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Coenzyme Q_{10} as Adjunctive Therapy for Cardiovascular Disease and Hypertension: A Systematic Review

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ABSTRACT

Background: Mitochondrial ATP production requires a small electron carrier, coenzyme Q_{10} (CoQ_{10}), which has been used as adjunctive therapy in patients with cardiovascular disease (CVD) and hypertension (HTN) because of its bioenergetics and antioxidant properties. Randomized controlled trials (RCTs) beyond the last 2 decades evaluating CoQ_{10} added to conventional therapy resulted in mixed results and were underpowered to address major clinical endpoints.

Objectives: The objective of this systematic review was to examine the impact of CoQ_{10} supplementation on older adults with CVD or HTN in the last 2 decades (2000–2020).

Methods: PubMed/Medline, Cochrane Database, CINAHL, and Google Scholar databases were searched systematically, and references from selected studies were manually reviewed, to identify RCTs or crossover studies evaluating the efficacy of CoQ_{10} supplementation. Data extracted from selected studies included trial design and duration, treatment, dose, participant characteristics, study variables, and important findings.

Results: A total of 14 studies (1067 participants) met the inclusion criteria. The effect of CoQ_{10} supplementation was examined among predominantly older adult males with heart failure (HF) ($n = 6$), HTN ($n = 4$), and ischemic heart disease ($n = 3$), and preoperatively in patients scheduled for cardiac surgery ($n = 1$). CoQ_{10} supplementation in patients with HF improved functional capacity, increased serum CoQ_{10} concentrations, and led to fewer major adverse cardiovascular events. CoQ_{10} had positive quantifiable effects on inflammatory markers in patients with ischemic heart disease. Myocardial hemodynamics improved in patients who received CoQ_{10} supplementation before cardiac surgery. Effects on HTN were inconclusive.

Conclusions: In predominantly older adult males with CVD or HTN, CoQ_{10} supplementation added to conventional therapy is safe and offers benefits clinically and at the cellular level. However, results of the trials need to be viewed with caution, and further studies are indicated before widespread usage of CoQ_{10} is recommended in all older adults. *J Nutr* 2022;152:1666–1674.

Keywords: cardiac surgery, coenzyme Q_{10}, congestive heart failure, hypertension, ischemic heart disease, mitochondria

Introduction

The use of dietary supplements in complementary and alternative medicine (CAM) practices is now common among adults in the United States and worldwide (1, 2). Decades of literature suggest that some alternative approaches may be beneficial as adjunctive therapy to conventional management of cardiovascular disease (CVD) and hypertension (HTN) (3). One alternative complementary medication which has been shown to provide benefits in adults with CVD and HTN in several small randomized controlled trials (RCTs) over previous decades is coenzyme Q_{10} (CoQ_{10}), a fat-soluble quinone found in high concentrations in the mitochondria of the heart and other tissues, where it provides an important function in cellular respiration (3).

CoQ_{10} has 2 important and well-defined roles in regards to ATP generation, because it is an essential component of

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Abbreviations used: BP, blood pressure; CAM, complementary and alternative medicine; CoQ_{10}, coenzyme Q_{10}; CVD, cardiovascular disease; HF, heart failure; HFpEF, heart failure preserved ejection fraction; HTN, hypertension; MACE, major adverse cardiovascular events; NYHA, New York Heart Association; Q-SYMBIO, Effect of Coenzyme Q_{10} on Morbidity and Mortality in Chronic Heart Failure; RCT, randomized controlled trial.

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the mitochondrial electron transport chain (4). This coenzyme plays a vital role in myocardial bioenergetics where there is a high metabolic demand within the cardiac myocytes (5). Thus, CoQ_{10} myocardial tissue concentration becomes deficient, particularly in patients who suffer with CVD and HTN, as well as in conditions that create high oxidative stress (5). Furthermore, deficient concentrations in myocardial tissues of patients with CVD coupled with lower absorption of CoQ_{10} from the gut often lead to CoQ_{10}-deficient cells (6, 7). CoQ_{10} also acts as an antioxidant protecting cells against DNA damage and oxidative stress, which results from the imbalance between the production and degradation of reactive oxygen species (8, 9). By reducing oxidative stress damage, CoQ_{10} inhibits inflammation and plays a positive role in inhibiting atherosclerosis formation, which results in protective effects at the cellular level as well as improved clinical outcomes in patients with CVD and those undergoing cardiac surgery (10–12).

