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# Evaluating the Therapeutic Impact of L-Carnitine on Postoperative Left Ventricular Ejection Fraction in Patients Undergoing Coronary Artery Bypass Grafting: A Meta-Analysis

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## ABSTRACT

**Background:** L-Carnitine (LC) plays a crucial role in transporting long-chain fatty acids into mitochondria for oxidation, which is particularly important for the heart and skeletal muscles. Additionally, it acts as an antioxidant and anti-inflammatory agent, helping to protect tissues from damage caused by reactive oxygen species (ROS). This study aims to evaluate the effect of LC on postoperative left ventricular ejection fraction (LVEF) in patients undergoing coronary artery bypass grafting (CABG).

**Methods:** This systematic review adhered to PRISMA guidelines and searched Google Scholar, PubMed, and ScienceDirect for randomized controlled trials (RCTs) comparing L-Carnitine to placebo in CABG patients. We focused on outcomes related to left ventricular ejection fraction (LVEF) and serum creatine kinase-MB (CK-MB) levels. Data were analyzed using a random-effects model, with results reported as weighted mean differences (WMD) and 95% confidence intervals (CI), considering statistical significance at $p < 0.05$.

**Results:** The analysis included five RCTs involving 365 CABG patients, with LC doses ranging from 2 to 6 g per day, administered from one month before to 180 days after surgery. The results showed that LC significantly improved LVEF (Weighted Mean Difference [WMD]: 3.22%, 95% Confidence Interval [CI]: 0.28 to 6.16, P = 0.0001). Additionally, LC treatment resulted in a reduction of serum creatine kinase-MB (WMD: -12.75, 95% CI: -22.46 to -3.05, P = 0.01). However, there was no significant difference in cardiopulmonary bypass time between the LC and control groups (WMD: 0.78%, 95% CI: 0.37 to 1.20, P = 0.51).

**Conclusion:** L-Carnitine is effective in improving LVEF and reducing serum CK-MB levels in patients with heart disease undergoing CABG. This suggests it may contribute to a more favourable postoperative recovery.

**Keywords:** L-Carnitine, left ventricular ejection fraction (LVEF), CK-MB levels, coronary artery bypass grafting (CABG)

## INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death globally, with coronary artery bypass grafting (CABG) being a prevalent surgical intervention. Despite its commonality, CABG is often associated with considerable morbidity and mortality. Factors such as preoperative renal impairment, heart failure

(characterized by decreased ejection fraction), diabetes mellitus, and prolonged cardiopulmonary bypass (CPB) duration are independent risk factors that heighten postoperative complications (Afrasiabirad et al., 2015).

L-Carnitine (LC) is a naturally occurring, non-protein amino acid derived from lysine and methionine. It plays a crucial role in fatty acid metabolism by facilitating the transport of long-chain fatty acids into mitochondria for oxidation, particularly in heart and skeletal muscle tissues (Hua, 2015). LC enhances carbohydrate metabolism and reduces toxic metabolite accumulation during ischemic conditions, offering protective effects against myocardial ischemia. By improving mitochondrial function and reducing reactive oxygen species (ROS) during CABG, LC helps mitigate oxidative stress and supports recovery post-surgery. Additionally, LC modulates the immune response by decreasing pro-inflammatory cytokines such as TNF-α and IL-6, thereby aiding in recovery and preserving heart function (Xue, 2017).

LC has demonstrated benefits, including reduced infarct size, decreased ventricular arrhythmias, reduced heart failure incidence, and improved survival in patients with acute myocardial infarction. Supplementing with LC (2000 mg/day) enhances antioxidant enzyme activity, offering therapeutic potential for chronic diseases. High-dose LC supplementation (≥2000 mg/day) has shown protective effects on cardiac metabolism and function in ischemic heart disease (da Silva et al,, 2017). Administering LC pre- and post-surgery may enhance heart resilience and aid recovery. Effective myocardial preservation during cardiac surgery is critical. Recent studies suggest that adding LC to cardioplegic solutions can improve myocardial ATP levels and mitochondrial function during cardioplegia (da Silva et al., 2017). This study aims to evaluate LC's effect on postoperative cardiac performance, morbidity, and complications in CABG patients.

