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REVIEW ARTICLE

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Major cardiovascular, metabolic, and hypertension outcomes of coenzyme Q10 supplementation in elderly patients: a systematic review and meta-analysis

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Abstract

Introduction: The aging of the world's population poses unprecedented challenges to maintaining the health of the 9.1 billion people who will inhabit the planet by 2050. Dietary habits, which lead to the development of cardiovascular and metabolic diseases, significantly increase the risk of death. **Objective:** This was to conduct a systematic review to present and correlate the main outcomes of clinical studies on the dosages and bioavailability of coenzyme Q10, in monotherapy or associated with other supplements, for the best treatment and prevention of cardiovascular and metabolic diseases and arterial hypertension in the elderly. **Methods:** The systematic review rules of the PRISMA Platform were followed. The search was carried out from January to April 2026 in the Web of Science, Scopus, Embase, PubMed, ScienceDirect, Scielo, and Google Scholar databases. The quality of the studies was based on the GRADE and AMSTAR-2 instruments and the risk of bias was adequately analyzed, according to the Cochrane instrument. **Results and Conclusion:** A total of 154 articles were found, and 37 articles were fully evaluated and included in this article, of which 17 were included in the systematic review. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 25 studies with a high risk of bias and 29 studies that did not reach GRADE. Most studies presented homogeneity in their results, with X^2=64.5%>50%. It was concluded that supplementation with selenium and coenzyme Q10 for an elderly population significantly reduces systemic oxidative stress, with a reduction in the risk of cardiovascular mortality and presenting a lower rate of cardiovascular mortality after a median follow-up of 10 years. There was also preservation of leukocyte

telomeres, fibrosis reduction, and fibroblast growth factor 23 after selenium and Coenzyme Q10 supplementation. In patients with metabolic syndrome, nutraceutical (NC) and Coenzyme Q10 supplementation were safe, well tolerated, and effective in improving clinical blood pressure, lipid, and glycemic profiles. The combination of nutraceuticals and Coenzyme Q10 demonstrated clinical efficacy in reducing total cholesterol, non-HDL, LDL, and triglycerides, while improving the level of hepatic transaminases and high-sensitivity C-reactive protein.

Keywords: Coenzyme Q10. Supplements. Cardiovascular diseases. Metabolism. Arterial hypertension. Elderly.

Introduction

The aging of the global population poses unprecedented challenges to maintaining the health of the 9.1 billion people who will inhabit the planet by 2050. Population aging is a significant social, medical, and economic problem due to the increased prevalence of chronic diseases in the elderly population. Dietary habits that lead to the development of cardiovascular and metabolic diseases significantly increase the risk of death. The use of dietary supplements in complementary and alternative medicine (CAM) practices is common among adults worldwide **[1,2]**. Some alternative approaches may be beneficial as adjunctive therapy to conventional management of cardiovascular disease (CVD) and systemic arterial hypertension (SAH) **[3]**.

In this sense, an alternative complementary medication that has been shown to provide benefits in adults with CVD and SAH in several small randomized controlled trials in recent decades is coenzyme Q10, an endogenous lipophilic quinone found in high concentrations in the mitochondria of the heart and other tissues, where it plays an important role in the cell **[3,4]**. Coenzyme Q10 plays an important role in cellular bioenergetics, acting as an electron carrier between mitochondrial respiratory complexes, alternating between its oxidized (ubiquinone) and reduced (ubiquinol) form. Tissues characterized by high respiratory demand and energy turnover, such as cardiac muscle, are particularly rich in coenzyme Q10 **[5]**.

In its reduced form, coenzyme Q10 is also endowed with critical antioxidant properties in the lipid environment. In particular, at the extracellular level, coenzyme Q10 is transported in plasma by lipoproteins, being present in more than 90% in the form of ubiquinol. Among lipoproteins, low-density lipoproteins (LDL) constitute the main transporters where ubiquinol, synergistically with vitamin E, plays a key role in the inhibition of lipid peroxidation **[1,5,6]**.

In this scenario, the concentration of coenzyme Q10 in the myocardial tissue becomes deficient, particularly in patients suffering from CVD and hypertension, as well as in conditions that generate high oxidative stress. Furthermore, deficient concentrations in the myocardial tissues of patients with CVD together with reduced absorption of coenzyme Q10 from the intestine generally lead to coenzyme Q10 -deficient cells **[5,6]**. Furthermore, coenzyme Q10 also acts as an antioxidant protecting cells against DNA damage, which results from the imbalance between the production and degradation of reactive oxygen species **[7,8]**.

As a corollary of this, by reducing oxidative stress damage, coenzyme Q10 inhibits inflammation and the formation of atherosclerosis, which results in protective effects at the cellular level, as well as improved clinical outcomes in patients with CVD and undergoing cardiac surgery **[8,9]**. The antioxidant properties of coenzyme Q10 and its localization within mitochondria have allowed researchers to focus on its therapeutic use as an adjunctive therapy for a variety of CVD **[9]**. Observational studies have reported that plasma coenzyme Q10 concentration is an independent predictor of mortality in patients with congestive heart failure (CHF) **[1]**.

Also, coenzyme Q10 synthesis in humans progressively decreases after the age of 20 years, as do the activities of the reductases responsible for activating coenzyme Q10 to its reduced form **[10]**. Therefore, age-related coenzyme Q10 deficit is related to increased cardiovascular risk. In this context, the cardiovascular benefits of coenzyme Q10 supplementation are among its best-documented clinical effects. This is mainly associated with its ability to protect LDL from oxidation and to counteract endothelial dysfunction through the modulation of endogenous antioxidant defenses. Coenzyme Q10, due to its bioenergetic role, has also been shown to support myocardial contractility **[1,5]**.