The antioxidant properties of CoQ_{10} and its location within the mitochondria allowed researchers to focus on its therapeutic usage as adjunctive therapy for a variety of cardiovascular disorders (13, 14). Previous studies and meta-analyses sought to pinpoint ideal dosing, bioavailability of the drug, and dose timings in relation to efficacy of the supplement, but conclusive evidence is lacking (15). An examination of CVD and HTN at the cellular level may hold the answer.

Previous studies examining the effect of CoQ_{10} for treating CVD include older studies dating back to 1985 (16, 17). The purpose of this literature review was to focus on more recent studies published during the past 2 decades (2000–2020) which examined the effects of CoQ_{10} as adjunctive therapy for treating CVD [i.e., congestive heart failure (HF), ischemic heart disease] and HTN, and during cardiac surgery.

Methods

Search strategy

Four computerized databases (PubMed/Medline, Cochrane Database, CINAHL, and Google Scholar) were searched for relevant studies meeting the inclusion criteria (listed in what follows) that were published between January 2000 and January 2020. The reference sections of selected articles set aside for review were manually searched for additional articles. The validated search filters incorporated a combination of keywords and Medical Subject Headings (MESH) terms depending upon the database being queried. Terms germane to all searches included CoenzymeQ$_{10}$ and randomized controlled trial (RCT). Other search terms included CoQ_{10}, coronary artery disease, ischemic heart disease, congestive heart failure, heart failure, cardiac surgery, coronary artery bypass graft surgery, and hypertension. Studies were eligible for inclusion if they were randomized, parallel or crossover, placebo-controlled, double-blinded trials involving adult humans $\geq$ 25 y of age, published and unpublished studies in the English language, and if the intervention group received CoQ_{10} supplementation.

Results

A search of the 4 databases yielded a combined total of 834 titles and abstracts reporting on the impact of CoQ_{10} supplementation on older adults with CVD or HTN, which were reviewed by 2 independent reviewers to determine eligibility criteria. After deduplication, 622 abstracts and articles remained which were selected for full review. Further review eliminated editorials, abstracts, review articles, articles not of interest, and duplicate citations. **Figure 1** outlines the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart. One crossover, double-blinded, placebo-controlled trial (18) and 13 randomized, placebo-controlled, double-blinded trials (19–31) met the inclusion criteria. A variety of outcome variables including cardiac functional status, endothelial function, left ventricular contractility, brachial flow-mediated dilatation, different CoQ_{10} supplementation doses, and duration of therapy were evaluated among persons with HF ($n = 6$), HTN ($n = 4$), and ischemic heart disease ($n = 3$), and preoperatively in persons scheduled for cardiac surgery ($n = 1$). Most studies were conducted in countries outside the United States (Asia, $n = 2$; Australia, $n = 5$; Europe, $n = 3$; Middle East, $n = 2$; New Zealand, $n = 1$; United States, $n = 1$).

CoQ_{10} and HF

A total of 5 RCTs (19–23) and 1 crossover, double-blinded, placebo-controlled study (18) examined CoQ_{10} therapy among persons with HF (**Table 1**). Study participants in the selected studies were reported as having New York Heart Association (NYHA) class II–IV HF symptoms. Supplemental CoQ_{10} administration varied from 60 mg/d to a maximum dosage of 320 mg/d. The attrition rate in all studies varied between 0% and 16%. Functional status and exercise tolerance were evaluated using a cardiopulmonary exercise test or dobutamine stress echocardiography. HPLC with an electrochemical detector measured CoQ_{10} concentrations in selected studies (Table 1). Three studies (18, 19, 21) reported a 3- to 4-fold increase in serum CoQ_{10} concentrations after CoQ_{10} supplementation. One study showed a 2-fold increase in the serum CoQ_{10} concentration (22). Degree of increase in serum concentrations showed no correlation with different dosages or dosing timing in relation to meals. The impact of CoQ_{10} among adults with chronic HF resulted in significant improvements ($P < 0.05$) in exercise capacity, functional class, and a decrease in HF symptoms (18–21, 23). More recently, Mortensen et al. (23) conducted the Q-SYMBIO (Effect of Coenzyme Q_{10} on Morbidity and Mortality in Chronic Heart Failure) trial to determine the efficacy of CoQ_{10} in patients with chronic HF. This large trial evaluated endpoints which focused on functional class, mortality, and major adverse cardiovascular events (MACE). At 2 y, the CoQ_{10}-treated group demonstrated significant improvement in mortality, functional class, and reduction in MACE (23). Overall, CoQ_{10} was well tolerated by study participants, with only 1 study reporting gastrointestinal symptoms in 1 of 32 study patients, which were drug-induced (19). The participants in this study suffered with end-stage HF, and all were heart transplantation candidates.