## METHODS

### Eligibility Criteria

The study followed the PICOS framework: "P" (Patient) – effects of L-Carnitine (LC) in humans undergoing coronary artery bypass grafting (CABG); "I" (Intervention) – intravenous LC treatment; "C" (Comparison) – LC supplementation compared to placebo; "O" (Outcome) – improvements in left ventricular ejection fraction, reductions in CK-MB levels, and duration of CPB; "S" (Study Design) – randomized controlled trials (RCTs). Exclusion criteria included studies not in English, articles without full text, reviews, and case reports. Additional criteria for inclusion required: a) human subjects undergoing CABG; b) provision of LC; c) no illegal drug use; d) no multi-ingredient supplementation.

### Search Strategy

A systematic review was conducted according to PRISMA guidelines, targeting intervention studies. RCTs were identified through a comprehensive search of major databases including Google Scholar, PubMed, and ScienceDirect, covering the

years 2014-2024. The search terms used were: (“L-carnitine” OR “L-karnitin” AND “Coronary artery bypass grafting”).

**Study Selection**

Initial selection involved removing duplicates via title verification across databases. Subsequently, abstracts were reviewed to exclude non-English, incomplete text, review articles, case reports, animal, and in-vitro studies. The final selection was based on full-text analysis according to the established eligibility criteria.

**Data Collection Process**

Data extracted for each study included author, publication year, study type, supplementation duration, dose, and main outcomes. Thematic analysis was conducted to synthesize and interpret the data. The entire process of paper selection, data extraction, and quality assessment was independently conducted by the author.

**Statistical Analysis**

A meta-analysis was performed using Review Manager 5.0.4. For continuous outcomes, results were presented as mean differences with 95% confidence intervals (CIs). Heterogeneity among studies was assessed using the $I^2$ statistic: $I^2$ <30% indicated low heterogeneity, $I^2$ = 30-50% moderate, and $I^2$ >50% substantial heterogeneity. A fixed effects model was used for low heterogeneity, while a random effects model was applied when heterogeneity was present. A P-value <0.05 was deemed statistically significant for all analyses.

## RESULTS

The study identification process is illustrated in Figure 1. Out of 243 initial reports, five randomized controlled trials (RCTs) met the inclusion criteria for analysis. These studies included patient characteristics and L-Carnitine (LC) doses ranging from 2 to 6 g/day, administered from one month before surgery up to 180 days after surgery. A summary of the reviewed articles is presented in Table 1.

**Effect of LC on Left Ventricular Structure and Function**

Five studies provided data on left ventricular ejection fraction (LVEF). Due to the high heterogeneity among the studies ($I^2$ = 85%, P < 0.0001), a random effects model was used, revealing a significant improvement in LVEF among patients receiving LC therapy (Weighted Mean Difference [WMD]: 3.22%, 95% Confidence Interval [CI]: 0.28 to 6.16, P = 0.0001).

**Effect of LC on Serum CK-MB Levels**

Among the five studies reviewed, two examined serum creatine kinase-MB (CK-MB) levels. High heterogeneity was noted ($I^2$ = 94%, P < 0.0001), prompting the use of a random effects model. This analysis showed that serum CK-MB levels were significantly reduced in the LC group compared to the control group (WMD: -12.75, 95% CI: -22.46 to -3.05, P = 0.01).

**Effect of LC on CPB Duration**

Three studies reported on the duration of cardiopulmonary bypass (CPB). The analysis indicated no statistically significant difference in CPB duration between the LC and control groups, with an overall mean difference showing no significance ($I^2$

= 0%, P = 0.51). Using a random effects model, the observed CPB time was similar in patients receiving LC therapy (WMD: 0.78%, 95% CI: 0.37 to 1.20, P = 0.51).

