospital stays were all significantly reduced, and NYHA class improved for the CoQ10 group as well.

The optimum CoQ10 dosage for HF is still undetermined, but most practitioners initially prescribe 100 to 300 mg daily.[41] Caution is advised for those taking anticoagulation therapy because of possible procoagulant activity, likely as a result of CoQ10's structural similarity to vitamin K. Patients taking statins may benefit from CoQ10 supplementation, particularly in terms of statin-related muscle pain.

## **HAWTHORN (CRATAEGUS SP.)**

Hawthorn leaves and flowers are used to make a slow-acting cardiac tonic that has long been favored in Europe. Hawthorn's active constituents include flavonoids and oligomeric proanthocyanidins, which seem to have anti-inflammatory, antioxidant, anti-arrhythmic coronary vasodilator, and inotropic effects.[44] It seems to protect the myocardium from ischemic damage, reperfusion injury, and hypertension-related damage while improving function of the inner walls of the arteries and synthesis of nitric oxide.[45] Hawthorn possesses slight hypotensive activity and may offer some ACE-inhibition.[46]

Older data reported both subjective and objective improvement in patients with mild forms of heart failure (New York Heart Association [NYHA] classes I and II), but many of these studies were completed before the advent of pharmacotherapy now considered a standard part of HF management, such as ACE inhibitors and beta blockers.[44] Studies done in 2009-2010 questioned hawthorn's safety and efficacy.[5]



In terms of recent reviews, it seems that review findings vary. A 2020 Australian review concluded that there is “insufficient evidence to recommend.”[37] In contrast a slightly earlier review noted that it does have benefit for NYHA class II or III heart failure. That review concluded that hawthorn “...increases functional capacity, alleviates disabling symptoms, and improves health-related quality of life...” with a favorable benefit-risk assessment.[44] Another recent review also supported its multiple cardiovascular benefits.[46]

Hawthorn is usually standardized to its content of flavonoids (2.2%) or oligomeric proanthocyanidins (18.75%). The recommended daily dosage ranges from 160-1800 milligrams daily, but it appears to be more effective at daily doses ranging from 600-1800 milligrams. Side effects are mild and include mild rash, headaches, dizziness, GI symptoms, and sweating.[38,44]

## **L-CARNITINE**

Levocarnitine (commonly known as L-carnitine) acts as a specific carrier of fatty acids required for energy production.[47] Myocardial carnitine is most highly concentrated within the left ventricle, and levels are low in patients with HF. L-carnitine may improve muscle metabolism, ventricular performance and exercise tolerance; it prevents ventricular fibrosis and HF in people with hypertensive heart disease.[48] L-carnitine has been reported to cause an unpleasant body odor in extremely high doses. When used, the effective dosage is 1-3 gm daily (the optimal dose after a heart attack is 3 gm daily).[48]

## **ADDITIONAL SUPPLEMENTS TO BE AWARE OF**

- Levo-carnosine. L-carnosine has shown, in preliminary studies, to benefit exercise performance and quality of life in stable HF.[49]
- L-arginine. Abnormal transport of this essential amino acid contributes to HF.[50] It possesses vasodilatory effects and seems to improve overall quality of life.[51] One study suggested increased mortality, and it may increase potassium levels when combined with potassium-sparing agents.[5]
- D-ribose is a possible metabolic substrate that provides additional energy to myocytes. A pilot study found that it may help some people with tissue Doppler velocity and diastolic filling speed.[52] More research is needed.
- Curcumin, most commonly used as an anti-inflammatory supplement, also shows some potential cardiovascular benefits, largely in animal and in vitro studies at this point.[53]

## **RESOURCE LINKS**

- [Heart Health](https://wholehealth.wisc.edu/overviews/heart-health/): <https://wholehealth.wisc.edu/overviews/heart-health/>
- [Passport to Whole Health](https://wholehealth.wisc.edu/wp-content/uploads/sites/414/2018/09/Passport-to-Whole-Health-3rd-Edition-2018.pdf): <https://wholehealth.wisc.edu/wp-content/uploads/sites/414/2018/09/Passport-to-Whole-Health-3rd-Edition-2018.pdf>