CoQ_{10} and HTN

Four RCTs (24–27) examined CoQ_{10} supplementation among persons with HTN (**Table 2**). Study participants' mean age ranged from 57 to 64 y, with all participants having $\geq$1 comorbid risk factor. A dosage of 200 mg CoQ_{10}/d was used in all 4 studies. Twenty-four-hour ambulatory systolic and diastolic blood pressure (BP) recordings were performed for the duration of the trials. In 3 trials (25–27), all study participants received conventional antihypertensive therapy, whereas only 50% of patients were treated with antihypertensive medications in the fourth trial (24). Three RCTs (24–26) reported no statistical reduction in systolic or diastolic 24-h ambulatory BP. However, Young et al. (27) reported a significantly lowered daytime diastolic BP load during CoQ_{10} administration. The

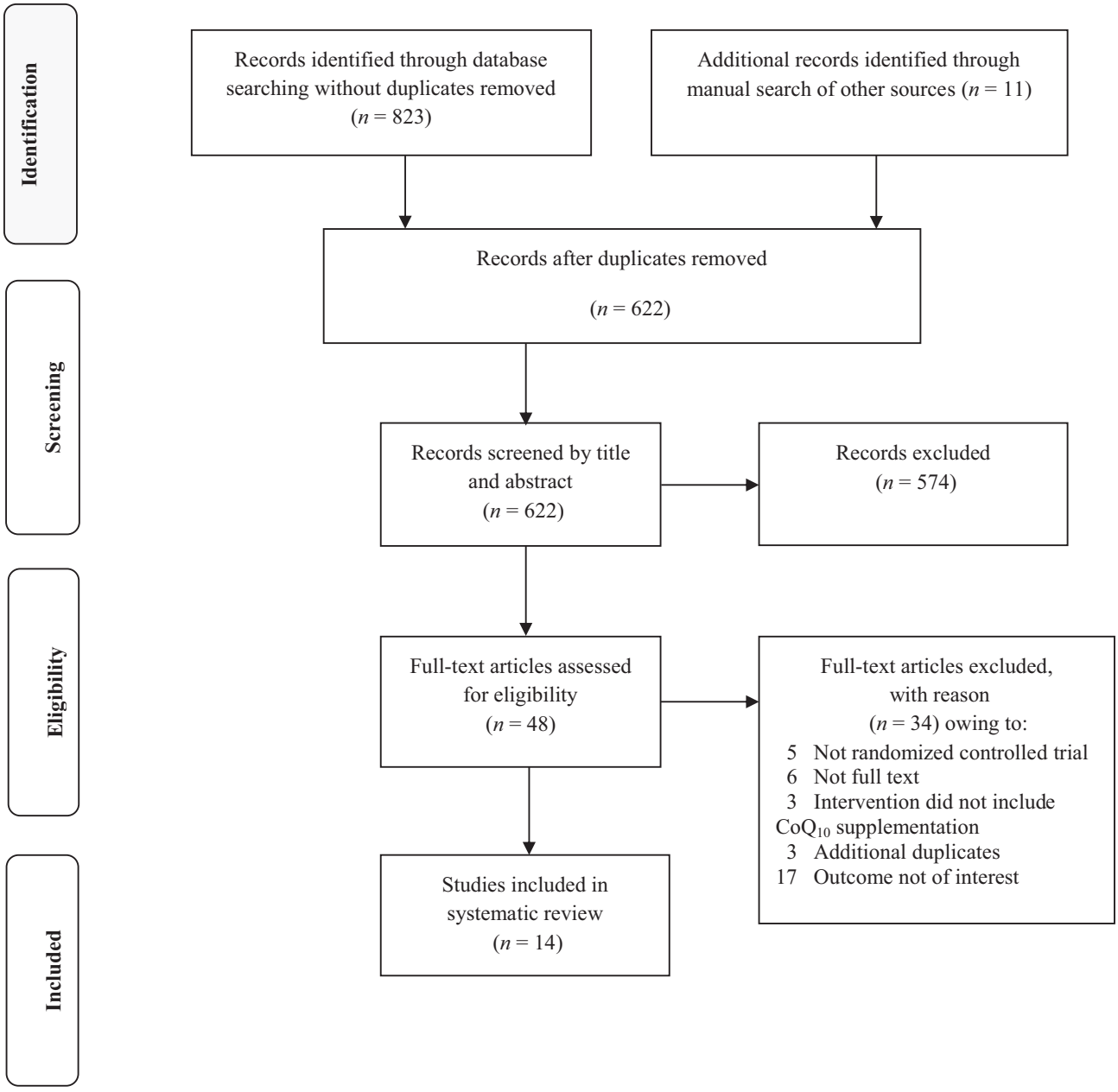

FIGURE 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram of studies. CoQ_{10}, coenzyme Q_{10}.

findings in this trial need to be viewed with caution, given the small sample size and number of BP variables, and all patients suffered with the metabolic syndrome (27). In contrast, CoQ_{10} independently lowered diastolic BP by a small (−2.2 mm Hg) but statistically significant amount ($P < 0.001$) (24), and improved 24-h systolic and diastolic BP control ($P < 0.0001$) (25). Overall, the impact of CoQ_{10} supplementation on BP control is inconclusive and warrants further investigation. CoQ_{10} supplementation was well tolerated in these studies with no major side effects reported.

CoQ_{10} and ischemic heart disease

Three RCTs (28–30) examined CoQ_{10} as adjunctive therapy in older adults with ischemic heart disease (Table 3). All studies were double-blind and placebo-controlled, and the majority of participants were men. The mean age of study participants ranged from 55 to 77 y. The studies analyzed the impact of CoQ_{10} supplementation on either endothelial function or inflammatory markers (28–30). All 3 RCTs showed statistically significant improvements in endothelial function and reduction in oxidative stress after CoQ_{10} supplementation (all P values < 0.05). Two studies reported 3- to 4-fold increases in plasma CoQ_{10} concentrations after supplementation (28, 30). The third study reported an increase in CoQ_{10} concentration, but no concentrations were recorded (29). Lee et al. (29) studied the effects of 2 dosages (60 mg/d and 150 mg/d) of CoQ_{10} on inflammatory markers (high-sensitivity C-reactive protein, IL-6, and homocysteine) in 51 patients with known coronary artery disease. After a 12-wk intervention, the authors noted a significant decrease in the inflammatory marker IL-6 ($P = 0.03$) in the 150 mg/d group. In summary, these studies demonstrate positive effects on endothelial function and inflammatory markers, but the results are biased because the participants were predominantly male.