Coenzyme Q10 supplementation has been shown to improve some cardiovascular indices, such as left ventricular ejection fraction (LVEF), cardiac output (CO), and stroke index (SI). In cardiac surgery, coenzyme Q10 supplementation has been shown to improve the protection of mitochondria and myofilaments against oxidative stress, contributing to the maintenance of efficient energy production and improving contractile recovery **[1-3]**.

Although several trials have evaluated the effect of coenzyme Q10 supplementation on blood pressure in patients with metabolic diseases, the results are controversial. The results showed that coenzyme Q10 supplementation significantly decreased systolic blood pressure (SBP). However, coenzyme Q10 supplementation decreased diastolic blood pressure (DBP), but this was not statistically significant **[11]**. Even with important scientific evidence on the real effects of coenzyme Q10 on cardiovascular protection and hypertension, there is still a lack of systematic review studies to identify the ideal dosage, the bioavailability of the medication and the dose/schedule in relation to the effectiveness of the supplement, especially in the elderly population.

Therefore, the present study aimed to conduct a systematic review in order to present and correlate the main outcomes of clinical studies on the dosages and bioavailability of coenzyme Q10, in monotherapy or associated with other supplements, for the best treatment and prevention of cardiovascular, metabolic and arterial hypertension diseases in the elderly.

Methods

Study Design

The PRISMA (preferred reporting items for systematic reviews and meta-analysis) rules were followed. Available at: http://www.prisma-statement.org/?AspxAutoDetectCookieSupport=1. Accessed on: 03/11/2025. The AMSTAR-2 (Assessing the methodological quality of systematic reviews) methodological quality standards were also followed. Available at: https://amstar.ca/. Accessed on: 03/11/2025. Table 1 presents the PICOS (Patients; Intervention; Control; Outcomes and Study Design) literary search strategy.

Table 1. Literature search strategy - PICOS.

PARTICIPANTS	• Elderly participants over 60 years of age.
INTERVENTION	• Coenzyme Q10 supplementation in monotherapy or combination with other supplements.
CONTROL	• Elderly participants without coenzyme Q10 supplementation and with only pharmacological treatment for cardiovascular diseases and arterial hypertension.
OUTCOMES	• Better clinical results (cardiovascular, arterial hypertension, metabolism) with the use of coenzyme Q10 or in combination with other supplements.
STUDIES	• Randomized, prospective, retrospective observational clinical studies, systematic reviews, and meta-analyses.

Source: Own authorship.

Study Quality, Study Eligibility Criteria, and Risk of Bias

The scientific quality of the studies was assessed as high, moderate, low, or very low, according to the risk of bias in the evidence, sample size, clarity of comparisons, precision, and consistency in the effects of the analyses. High-quality evidence was assessed by randomized or prospective controlled clinical trials, observational epidemiological clinical trials with a significant sample size, several participants in the studies above 40, methodological design and statistically well-developed results, inclusion of studies published in indexed journals, identification of studies that clearly showed the dosage, route of delivery of coenzyme Q10 and follow-up of participants and identification of advantages and disadvantages. Low-quality evidence was attributed to case reports, editorials, and brief communications. The risk of bias was analyzed according to the Cochrane tool (Available at: https://sites.google.com/site/riskofbiastool/. Accessed on 02/15/2025) by analyzing the Funnel Plot graph (Sample size versus Effect size), using Cohen's test (d).

Inclusion and Exclusion Criteria of Participants

As inclusion criteria, articles were selected that included participants over 60 years of age, coenzyme Q10 supplementation alone or in combination, randomized controlled or non-randomized and controlled clinical studies, and systematic review and meta-analysis studies. Articles that did not report the search strategy presented in Table 1 and that did not meet the GRADE quality criteria were excluded.

Data Sources, Search Strategy, and Study Time

The following health descriptors (DeCS/MeSH Terms) were used *"Cardiovascular diseases; Arterial hypertension; Metabolism; Elderly; Coenzyme Q10; and Supplementation"*. Search filters designated as clinical studies or systematic reviews/meta-analysis were used (Table 2). The research and development of the work were carried out from January to April 2026 in the databases Web of Science, Scopus, Embase, PubMed, OVID, Science Direct, LILACS, and EBSCO, using scientific articles from the last 10 years.

Table 2. For example, in the search structure in PubMed, the same search strategy was used in the other databases.

PubMed	*Cardiovascular diseases* ***OR*** *Arterial hypertension* ***OR*** *Metabolism*
	AND
PubMed	*Elderly* ***OR*** *Coenzyme Q10* ***OR*** *Supplementation*
	AND
PubMed	*Prospective Clinical studies* ***OR*** *Retrospective Clinical studies* ***OR*** *Randomized clinical trials OR Systematic Reviews OR Meta-analysis*
	NOT
PubMed	*Editorials* ***OR*** *Short communications* ***OR*** *Case Report*

Source: Own authorship.