- [Personal Development](https://wholehealth.wisc.edu/overviews/personal-development/): <https://wholehealth.wisc.edu/overviews/personal-development/>
- [Spirit & Soul](https://wholehealth.wisc.edu/overviews/spirit-soul/): <https://wholehealth.wisc.edu/overviews/spirit-soul/>
- [The DASH Diet](https://wholehealth.wisc.edu/tools/dash-diet/): <https://wholehealth.wisc.edu/tools/dash-diet/>
- [Depression](https://wholehealth.wisc.edu/overviews/depression/): <https://wholehealth.wisc.edu/overviews/depression/>
- [Breathing](https://wholehealth.wisc.edu/tools/breathing/): <https://wholehealth.wisc.edu/tools/breathing/>

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## REFERENCES

1. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *Circulation*. 2013;128(16):1810-1852.
2. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2013;62(16):e147-239.
3. Jackevicius CA, Page RL, Buckley LF, Jennings DL, Nappi JM, Smith AJ. Key articles and guidelines in the management of heart failure: 2018 update. *J Pharm Pract*. 2019;32(1):77-92.
4. Freeman JV, Yang J, Sung SH, Hlatky MA, Go AS. Effectiveness and safety of digoxin among contemporary adults with incident systolic heart failure. *Circ Cardiovasc Qual Outcomes*. 2013;6(5):525-533.
5. Greenfield R. Congestive Heart Failure. In: Rakel D, ed. *Integrative Medicine*. 4th ed. Philadelphia: Saunders Elsevier; 2017.
6. Aggarwal M, Bozkurt B, Panjra G, et al. Lifestyle modifications for preventing and treating heart failure. *J Am Coll Cardiol*. 2018;72(19):2391-2405.
7. Ozemek C, Phillips SA, Popovic D, et al. Nonpharmacologic management of hypertension: a multidisciplinary approach. *Curr Opin Cardiol*. 2017;32(4):381-388.
8. Shah AS, Langrish JP, Nair H, et al. Global association of air pollution and heart failure: a systematic review and meta-analysis. *Lancet*. 2013;382(9897):1039-1048.
9. Kallstrom M, Soveri I, Oldgren J, et al. Effects of sauna bath on heart failure: A systematic review and meta-analysis. *Clin Cardiol*. 2018;41(11):1491-1501.
10. Laukkanen JA, Laukkanen T, Kunutsor SK. Cardiovascular and other health benefits of sauna bathing: a review of the evidence. *Mayo Clin Proc*. 2018;93(8):1111-1121.
11. Sanches Machado d'Almeida K, Ronchi Spillere S, Zuchinali P, Correa Souza G. Mediterranean diet and other dietary patterns in primary prevention of heart failure