TABLE 1 Summary of CoQ_{10} as adjunct plus conventional therapy in older class II–IV HF patients[1]

Authors (ref), location	Design	*n*	Diagnosis	CoQ_{10} intervention daily dose and duration	Participants/controls, details	Study variables	Significant findings
Belardinelli et al. (18), Italy	Crossover	23	ICM	300 mg 4 wk	$n = 23$ Mean age: 59 y Women: 8%	Serum CoQ_{10} concentrations Functional capacity	↑ LV contractility ($P < 0.01$), endothelial function, and enhanced functional capacity; 4-fold increase in plasma concentrations ($P < 0.01$), with further increase after ET (ET main effect, $P = 0.07$). Attrition = 0%
Berman et al. (19), Israel	RCT	32	End-stage HF	60 mg 12 wk	$n = 14/13$ Mean age: 54.6 y Women: 8%	Endothelial function 6-min walk test NYHA classification Fatigue ANF concentrations Echo parameters	↑ Functional status, fatigue symptoms ($P < 0.01$), quality of life; no objective changes in ANF concentrations or echo measurements. Significant improvement in 6-min walk test ($P < 0.01$). Attrition = 16%
Fumagalli et al. (20), Italy	RCT	67	Stable CHF	150 mg 12 wk	$n = 35/32$ Mean age: 72 y Women: 15%	Physical performance 8-wk peak $\dot{V}O_2$	CoQ_{10} and creatine plus conventional therapy improved physical performance ($P < 0.05$). Attrition = 0%
Keogh et al. (21), Australia	RCT-pilot	39	ICM & DCM; NYHA II, III	150 mg 12 wk	$n = 17/18$ Mean age: 62 y Women: 23%	LV contractility NYHA classification CoQ_{10} concentrations 6-min walk test	↑ Cardiac functional status on maximum β-blockers ($P = 0.05$); 3-fold increase in CoQ_{10} concentrations in treated group (0.07 ± 2.1 μg/mL). Correlation between increase in exercise time and increase in CoQ_{10} concentration ($P = 0.02$). Attrition = 10%
Khatta et al. (22), USA	RCT	55	Symptomatic CHF; NYHA III, IV	200 mg 24 wk	$n = 23/23$ Mean age: 64 y Women: 6%	Peak oxygen consumption Exercise duration LVEF	Mean ± SD CoQ_{10} increased from 0.95 ± 0.62 μg/mL to 2.2 ± 1.2 μg/mL ($P < 0.001$). No improvement in peak oxygen consumption, exercise duration, and LVEF in both the CoQ_{10} and control groups. Attrition = 16%
Mortensen et al. (23), Denmark, Austria Australia, India, Poland	RCT	420	CHF; NYHA II–IV	300 mg 16 wk–2 y	$n = 180/204$ Mean age: 62 y Women: 27%	Changes in NYHA 6-min walk test NT-proBNP concentration Effect on MACE	CoQ_{10} supplementation improved cardiac function and reduced MACE over time. CoQ_{10} is safe as adjunctive therapy in chronic HF patients. Reduced cardiovascular mortality (9% vs. 16%, $P = 0.026$) and index HF hospitalization ($P = 0.033$). Attrition = 8%