Data Analysis

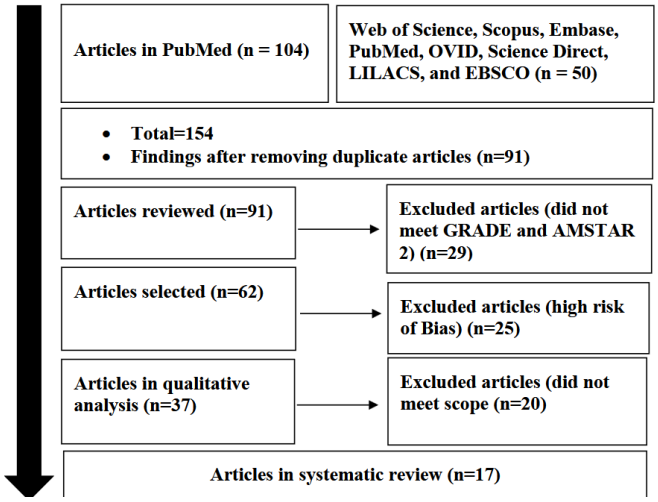
The data were entered into Excel spreadsheets and exported to Stata 17. The Cochrane Instrument was used to assess the risk of bias in the selected studies using Cohen's Test to calculate the effect size versus the Inverse of the Standard Error (precision or sample size) to determine the Risk of Bias in the studies using the Funnel Plot graph. The Heterogeneity Test (Chi-square Test, X^2) of the results between the studies was also determined, with $p<0.05$ showing no statistically significant difference, in the 95% CI, adopting codes for low association = <25%, medium association 25% <X<50%, and high association = >50%. Odds Ratio (OR), Confidence Interval (CI), and relative and comparative p-value were performed between each study, with CI =95% and p-value<0.05 with statistical significance by binary logistic regression analysis.

Results

Summary of Literature Findings

A total of 154 articles were found. Initially, duplicate articles were excluded. After this process, the abstracts were evaluated and a new exclusion was performed, removing articles that did not address the theme of this article, resulting in 91 articles. Thirty-seven articles were evaluated in full and included in this article, of which 17 were included in the systematic review (Figure 1). Considering the Cochrane tool for risk of bias, the overall assessment resulted in 25 studies with a high risk of bias and 29 studies that did not follow GRADE and AMSTAR-2. Most studies presented homogeneity in their results, with X^2=64.5%>50%.

Figure 1. Flowchart and eligibility of studies.



Source: Own authorship.

Figure 2 shows the Funnel Plot graph, performed using Cohen's statistical test, which presents symmetrical behavior in the lower part of the graph among the 8 studies with a small sample size (n<15), suggesting no significant risk of bias.

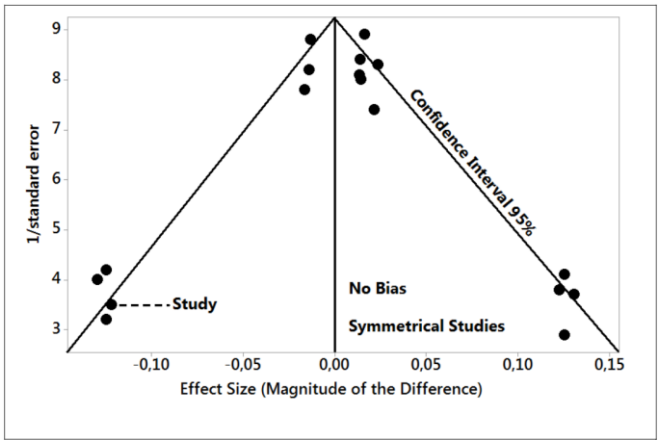


Figure 2. The symmetrical funnel plot suggests no risk of bias among the studies in the lower part of the graph (N=8 studies with a small sample size out of a total of 17 studies). Source: Own authorship.

Major Clinical Findings (N=17 randomized placebo-controlled clinical trials)

After selecting the clinical findings, it was evident that women have lower levels of coenzyme Q10 than men, probably explaining why women benefited more than men from supplementation. However, the reduction in lifetime risk with Coenzyme Q10 supplementation is significant and stable in all well-known risk populations, including those with cardiovascular disease (CVD) and systemic arterial hypertension (SAH).

In this sense, positive effects of coenzyme Q10 supplementation on endothelial function have also

been reported. Increased inflammatory activity and oxidative stress in the elderly are reduced by Coenzyme Q10 intervention. Furthermore, endothelial cells and platelets may be particularly vulnerable to oxidative stress, since they are surrounded by continuous oxygen transport in the circulation and also exposed to an increased inflammatory burden with age. The main effects of Coenzyme Q10 as monotherapy or in combination with other nutrients or vitamins in elderly patients in terms of cardiovascular and hypertension are described in Tables 3 and 4.

Table 3. Description of the main authors and outcomes of the clinical studies.