- and changes in cardiac function markers: a systematic review. *Nutrients*. 2018;10(1).
12. Dos Reis Padilha G, Sanches Machado d'Almeida K, Ronchi Spillere S, Correa Souza G. Dietary patterns in secondary prevention of heart failure: a systematic review. *Nutrients*. 2018;10(7).
  13. Miro O, Estruch R, Martin-Sanchez FJ, et al. Adherence to Mediterranean diet and all-cause mortality after an episode of acute heart failure: results of the MEDIT-AHF Study. *JACC Heart failure*. 2018;6(1):52-62.
  14. Dragan S, Buleu F, Christodorescu R, et al. Benefits of multiple micronutrient supplementation in heart failure: A comprehensive review. *Crit Rev Food Sci Nutr*. 2019;59(6):965-981.
  15. Mahtani KR, Heneghan C, Onakpoya I, et al. Reduced salt intake for heart failure: a systematic review. *JAMA Intern Med*. 2018;178(12):1693-1700.
  16. Tang WHW, Li DY, Hazen SL. Dietary metabolism, the gut microbiome, and heart failure. *Nat Rev Cardiol*. 2019;16(3):137-154.
  17. Liu H, Chen A. Roles of sleep deprivation in cardiovascular dysfunctions. *Life Sci*. 2019;219:231-237.
  18. Kanno Y, Yoshihisa A, Watanabe S, et al. Prognostic significance of insomnia in heart failure. *Circ J*. 2016;80(7):1571-1577.
  19. Cahalin LP, Arena RA. Breathing exercises and inspiratory muscle training in heart failure. *Heart Fail Clin*. 2015;11(1):149-172.
  20. Graven LJ, Grant JS. Social support and self-care behaviors in individuals with heart failure: an integrative review. *Int J Nurs Stud*. 2014;51(2):320-333.
  21. Andres E, Talha S, Zulfiqar AA, et al. Current research and new perspectives of telemedicine in chronic heart failure: narrative review and points of interest for the clinician. *J Clin Med*. 2018;7(12).
  22. Clark CC, Hunter J. Spirituality, spiritual well-being, and spiritual coping in advanced heart failure: review of the literature. *J Holist Nurs*. 2019;37(1):56-73.
  23. Di Palo KE. Psychological disorders in heart failure. *Heart Fail Clin*. 2020;16(1):131-138.
  24. Gok Metin Z, Ejem D, Dionne-Odom JN, et al. Mind-body interventions for individuals with heart failure: a systematic review of randomized trials. *J Card Fail*. 2018;24(3):186-201.
  25. Kwekkeboom KL, Bratzke LC. A systematic review of relaxation, meditation, and guided imagery strategies for symptom management in heart failure. *J Cardiovasc Nurs*. 2016;31(5):457-468.
  26. Dekker RL, Moser DK, Peden AR, Lennie TA. Cognitive therapy improves three-month outcomes in hospitalized patients with heart failure. *J Card Fail*. 2012;18(1):10-20.
  27. Cattadori G, Segurini C, Picozzi A, Padeletti L, Anza C. Exercise and heart failure: an update. *ESC heart failure*. 2018;5(2):222-232.
  28. Long L, Mordi IR, Bridges C, et al. Exercise-based cardiac rehabilitation for adults with heart failure. *Cochrane Database Syst Rev*. 2019;1:Cd003331.
  29. Gomes Neto M, Ferrari F, Helal L, Lopes AA, Carvalho VO, Stein R. The impact of high-intensity inspiratory muscle training on exercise capacity and inspiratory