[1] ANF, atrial naturetic factor; CHF, congestive heart failure; CoQ_{10}, coenzyme Q_{10}; DCM, dilated cardiomyopathy; echo, echocardiographic; ET, exercise training; HF, heart failure; ICM, ischemic cardiomyopathy; LV, left ventricular; LVEF, left ventricular ejection fraction; MACE, major adverse cardiovascular events; NT-proBNP, N-terminal pro-B type natriuretic peptide; NYHA, New York Heart Association; RCT, randomized controlled trial; $\dot{V}O_2$, oxygen uptake.

TABLE 2 Summary of CoQ_{10} as adjunct plus conventional therapy in older patients with HTN[1]

Authors (ref), location	Design	Anti-HTN treatment?	*n*	CoQ_{10} intervention daily dose and duration	Participants/controls, details	Study variables	Significant findings
Chew et al. (24), Australia	RCT	~50%	41	200 mg 24 wk	*n* = 16/20 Mean age: 62 y Women: 25%	24-h BP	Lowered 24-h systolic BP (−3.4 ± 0.09 mm Hg) ($P = 0.01$); no effect on HR. Attrition = 7%
Mohseni et al. (25), Iran	RCT	Yes	52	200 mg 12 wk	*n* = 26/26 Mean age: 61 y Women: 15%	Systolic and diastolic BP, serum lipid and fibrinogen concentrations	CoQ_{10} therapy improved 24-h systolic and diastolic BP control ($P < 0.001$). Serum lipid and fibrinogen concentrations also significantly reduced after CoQ_{10} supplementation ($P < 0.001$). Attrition = 0%
Mori et al. (26), Australia	RCT	Yes	42	200 mg 8 wk	*n* = 16/15 Mean age: 57 y Women: 30%	24-h ambulatory systolic and diastolic BP	No independent effect on systolic BP or diastolic BP, but increased HR. Attrition = 14%
Young et al. (27), New Zealand	RCT and crossover	Yes	30	200 mg 12 wk	*n* = 15/15 Mean age: 64 y Women: 50%	24-h ambulatory systolic and diastolic BP	No statistically significant reduction in systolic ($P = 0.60$) or diastolic ($P = 0.12$) 24-h ambulatory BP or HR in patients with metabolic syndrome. Attrition = 0%

[1] BP, blood pressure; CoQ_{10}, coenzyme Q_{10}; HR, heart rate; HTN, hypertension; RCT, randomized controlled trial.