Authors-date/type of study (All Randomized Controlled); N=17	***Main CVD, Hypertension and Metabolic Effects***
1. Dunning et al. 2023 [12]	Participants who received combined selenium and coenzyme Q10 supplementation had the lowest cardiovascular mortality rate after a median follow-up of 10 years.
2. Alehagen et al. 2023 [13]	Selenium/Q10 supplementation influenced the analyzed biomarkers in a way that indicated an anti-aging effect and, through the application of the SEM methodology, the interrelationships between two independent structural factors and age were validated.
3. Opstad et al. 2022 [14]	Preservation of leukocyte telomeres after selenium and coenzyme Q10 supplementation is associated with reduced cardiovascular mortality.
4. Alehagen et al. 2018 [15]	Reduction in fibrosis precedes the reported improvement in cardiac function, thus explaining some of the positive clinical effects caused by the intervention of selenium and coenzyme Q10.
5. Alehagen et al. 2016 [16]	In the evaluation of healthy elderly individuals, low mean serum concentrations of selenium and Coenzyme Q10 were found among participants, and cardiovascular mortality was higher in the subgroup with lower serum concentrations of selenium and Coenzyme Q10 compared with those with higher serum concentrations of selenium and Coenzyme Q10.
6. Zhang et al. 2018 [17]	Twenty-four weeks of treatment with Coenzyme Q10 improves multiple risk factors for cardiovascular disease. The versatility and safety of Coenzyme Q10 make it a potential candidate for the primary prevention of cardiovascular disease.
7. Alehagen et al. 2015 [18]	In a 10-year follow-up of a group of healthy elderly individuals who received four years of intervention with selenium and coenzyme Q10, a significant reduction in cardiovascular mortality was observed.
8. Alehagen et al. 2022 [19]	Selenium and coenzyme Q10 supplementation in a community-dwelling elderly population with low levels of both substances prevented an increase in fibroblast growth factor 23 (FGF-23) and also provided a reduction in cardiovascular risk.
9. Samuel et al. 2022 [20]	In elderly patients with preserved ejection fraction, Coenzyme Q10 treatment did not significantly affect echocardiographic indices of diastolic function and serum NT-proBNP levels.
10. Alehagen et al. 2022 [21]	Selenium reduces inflammation and oxidative stress. According to structural equation modeling (SEM) analysis, these effects reduced fibrosis and improved myocardial function, pointing to the importance of supplementation in those with low selenium and coenzyme Q10 status.
11. Mortensen et al. 2019 [22]	The therapeutic efficacy of Coenzyme Q10 demonstrated in the Q-SYMBIO study was confirmed in the European subpopulation in terms of safe reduction of major adverse cardiovascular events (MACE), all-cause mortality, cardiovascular mortality, hospitalization, and improvement of symptoms.
12. Alehagen et al. 2018 [23]	The authors followed for 12 years a group of healthy elderly people who were supplemented with selenium and coenzyme Q10 for four years. Even after twelve years, a significant reduction in the risk of cardiovascular mortality was observed in this group, as well as in subgroups of patients with diabetes, hypertension, ischemic heart disease, or impaired functional capacity.
13. Bagheri Nesami et al. 2015 [24]	Daily supplementation of 100 mg of coenzyme Q10 may be effective in decreasing some pro-inflammatory factors, such as IL6 and hs-CRP, and in increasing adiponectin.
14. Sharp et al. 2014 [25]	Coenzyme Q10 improved hemoglobin and red blood cell maturation in pulmonary arterial hypertension (PAH).
15. Mazza et al. 2018 [26]	In patients with metabolic syndrome (MS), supplementation with nutraceutical compounds (NC) and Coenzyme Q10 was safe, well tolerated, and effective in improving clinical blood pressure (BP), lipid, and glycemic profile.
16. Mortensen et al. 2014 [27]	Long-term treatment with Coenzyme Q10 in patients with chronic HF is safe, improves symptoms, and reduces major adverse cardiovascular events.
17. Cicero et al. 2017 [28]	The combination of nutraceuticals and Coenzyme Q10 has demonstrated clinical efficacy in reducing total cholesterol, non-HDL, LDL, and triglycerides while improving the level of hepatic transaminases and high-sensitivity C-reactive protein.

Source: Own authorship.

Table 4. Description of the main types of interventions and their effects compared to placebo, with determination of the relative and comparative Odds Ratio (OR), Confidence Interval (CI), and p-value values between each study, with CI = 95% and p-value <0.05 with statistical significance by binary logistic regression analysis.

Authors / Type of Intervention (N=17)	Significant Effects Compared to Placebo Control? (*The Odds Ratio (OR). Confidence Interval (CI). and p-value values are relative and comparative between each study)
1. Dunning et al. 2023 **[12]** - Selenium and coenzyme Q10	Yes; OR =3.72 (CI =1.582-4.454); p=0.032
2. Alehagen et al. 2023 **[13]** - Selenium and coenzyme Q10	Yes; OR =2.88 (CI =1.322-3.664); p=0.042
3. Opstad et al. 2022 **[14]** - Selenium and coenzyme Q10	Yes; OR =2.22 (CI =0.999-2.954); p=0.039
4. Alehagen et al. 2018 **[15]** - Selenium and coenzyme Q10	Yes; OR =3.89 (CI =1.652-4.234); p=0.012
5. Alehagen et al. 2016 **[16]** - Selenium and coenzyme Q10	Yes; OR =3.23 (CI =1.478-4.589); p=0.029
6. Zhang et al. 2018 **[17]** - Coenzyme Q10	Yes; OR =1.82 (CI =0.893-2.879); p=0.035
7. Alehagen et al. 2015 **[18]** - Selenium and coenzyme Q10	Yes; OR =2.78 (CI =1.334-4.356); p=0.019
8. Alehagen et al. 2022 **[19]** – Selenium and coenzyme Q10	Yes; OR =3.55 (CI =1.234-5.123); p=0.018
9. Samuel et al. 2022 **[20]** - Coenzyme Q10	Yes; OR =1.67 (CI =0.567-3.559); p=0.027
10. Alehagen et al. 2022 **[21]** - Selenium and coenzyme Q10	Yes; OR =4.66 (CI =1.956-6.477); p=0.021
11. Mortensen et al. 2019 **[22]** - Coenzyme Q10	Yes; OR =1.69 (CI =0.455-3.887); p=0.037
12. Alehagen et al. 2018 **[23]** - Selenium and coenzyme Q10	Yes; OR =3.47 (CI =0.882-5.346); p=0.028
13. Bagheri Nesami et al. 2015 **[24]** - Coenzyme Q10	Yes; OR =1.55 (CI =0.742-3.789); p=0.041
14. Sharp et al. 2014 **[25]** - Coenzyme Q10	Yes; OR =1.98 (CI =0.564-4.588); p=0.023
15. Mazza et al. 2018 **[26]** - Nutraceutical compounds and coenzyme Q10	Yes; OR =3.97 (CI =1.457-5.788); p=0.017
16. Mortensen et al. 2014 **[27]** - Coenzyme Q10	Yes; OR =1.87 (CI =0.346-3.777); p=0.030
17. Cicero et al. 2017 **[28]** - Nutraceutical compounds and coenzyme Q10	Yes; OR =3.78 (CI =0.887-5.245); p=0.027

Source: Own authorship.