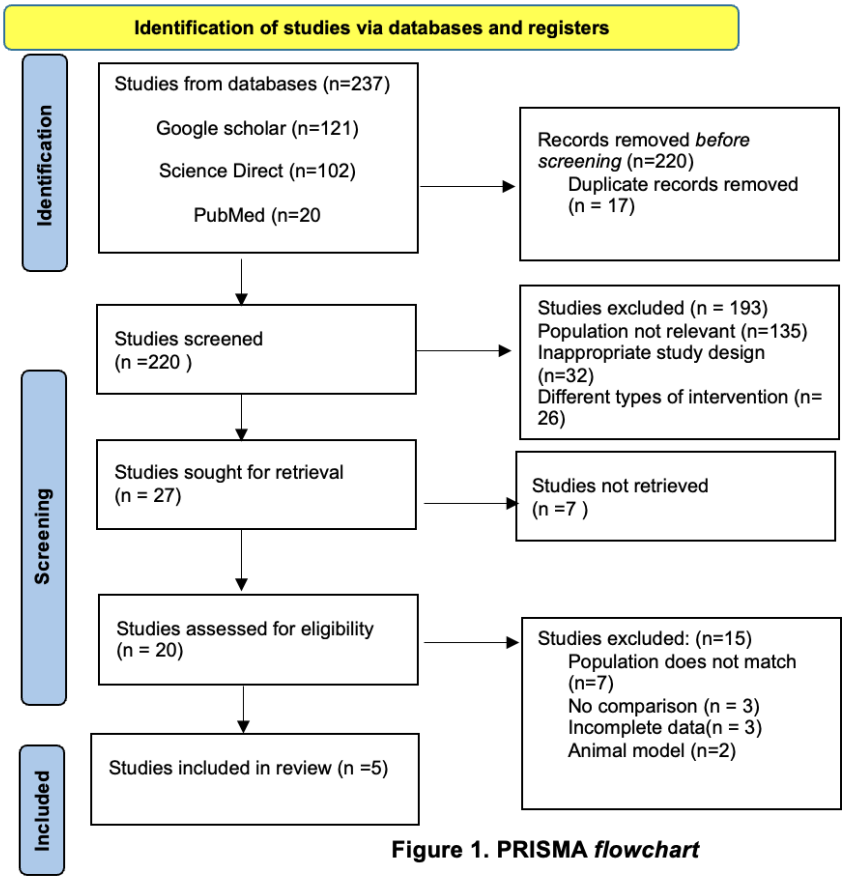


**Figure 1. PRISMA *flowchart***

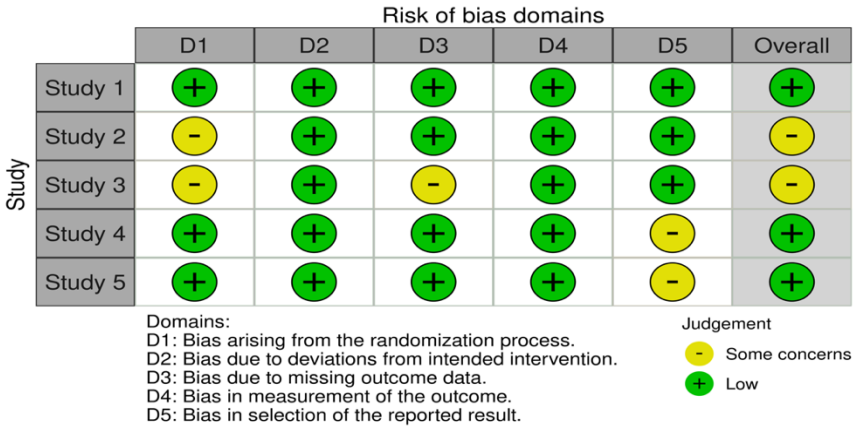


**Figure 2.** Risk of Bias Assessment

**Table 1.** Characteristics of included studies

| Author(s); Year; Country | Methods and Sample | Intervention | Outcome |
|---|---|---|---|
| Ming Li et al; 2016; China | RCT DB, 90 patients RHVD, NYHA II-III | Administered in crystalloid cardioplegic solution for the experimental group (6 g/L), while LC was not used in the control group | Higher mean arterial pressure and left ventricular ejection fraction (LVEF) levels were observed in the LC group compared with the control group 3 days after surgery (p=0.079) |
| Silva Guimaraes et al; 2017; Brazil | RCT DB, 26 patients with NYHA II-III HF undergoing CABG | LC at an oral dose of 50 mg/kg/day for 60 days starting 4 days after CABG | Evaluation in the LC group showed an increase in left ventricular ejection fraction by 37.1% (p = 0.002) and a decrease in systolic and diastolic diameters by 14.3% (p = 0.006) and 3.3% (p > 0.05), respectively) |
| Suchoun Xu et al; 2019; China | RCT DB, 129 patients RHVD with NYHA II-III undergoing CABG | 6 g/L-12 g/L LC added to the crystalloid cardioplegic solution | LC improves LVEF while reducing postoperative wall motion score index (WMSI) in patients with RVHD. Data are presented as mean ± SD (n = 43), P < 0.05, P < 0.01 and P < 0.001 vs preoperatively in the same group; P < 0.05 and P < 0.001<br><br>LC reduces levels of postoperative serum markers of myocardial injury in patients with rheumatic valvular heart disease (RVHD). Serum CK-MB as mean ± SD (n = 43), P < 0.05, P < 0.01 and P < 0.001 |