CoQ_{10} and cardiac surgery

One RCT (31) was identified which reported on preoperative oral CoQ_{10} therapy in patients undergoing cardiac surgery (Table 4). In this study, Rosenfeldt et al. (31) studied the impact of 300 mg/d of CoQ_{10} supplementation or placebo preoperatively on myocardial function in 121 patients. The mean age of participants in the study was 68 y; they were predominantly men. Analyses were performed on mitochondrial tissue obtained at the time of surgery, hemodynamic parameters, and on blood samples measuring CoQ_{10} concentrations. The study reported a statistically significant increase in myocardial and cardiac mitochondrial CoQ_{10} concentrations, improved mitochondrial efficiency, improved protection of mitochondria and myofilaments against oxidative stress (all P values < 0.01), and improvement in the contractile recovery force of myocardial trabeculae. Serum CoQ_{10} concentrations in the treatment group were ~4 times greater than those in the placebo group ($P = 0.001$) (31). This study demonstrated that CoQ_{10} supplementation administered before cardiac surgery provided benefits clinically and at the cellular level.

Discussion

This review confirms that data evaluating the supplementation of CoQ_{10} in different cardiovascular conditions remain controversial. A majority of the controversy arose from the design of the trials, baseline characteristics of the samples, and differing surrogate endpoints, all of which influenced outcomes. However, individual responses to CoQ_{10} supplementation affected by dosage, age, gender, diet, and drug preparation also contributed to mixed results. Nevertheless, CoQ_{10} supplementation as a therapeutic approach showed positive clinical applications in patients with chronic CVD and HTN, but results remain inconclusive. The consumer base expansion of CoQ_{10} usage underscores an urgent need to address CoQ_{10} deficiency, safety, efficacy, and formulation challenges.

Design flaws and baseline characteristics

In the last 2 decades (2000–2020), several small RCTs and 1 double-blind, placebo-controlled, crossover trial were conducted to assess the effects of CoQ_{10} supplementation in patients with congestive HF, ischemic heart disease, and HTN, and undergoing cardiac surgery. Most of the trials included small sample sizes varying between 20 and 60 patients, which were underpowered to address major clinical endpoints. In addition, the trials incorporated differing baseline characteristics among their samples, and were heterogeneous with a wide variation in age, dosing, and surrogate endpoints. The RCTs evaluating the effects of CoQ_{10} supplementation on BP control (24–27) used strict inclusion and exclusion criteria, which increased bias and limited generalizability to patients with fewer complex comorbidities.

We compared our systematic review with 3 other systematic reviews (32–34) which evaluated the role of CoQ_{10} supplementation in patients with ischemic heart disease. The selected RCTs for these reviews also included underpowered sample sizes with heterogeneous baseline characteristics and variable CoQ_{10} dosage ranges. Current evidence from RCTs incorporated in the reviews suggests that CoQ_{10} supplementation can indirectly affect the progression of ischemic heart disease through its impact on oxidative stress, as well as by reducing lipoprotein concentrations (32–34). However, Ayers et al. (32) questioned the routine use of CoQ_{10} in patients with ischemic heart disease,

TABLE 3 Summary of CoQ_{10} as adjunct plus conventional therapy in older patients with ischemic heart disease[1]

Authors (ref), location	Design	Anti-lipid treatment?	*n*	CoQ_{10} intervention daily dose and duration	Participants/ controls, details	Study variables	Significant findings
Dai et al. (28), China	RCT	Yes	56	300 mg 8 wk	*n* = 28/28 Mean age: 69 y Women: 7%	Brachial FMD Mitochondrial function Plasma CoQ_{10} concentration	Improved mitochondrial function and FMD ($P = 0.03$); did not alter nitroglycerin-mediated dilatation, blood pressure, or lipid profile. CoQ_{10} concentration increased 3-fold ($P < 0.01$). Absolute CoQ_{10} concentration correlated significantly with improvement in FMD ($P = 0.01$). Attrition = 0%
Lee et al. (29), Taiwan	RCT	No	51	60 mg (*n* = 19) 150 mg (*n* = 18) 12 wk	*n* = 28/12 Mean age: 77 y Women: 7%	Inflammatory markers (hs-CRP, IL-6, and homocysteine)	Significant anti-inflammatory effect on IL-6 ($P = 0.03$) in CoQ_{10}-150 group, but not on hs-CRP and homocysteine concentrations at CoQ_{10} dose (150 mg). Attrition = 21%
Tiano et al. (30), Italy	RCT	Unknown	38	300 mg 4 wk	*n* = 19/19 Mean age: 55 y Women: 13%	Nonfatal infarction cardiac deaths Brachial artery ED assessment Peak $\dot{V}O_2$ and O_2 Endothelium-bound ecSOD	Endothelial-bound ecSOD was enhanced ($P = 0.02$) and ED relaxation was also enhanced ($P < 0.01$) in the CoQ_{10}-treated group; peak $\dot{V}O_2$ increased significantly ($P = 0.03$) and O_2 also increased significantly ($P < 0.05$) compared with placebo. Attrition = 13%