Discussion

Selenium and coenzyme Q10 intervention inhibit the pathogenesis of irreversible, presumably structural, alterations that precede cardiovascular events. Selenium and coenzyme Q10 supplementation may improve systemic redox status. A study aimed to evaluate the effect of Selenium and coenzyme Q10 supplementation on serum-free thiols and to study associations with the risk of cardiovascular mortality in community-dwelling elderly individuals. In this randomized, double-blind, placebo-controlled study, serum Selenium and coenzyme Q10 were measured colorimetrically and adjusted for albumin in 434 subjects at baseline and after 48 months of intervention. Selenium yeast (200 µg/day) and coenzyme Q10 (200 mg/day) or placebo were provided as dietary supplements. After 48 months of intervention, Participants receiving combined Selenium and coenzyme Q10 supplementation demonstrated increased serum Selenium and coenzyme Q10 levels compared to placebo. In prospective association analysis, the highest cardiovascular mortality rate after a median follow-up of 10 years was observed in the lowest quartile (Q1) of Selenium and coenzyme Q10 levels. Serum Selenium and coenzyme Q10 adjusted for baseline albumin were significantly associated with the risk of cardiovascular mortality, even after adjustment for potential confounders **[12]**.

Furthermore, aging is associated with CVD. Since no biomarker reflects the complete aging process, a study investigated five markers related to cardiovascular disease and age, and the effects of intervention with Selenium and coenzyme Q10 to elucidate the mechanisms that may influence the course of aging. This is a substudy of a previous prospective clinical trial double-blind randomized. Placebo-controlled study that included 441 subjects with low Selenium status (mean age 77 years, 49% women). The active treatment group (n = 220) received 200 µg/day of Selenium and 200 mg/day of coenzyme Q10. Combined. Blood samples were collected at enrollment and after 48 months for measurements of intercellular adhesion molecule (ICAM-1), identifying adiponectin, leptin, stem cell factor (SCF), and osteoprotegerin (OPG) using ELISAs. To better understand and reduce the complexity of the relationship between biomarkers and age, factor analyses and structural equation modeling (SEM) were performed. Correlation analyses of biomarker values at inclusion to age and relevant markers related to inflammation, endothelial dysfunction, and fibrosis demonstrated the association of biomarkers with these pathological processes; however, only ICAM1 and adiponectin were directly correlated with age. SEM analyses showed, however, that the biomarkers ICAM-1, adiponectin, SCF, and OPG, but not leptin, had significant associations with age and formed two independent structural factors, both significantly

related to age. Although no differences were observed at inclusion, biomarkers changed differently in the active and placebo treatment groups (decreasing and increasing levels, respectively) at 48 months ($p \leq 0.02$ in all adjusted models), and in the SEM model, they showed an anti-aging impact **[13]**.

In this sense, short telomeres have been associated with aging and cardiovascular disease. The influence on leukocyte telomere length (LTL) of long-term intervention with Selenium combined with coenzyme Q10 was analyzed by a study that determined whether 42 months of Selenium and coenzyme Q10 supplementation prevented telomere shortening and increased cardiovascular mortality. The investigation is an exploratory substudy of a randomized trial. Double-blind, placebo-controlled. Low-selenium Swedish citizens (n=118) aged 70-80 years were included. The intervention time was 4 years, with a follow-up of 10 years. LTL was relatively quantified with CRP at baseline and after 42 months. At baseline, LTL (SD) was 0.954 (0.260) in the active treatment group and 1.018 (0.317) in the placebo group ($p = 0.23$). At 42 months, less LTL shortening was observed after active treatment compared to placebo (+0.019 vs. -0.129, respectively, $p = 0.02$), with a significant difference in change based on individual changes in LTL ($p < 0.001$). Individuals who suffered future death had significantly shorter LTL at 42 months than survivors [0.791 (0.190) vs. 0.941 (0.279). $p = 0.01$], with a significant difference in LTL change according to cardiovascular mortality and survival ($p = 0.03$) **[14]**.

In an intervention study where 221 healthy elderly individuals received Selenium and coenzyme Q10 as a dietary supplement and 222 received a placebo for 4 years, we observed improved cardiac function and reduced cardiovascular mortality. Since fibrosis is central to the aging process, the effect of the intervention on biomarkers of fibrogenic activity was investigated in a subanalysis of this intervention study. A total of 122 actively treated individuals and 101 controls were evaluated. The effect of treatment on eight biomarkers of fibrogenic activity was evaluated. These biomarkers were Cathepsin S., Endostatin, and Galectin 3. Growth Differentiation Factor-15 (GDF-15). Matrix Metalloproteinases 1 and 9. Tissue Inhibitor of Metalloproteinases 1 (TIMP 1) and Suppression of Tumorigenicity 2 (ST-2). Blood concentrations of these biomarkers after 6 and 42 months were analyzed using T-tests, repeated measures of variance, and factor analysis. Compared with placebo, in those receiving Selenium and coenzyme Q10 supplementation, all biomarkers, except ST-2, showed significantly decreased blood concentrations. Changes in concentrations, i.e., partial effect sizes given by ST-2, caused by the intervention were considered small to medium. The significantly decreased concentrations of biomarkers in those on active treatment with Selenium and coenzyme Q10 compared with those receiving placebo after 36 months of intervention probably reflect less fibrogenic activity as a result of the intervention **[15]**.