- muscle strength in heart failure with reduced ejection fraction: a systematic review and meta-analysis. *Clin Rehabil.* 2018;32(11):1482-1492.
30. Chen YW, Hunt MA, Campbell KL, Peill K, Reid WD. The effect of Tai Chi on four chronic conditions-cancer, osteoarthritis, heart failure and chronic obstructive pulmonary disease: a systematic review and meta-analyses. *Br J Sports Med.* 2016;50(7):397-407.
  31. Gu Q, Wu SJ, Zheng Y, et al. Tai Chi exercise for patients with chronic heart failure: a meta-analysis of randomized controlled trials. *Am J Phys Med Rehabil.* 2017;96(10):706-716.
  32. Pullen PR, Seffens WS, Thompson WR. Yoga for heart failure: a review and future research. *Int J Yoga.* 2018;11(2):91-98.
  33. Liang B, Yan C, Zhang L, et al. The effect of acupuncture and moxibustion on heart function in heart failure patients: a systematic review and meta-analysis. *Evid Based Complement Alternat Med.* 2019;2019:6074967.
  34. Lee H, Kim TH, Leem J. Acupuncture for heart failure: a systematic review of clinical studies. *Int J Cardiol.* 2016;222:321-331.
  35. Ni YM, Frishman WH. Acupuncture and cardiovascular disease: focus on heart failure. *Cardiol Rev.* 2018;26(2):93-98.
  36. Cicero AFG, Colletti A. Nutraceuticals and dietary supplements to improve quality of life and outcomes in heart failure patients. *Curr Pharm Des.* 2017;23(8):1265-1272.
  37. Hopper I, Connell C, Briffa T, et al. Nutraceuticals in patients with heart failure: a systematic review. *J Card Fail.* 2020;26(2):166-179.
  38. Cicero AFG, Colletti A, von Haehling S, et al. Nutraceutical support in heart failure: a position paper of the International Lipid Expert Panel (ILEP). *Nutr Res Rev.* 2020:1-25.
  39. Khairallah RJ, Kim J, O'Shea KM, et al. Improved mitochondrial function with diet-induced increase in either docosahexaenoic acid or arachidonic acid in membrane phospholipids. *PLoS One.* 2012;7(3):e34402.
  40. Ghio S, Scelsi L, Latini R, et al. Effects of n-3 polyunsaturated fatty acids and of rosuvastatin on left ventricular function in chronic heart failure: a substudy of GISSI-HF trial. *Eur J Heart Fail.* 2010;12(12):1345-1353.
  41. Sharma A, Fonarow GC, Butler J, Ezekowitz JA, Felker GM. Coenzyme Q10 and heart failure: a state-of-the-art review. *Circ Heart Fail.* 2016;9(4):e002639.
  42. Folkers K, Vadhanavikit S, Mortensen SA. Biochemical rationale and myocardial tissue data on the effective therapy of cardiomyopathy with coenzyme Q10. *Proc Natl Acad Sci U S A.* 1985;82(3):901-904.
  43. Mortensen SA, Rosenfeldt F, Kumar A, et al. The effect of coenzyme Q10 on morbidity and mortality in chronic heart failure: results from Q-SYMBIO: a randomized double-blind trial. *JACC Heart failure.* 2014;2(6):641-649.
  44. Holubarsch CJF, Colucci WS, Eha J. Benefit-risk assessment of Crataegus Extract WS 1442: an evidence-based review. *Am J Cardiovasc Drugs.* 2018;18(1):25-36.
  45. Koch E, Chatterjee S. Crataegus extract WS-1442 enhances coronary flow in the isolated rat heart by endothelial release of nitric oxide. *Naunyn-Schmiedeberg's Arch Pharmacol.* 2000;4(Suppl.):R48 Abstract 180.

46. Orhan IE. Phytochemical and pharmacological activity profile of *Crataegus oxyacantha* L. (Hawthorn) - a cardiogenic herb. *Curr Med Chem.* 2018;25(37):4854-4865.
47. Ferrari R, Merli E, Cicchitelli G, Mele D, Fucili A, Ceconi C. Therapeutic effects of L-carnitine and propionyl-L-carnitine on cardiovascular diseases: a review. *Ann N Y Acad Sci.* 2004;1033:79-91.
48. Shang R, Sun Z, Li H. Effective dosing of L-carnitine in the secondary prevention of cardiovascular disease: a systematic review and meta-analysis. *BMC Cardiovasc Disord.* 2014;14:88.
49. Lombardi C, Carubelli V, Lazzarini V, et al. Effects of oral administration of orodispersible levo-carnosine on quality of life and exercise performance in patients with chronic heart failure. *Nutrition.* 2015;31(1):72-78.
50. Williams D, Venardos KM, Byrne M, et al. Abnormal mitochondrial L-arginine transport contributes to the pathogenesis of heart failure and reoxygenation injury. *PLoS One.* 2014;9(8):e104643.
51. Fontanive P, Saponati G, Iurato A, et al. Effects of L-arginine on the Minnesota Living with Heart Failure Questionnaire quality-of-life score in patients with chronic systolic heart failure. *Med Sci Monit.* 2009;15(12):Cr606-611.
52. Bayram M, St Cyr JA, Abraham WT. D-ribose aids heart failure patients with preserved ejection fraction and diastolic dysfunction: a pilot study. *Ther Adv Cardiovasc Dis.* 2015;9(3):56-65.
53. Saeidinia A, Keihanian F, Butler AE, Bagheri RK, Atkin SL, Sahebkar A. Curcumin in heart failure: a choice for complementary therapy? *Pharmacol Res.* 2018;131:112-119.