[1] CoQ_{10}, coenzyme Q_{10}; ecSOD, extracellular superoxide dismutase; ED, endothelial-dependent; FMD, flow-mediated dilatation; hs-CRP, high-sensitivity C-reactive protein; RCT, randomized controlled trial; $\dot{V}O_2$, oxygen uptake.

unless they were high-risk patients with statin intolerance. Four other meta-analyses of similar RCTs (35–38) indicated that CoQ_{10} supplementation positively affected oxidative stress markers such as superoxide dismutase, catalase, C-reactive protein, and IL-6, whereas a more recent review (39) showed improvement of inflammation-related diseases in individuals under a CoQ_{10} supplementation protocol. Despite design flaws and variable baseline characteristics, these trials demonstrate that supplementation of CoQ_{10} in patients with CVD or HTN over a relatively short period of time resulted in clinical benefits through direct interactions at the cellular level.

CoQ_{10} supplementation issues

Our recent systematic review also demonstrated that dosages of CoQ_{10} and duration of treatment varied widely, which probably affected surrogate endpoints. The absorption of CoQ_{10} from the intestines is poor because it has a high molecular weight, is lipophilic, and is insoluble in the aqueous phase, all of which leads to low oral bioavailability (40). This characteristic of ingested CoQ_{10} often leads to a wide variation in serum concentrations at different dosages. In the majority of RCTs included in this review, dosage of CoQ_{10} ranged from 100 mg/d to 300 mg/d, with limited data on the amount of CoQ_{10} absorbed from the gastrointestinal tract. Six RCTs (18, 19, 21, 22, 28, 30) reported a 2- to 4-fold increase in plasma CoQ_{10} concentrations. In all 6 RCTs, the surrogate endpoints were achieved, suggesting that higher dosages of CoQ_{10} contribute to increased serum concentrations which have a positive impact on CVD through its effects on inflammatory and oxidative stress markers (35–38). However, patients with end-stage HF who received a lower dosage of CoQ_{10} (60 mg/d) also showed improved functional status and decrease in dyspnea (19). This unexpected result appears related to a 4-fold increase in plasma CoQ_{10} concentration, which correlated to special dosing preparations to increase intestinal absorption, because these elevated concentrations cannot be achieved with low oral doses (18, 19, 40). The RCTs in this review incorporated higher CoQ_{10} concentrations to exceed a threshold of 2.5 μg/mL which is needed to ameliorate symptoms (18). Previous research supports these findings (3, 29, 41).

CoQ_{10} supplementation and HF

CoQ_{10} becomes a potent lipophilic antioxidant in its reduced form, ubiquinol, which is capable of providing benefits to individuals suffering with poor exercise tolerance related to chronic HF (42, 43). Thus, the severity of HF in patients with chronic mitochondrial diseases correlates inversely with the severity of CoQ_{10} deficiency (32, 44). CoQ_{10} supplementation in patients with chronic HF appears to offer beneficial effects clinically and at the cellular level as shown in trials spanning 2 decades (18–23). The majority of patients in these trials suffered with HF reduced ejection fraction (HFrEF), left ventricular ejection fraction $\leq 50\%$, and received dosages of CoQ_{10} varying from 60 mg/d to 300 mg/d. Overall evidence from these trials is low-quality based on the relatively small sample sizes, heterogeneity among patients, variable CoQ_{10} supplementation dosages, and surrogate endpoints, making generalizability to other HF populations difficult. As such, Mortensen et al. (23) designed a more recent trial (Q-SYMBIO) involving 420 patients, a larger dosage of CoQ_{10} (300 mg/d), and a longer duration (2 y) to address mortality, functional status, and MACE. Even though the results of Q-SYMBIO were impressive, extrapolation to patients with HF preserved ejection fraction (HFpEF), older women, and other ethnic groups should be

TABLE 4 Summary of the effects of CoQ_{10} on myocardium in older patients undergoing cardiac surgery[1]