In addition, selenium is required by all living cells to ensure the optimal functioning of several enzyme systems. Previous reports indicate that dietary supplementation with Selenium could reduce cardiovascular disease, but mainly in populations in areas with low Selenium content. A randomized, double-blind study. A placebo-controlled study aimed to determine whether the effects on cardiovascular mortality of supplementation with a fixed dose of combined selenium and coenzyme Q10 during a four-year intervention were dependent on baseline selenium levels. In 668 healthy elderly individuals from a municipality in Sweden, serum selenium levels were measured. Of these, 219 individuals received daily supplementation with combined selenium (200 µg Se as selenized yeast) and coenzyme Q10 (200 mg) for four years. The remaining participants (n = 449) received a placebo (n=222) or no treatment (n = 227). All cardiovascular mortality was recorded. No participants were lost to follow-up during a mean of 5.2 years. The mean serum selenium concentration among participants at baseline was low, 67.1 µg/L. Based on the distribution of selenium concentrations at baseline, the supplemented group was divided into three groups: <65 µg/L. 65-85 µg/L and >85 µg/L (45th and 90th percentiles) and the remaining participants were distributed accordingly. Among the untreated participants, lower cardiovascular mortality was found in the high-selenium group compared to the low-selenium group (13.0% vs. 24.1%; p=0.04). In the group with the lowest baseline selenium concentration, those who received a placebo or no supplementation had a mortality of 24.1%. Mortality was 12.1% in the group receiving the active substance, which represented an absolute risk reduction of 12%. In the medium-selenium concentration group, a mortality of 14.0% was demonstrated in the untreated group and 6.0% in the actively treated group; thus, there was an absolute risk reduction of 8.0%. In the group with serum concentration >85 µg/L. cardiovascular mortality of 17.5% was observed in the untreated group and 13.0% in the actively treated group **[16]**.

The use of coenzyme Q10 as an adjunctive treatment to routine clinical therapy against metabolic diseases has also shown benefits. A study investigated

the effect of coenzyme Q10 on CVD risk factors in dyslipidemic patients. A randomized, double-blind, placebo-controlled study was conducted with 101 dyslipidemic individuals not taking any hypoglycemic or lipid-lowering medications who received 120 mg of coenzyme Q10 or placebo daily for 24 weeks. Anthropometric parameters, lipid and glycemic profile, biomarkers of inflammation, and antioxidant capacity were assessed before and after 12 and 24 weeks of intervention. All 101 subjects were included in the analysis. At week 12, compared with placebo, coenzyme Q10 supplementation decreased systolic (p=0.010) and diastolic (p=0.001) blood pressure and increased serum total antioxidant capacity (TAC; p=0.003). At week 24, compared with placebo, coenzyme Q10 supplementation further reduced blood pressure and TAC. It reduced triglycerides (p=0.020) and low-density lipoprotein cholesterol (p = 0.016), and increased ApoA-I (p<0.001) while decreasing the homeostasis model assessment of insulin resistance index (p = 0.009). Adjustment for changes in physical activity and energy intake did not alter the effect of coenzyme Q10 on the above parameters but led to a significant decrease in non-high-density lipoprotein cholesterol in the coenzyme Q10 group compared with placebo (p=0.031) **[17]**.

One study analyzed cardiovascular mortality up to 10 years after the intervention to assess whether mortality differed in subgroups differentiated by sex, diabetes, ischemic heart disease (IHD), and functional class. We included 443 healthy elderly individuals from a rural municipality in Sweden. All cardiovascular mortality was recorded and no participants were lost to follow-up. Based on death certificates and autopsy results, mortality was recorded. A significant reduction in cardiovascular mortality was observed in those who received intervention with Selenium and coenzyme Q10. A multivariate Cox regression analysis demonstrated a reduced risk of cardiovascular mortality in the active treatment group (HR: 0.51; 95% CI 0.36-0.74; p = 0.0003). The reduced mortality could persist over the next 10 years. Subgroup analysis showed positive effects in both sexes. An equally positive risk reduction could be observed in those with ischemic heart disease (HR: 0.51; 95% CI 0.27-0.97; p = 0.04). But, also in the different functional classes **[18]**.

Also, fibroblast growth factor 23 (FGF-23) acts primarily on the metabolism of vitamin D and phosphorus. However, there are indications that FGF-23 may also provide information on both cardiovascular function and prognosis. A study evaluated the effect of supplementation with Selenium and coenzyme Q10 on FGF-23 concentrations in an elderly population with low Selenium and coenzyme Q10 concentrations and in which supplementation improved cardiac function and mortality. In a randomized, double-blind, placebo-controlled trial, FGF-23 was measured in 219 subjects at baseline and after 48 months. Selenium yeast (200 µg/day) and coenzyme Q10 (200 mg/day) (n = 118) or placebo (n = 101) were administered as a dietary supplement. The intervention time was 48 months. After supplementation with Selenium and coenzyme Q10. a significantly lower level of FGF-23 could be observed (p = 0.01). Applying 10 years of follow-up, those who subsequently died of cardiovascular death had a significantly higher FGF-23 concentration after 48 months compared to those who survived (p = 0.036), and a significantly lower FGF-23 concentration could be observed in those with normal renal function compared to those with impaired renal function (p = 0.027). Supplementation with Selenium and coenzyme Q10 to a community-dwelling elderly population with low levels of both substances prevented an increase in FGF-23 and also provided a reduction in cardiovascular risk **[19]**.

Heart failure with preserved ejection fraction (HFpEF) is common in the elderly and its prevalence is increasing. Coenzyme Q10 is an essential cofactor for energy production, with reduced levels observed in HF. Previous studies have suggested a possible role for coenzyme Q10 in the treatment of HF. This study examined the effect of Coenzyme Q10 supplementation on diastolic function in patients with HFpEF. A prospective, randomized, double-blind, placebo-controlled study was conducted including patients aged >55 years with symptoms of New York Heart Association class II-IV heart failure and left ventricular ejection fraction >50%, with impaired diastolic function. Echocardiography and serum N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels were performed at baseline and after 4 months of coenzyme Q10 or placebo supplementation. A total of 39 patients were enrolled, 19 in the coenzyme Q10 group and 20 in the placebo group. Baseline clinical characteristics were similar between groups, while adherence was high and also similar between the coenzyme Q10 and placebo groups. There was no significant effect of treatment on indices of diastolic function (difference in lateral E/e' ratio: -0.86 ± 6.57 in the coenzyme Q10 group. +0.18±3.76 in the placebo group; p=0.561) or on serum NT-proBNP levels (-72 pg/mL vs. -42 pg/mL; p=0.195) **[20]**.

A randomized placebo-controlled clinical trial using selenium yeast (200 µg/day) and coenzyme Q10 (200 mg/day) or placebo was administered to 443 community-dwelling elderly individuals for 48 months. Structural Equation Modeling (SEM) was used to

investigate the statistical interrelationships between biomarkers related to inflammation, oxidative stress, insulin-like growth factor 1, microRNA expression, fibrosis, and endothelial dysfunction and their impact on clinical effects. In addition to the positive clinical effects, the intervention with selenium and coenzyme Q10 was also associated with favorable effects on cardiovascular risk biomarkers. Using these results in the SEM model, it was shown that the weights of the first-order factors inflammation and oxidative stress were high, together forming a second-order factor inflammation/oxidative stress influencing the factors fibrosis (β=0.74; p<0.001) and myocardium (β=0.65; p<0.001). According to the model, the intervention impacted fibrosis and myocardium through these factors, resulting in improved cardiac function and reduced CV mortality **[21]**.

A study evaluated the consistency of the treatment effect of coenzyme Q10 in the European subpopulation of Q-SYMBIO, a multinational randomized, double-blind, trial of coenzyme Q10 treatment, in addition to standard therapy in chronic HF. Patients with moderate to severe HF were randomized to coenzyme Q10 300 mg daily or placebo in addition to standard therapy. At 3 months, the primary short-term outcomes were changes in the New York Heart Association (NYHA) functional class. 6-minute walk test, and N-terminal pro-B-type natriuretic peptide levels. At 2 years, the primary long-term outcome was MACE. There were no significant changes in short-term outcomes. The primary long-term outcome of MACE was achieved by significantly fewer patients in the Coenzyme Q10 group (n=10.9%) compared with the placebo group (n=33.27%, p = 0.001). The following secondary outcomes were significantly improved in the coenzyme Q10 group compared with the placebo group: all-cause and cardiovascular mortality, NYHA classification, and left ventricular ejection fraction (LVEF). In the European subpopulation, when compared with the entire group, there was greater adherence to guideline-directed therapy and similar results for short- and long-term endpoints. A novel finding revealed a significant improvement in LVEF **[22]**.

In this context, an intervention trial was carried out using selenium and coenzyme Q10 for four years as a dietary supplement, aiming to determine whether the reduction in cardiovascular (CV) mortality persisted after 12 years in the supplemented population or in subgroups with diabetes, hypertension, ischemic heart disease or reduced functional capacity due to impaired cardiac function. A total of 443 healthy elderly individuals were included. All cardiovascular mortality was recorded and no participants were lost to follow-up. After 12 years, a significantly reduced CV mortality could be observed in those who received supplementation with Selenium and coenzyme Q10, with a CV mortality of 28.1% in the active treatment group and 38.7% in the placebo group. A multivariate Cox regression analysis demonstrated a reduced risk of CV mortality in the active treatment group (HR: 0.59; 95% CI 0.42-0.81; p=0.001). In those with ischemic heart disease, diabetes, hypertension, and impaired functional capacity, a significant reduction in the risk of CV mortality was demonstrated **[23]**.

There is considerable evidence that hypertension can increase cytokine levels through endothelial stimulation and can stimulate inflammatory reactions. Thus, a study evaluated the effect of oral supplementation with coenzyme Q10 on pro-inflammatory factors and adiponectin in mildly hypertensive patients. A 12-week randomized double-blind placebo-controlled clinical trial was conducted. A total of 60 mildly hypertensive patients were randomly divided into two groups: placebo (PG, n = 30) and coenzyme Q10 (HQ, n = 30). HQ received 1 capsule containing 100 mg of Q10 per day. PG received 1 capsule of the same size and color as the Q10 capsules but containing 100 mg of lactose. Plasma pro-inflammatory factors (IL6, IL2, and TNF-α). Adiponectin and hs-CRP were determined before and after the intervention. The mean increase in adiponectin in HQ was significantly greater than that in PG (from 21.1 ± 14.5 to 24.2 ± 15.5 ng/ml. p=0.04). Significant declines in median IL6 (from 23 to 16 pg/ml. p=0.001) and mean hs-CRP were also observed in HQ after intervention (from 3.53 ± 3.36 to 2.62 ± 2.51 mg/L. P=0.03). In both groups, no statistically significant changes were observed in median TNF-α and IL2. Therefore, daily supplementation of 100 mg of coenzyme Q10 may be effective in decreasing some pro-inflammatory factors, such as IL6 and hs-CRP, and in increasing adiponectin **[24]**.

In this regard, mitochondrial dysfunction is a fundamental abnormality in the vascular endothelium and smooth muscle of patients with pulmonary arterial hypertension (PAH). Since coenzyme Q10 is essential for mitochondrial function and efficient utilization of oxygen as an electron carrier in the inner mitochondrial membrane, it was hypothesized that coenzyme Q10 would improve mitochondrial function and benefit patients with PAH. To test this, oxidized and reduced coenzyme Q10 levels were assessed. Cardiac function by echocardiography, mitochondrial functions of heme synthesis and cellular metabolism were assessed in patients with PAH (N=8) compared with healthy controls (N=7). At baseline and after 12 weeks of oral coenzyme Q10 supplementation.