Authors (ref), location	Design	*n*	CoQ_{10} intervention daily dose and duration	Participants/controls, details	Study variables	Significant findings
Rosenfeldt et al. (31), Australia	RCT	121	300 mg 2 wk	*n* = 62/59 Mean age: 68 y Women: 19%	CoQ_{10} concentrations Mitochondrial function Cardiac myocardium protection Cardiac myocardium recovery postsurgery	Preoperative CoQ_{10} therapy increases cardiac mitochondrial and myocardial concentrations ($P = 0.01$); myocardial tolerance to in vitro hypoxia-reoxygenation also increases ($P = 0.01$). Attrition = 0%

[1] CoQ_{10}, coenzyme Q_{10}; RCT, randomized controlled trial.

interpreted with caution (32, 44). A recent prospective RCT (45) in elderly (≥55 y) patients with HFpEF also demonstrated limited effect on indexes of diastolic function. However, some evidence (23) supports CoQ_{10} supplementation therapy in selected HF patients and in patients with diastolic HF, possibly related to a statin-associated cardiomyopathy (43, 46).

CoQ_{10} usage and safety

Nevertheless, all RCTs in this review indicate that CoQ_{10} is safe, well tolerated, and has the potential to improve functional status and quality of life in patients having NYHA class II, III, or IV congestive HF symptoms (7, 47). Many patients use CoQ_{10} worldwide as an adjunctive therapy because of its safety profile and presumed efficacy. It is now the third most consumed dietary supplement in developing countries because of its anti-inflammatory properties, but also to improve endothelial and mitochondrial dysfunction in patients with ischemic heart disease at dosages between 60 mg/d and 300 mg/d (7, 38, 47). In regards to cardiac surgery, CoQ_{10} showed a benefit at the cellular level, increasing protection of the mitochondria and myofilaments against oxidative stress when administered 2 wk before surgery.

Currently, the use of CAM such as CoQ_{10} is not included in nursing and medicine schools' curricula in the United States or other countries (48), and nurses' knowledge and attitudes vary according to beliefs and practices (49, 50). Based on the results of this review, educators, nurse managers, and other health care professionals need to recognize the mechanism of actions and clinical applications of CoQ_{10} as an antioxidant and its efficacy as a supplement when combined with conventional medications in HF patients. Patients using CoQ_{10} supplements for CAM must also understand that this therapy should be used as an adjunctive therapy combined with conventional treatment of conditions such as CVD or HTN, and only under the supervision of a qualified provider (51).

Strengths and limitations

This review has several strengths. Only RCTs that had both CoQ_{10} and placebo-controlled groups were selected, which made this review less subject to bias. This review examined studies published during the last 2 decades, a period in which most patients with CVD were treated with evolving standard accepted therapy, including angiotensin-converting enzyme (ACE) inhibitors, β-blockers, diuretics, and nitrates. In comparison, previous meta-analyses were conducted during a period when the standard of care for CVD changed considerably, and the latest meta-analysis on CoQ_{10} supplementation spanned 2 decades (16). Most studies were performed in countries outside the United States (Tables 1–4), with comparisons among different ethnic groups lacking.

Our review has some limitations. First, this review was not a meta-analysis and thus the analysis was unable to generate a more quantitative estimate of the studied phenomenon. The size of the trials in both recent and previous studies was small, and the duration of most trials was short (2–12 wk). In addition, limited information was reported on study characteristics such as race/ethnicity, BP, comorbid risk factors, and medication regimens.

Furthermore, only 4 computerized databases were screened for inclusion criteria, and the search was limited to English-language studies published in the past 2 decades (January 2000–January 2020). Lastly, comparison among studies was limited by the variation in outcomes assessed, differences in study design, and the amount and type of study variables evaluated in each trial.

Implications for practice

- CoQ_{10} helps cells to produce energy.
- CoQ_{10} acts as an antioxidant and improves dysfunctional bioenergetics.
- CoQ_{10} concentrations decrease with age and in patients with CVD.
- CoQ_{10} supplements may increase serum CoQ_{10} in humans.
- Nursing professionals should consider CoQ_{10} as an adjunctive therapy.

Conclusion

CoQ_{10} appears to be safe and clinically effective when used as an adjunctive therapy among adults with CVD. The effects on HTN are inconclusive. Because of the limited number of studies and participants included in this review, the results of the RCTs should be viewed with caution. Nonetheless, CoQ_{10} supplementation as adjunctive therapy in adults with CVD appears to provide benefits clinically and at the cellular level, which results in improved cardiac function, enhanced quality of life, and reduced MACE.

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