Coenzyme Q10 levels were similar between PAH and control subjects and increased in all subjects with coenzyme Q10 supplementation. Patients with PAH had higher coenzyme Q10 levels than supplemented controls and a trend toward a higher proportion of reduced to oxidized coenzyme Q10. Cardiac parameters improved with coenzyme Q10 supplementation, although 6-minute walk distances and BNP levels did not change significantly. Consistent with improved mitochondrial synthetic function, hemoglobin increased and red cell distribution width (RDW) decreased in PAH patients with coenzyme Q10, whereas hemoglobin decreased slightly and RDW did not change in healthy controls. In contrast, metabolic and redox parameters, including lactate, pyruvate, and reduced or oxidized glutathione, did not change in PAH patients with coenzyme Q10 **[25]**.

It is also observed that metabolic syndrome (MS) is a worldwide epidemic disease with increased risk of morbidity and mortality. Treatment strategies for MS include pharmacological and non-pharmacological interventions and, in this regard, a relevant role for nutraceutical compounds (NC) has been demonstrated. A study investigated the efficacy and safety of NCs incorporated into a diet with coenzyme Q10 and lifestyle management versus diet alone in reducing blood pressure (BP) values and improving lipid and glycemic profiles in a group of hypertensive and hypercholesterolemic patients with MS. A total of 104 individuals with MS (mean age 57.4 ± 8.8 years; 51% men) without a history of CVD were included in the study. 52 individuals were treated with a once-daily oral formulation of NC containing red yeast rice and coenzyme Q10 added to the diet for 2 months and were compared with 52 patients who followed a diet program. Differences in BP, serum total cholesterol (TC), low- and high-density lipoprotein cholesterol (LDLC and HDLC), triglycerides (TG), and glucose values were compared by analysis of variance. A significant reduction in BP, TC, TG, LDLC, and glucose levels was observed in both treatment groups. However, a greater reduction in systolic BP (-5.2 vs. -3.0 mmHg), diastolic BP (-4.9 vs. 2.9 mmHg), total cholesterol (-17.2%), LDLC (-21.8%), TG (-16.0%), and serum glucose (-3.4%) was observed in the treatment group compared to control ($p < 0.001$ for all); HDLC remained unchanged (p=NS). No gender difference was found in either group (p=NS) **[26]**.

A multicenter, randomized controlled trial evaluated coenzyme Q10 as an adjunctive treatment in chronic HF. Patients with moderate to severe HF were randomized in a 2-year prospective study to receive either 100 mg coenzyme Q10 3 times daily or placebo in addition to standard therapy. The primary short-term outcomes at 16 weeks were changes in the New York Heart Association (NYHA) functional class, a 6-minute walk test, and N-terminal pro-B-type natriuretic peptide levels. The primary long-term outcome at 2 years was a composite of major adverse cardiovascular events, as determined by time-to-first event analysis. A total of 420 patients were enrolled. There were no significant changes in short-term outcomes. The primary long-term outcome was achieved by 15% of patients in the coenzyme Q10 group versus 26% in the placebo group (hazard ratio: 0.50; 95% confidence interval: 0.32 to 0.80, p=0.003) by intention-to-treat analysis. The following secondary outcomes were significantly lower in the coenzyme Q10 group compared with the placebo group: cardiovascular mortality (9% vs. 16%, p= 0.026), all-cause mortality (10% vs. 18%, p=0.018), and incidence of hospitalizations for HF (p=0.033). In addition, a significant improvement in the NYHA class was found in the coenzyme Q10 group after 2 years (p=0.028) **[27]**.

Finally, there is a growing interest in combined nutraceuticals that can act on multiple points of lipid and glucose metabolism for preventive purposes. However, the simple combination of nutraceuticals with potentially additive mechanisms of action needs to be clinically tested. To evaluate the effects of a combination of nutraceuticals based on artichoke, red yeast rice, banaba, and coenzyme Q10, a double-blind, crossover versus placebo trial was conducted in 30 adults with suboptimal LDL cholesterol in the primary prevention of cardiovascular disease. After 3 weeks of dietary correction, patients began 6 weeks of treatment with nutraceutical or placebo, followed by a 2-week washout period and finally a 6-week crossover period. Data related to lipid patterns, insulin resistance, renal function, liver function, and CPK were obtained at each visit. After nutraceutical treatment, enrolled patients experienced a significant improvement in total cholesterol (-13.6%), LDL-C (-18.2%), non-HDL-C (-15%), glutamic oxaloacetic transaminase (-10%), glutamate-pyruvate transaminase (-30.9%), and hs-CRP (-18.2%) versus placebo. No changes were observed in the other parameters investigated in either group. Therefore, the combination of nutraceuticals with Coenzyme Q10 demonstrated clinical efficacy in reducing total cholesterol, non-HDL, LDL, and triglycerides, while improving the level of hepatic transaminases and high-sensitivity C-reactive protein **[28]**.

Conclusion

It was concluded that supplementation with selenium and coenzyme Q10 for an elderly population

significantly reduces systemic oxidative stress, with a reduction in the risk of cardiovascular mortality and a lower cardiovascular mortality rate after a median follow-up of 10 years. There was also preservation of leukocyte telomeres, fibrosis reduction, and fibroblast growth factor 23 after supplementation with Selenium and coenzyme Q10. In patients with metabolic syndrome, supplementation with nutraceutical compounds and coenzyme Q10 was safe, well tolerated, and effective in improving clinical blood pressure, lipid, and glycemic profile. The combination of nutraceuticals and coenzyme Q10 demonstrated clinical efficacy in reducing total cholesterol, non-HDL, LDL, and triglycerides, while improving the level of hepatic transaminases and high-sensitivity C-reactive protein.

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