| Cevdet Furat et al; 2018; Turkey | RCT DB, 60 patients NYHA II-III undergoing CABG | 6 g/L-12 g/L LC added to the crystalloid cardioplegic solution | Patients who received LC had significantly increased left ventricular stroke work immediately after CABG in the first postoperative hour (p=0.01)<br><br>CK-MB showed a significant decrease in group C, compared with the control group (p=0.001) |

| Author(s); Year; Country | Methods and Sample | Intervention | Outcome |
|---|---|---|---|
| Wael el et al; 2024; Korea Selatan | RCT DB, 60 patients aged 2 years with CHD who will undergoing CABG surgery | Patients were given 50 mg/kg/day once daily for one month before cardiac surgery | CK-MB levels (p=0.286) in the LC group were significantly lower than those in the control group<br><br>Postoperative LVEF was significantly higher in patients receiving LC (p=0.003) compared with the control group |

RCT DB=Randomized Controlled Trial Double-Blind, LC= l-carnitine, RHVD= rheumatic heart valvular disease, CHD= chronic heart disease, CABG= coronary artery bypass grafting, LVEF= left ventricular ejection fraction, CK-MB= creatinine kinase-MB, NYHA = New York Heart Association.

**Figure 2. Risk of Bias Assessment**

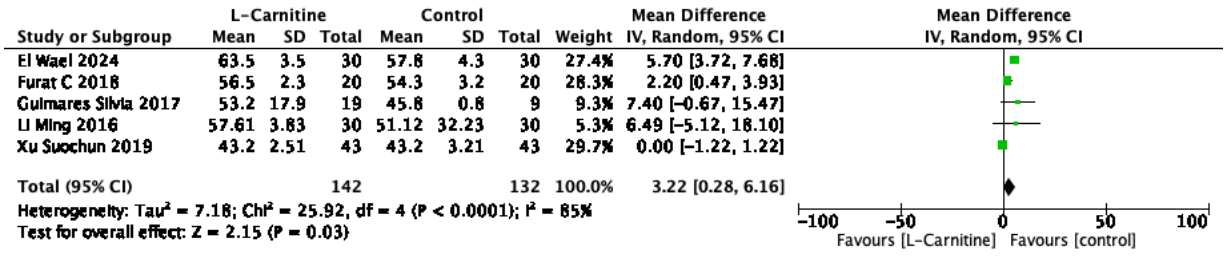


Figure 3.

**Figure 3.** Forest Plot for LVEF

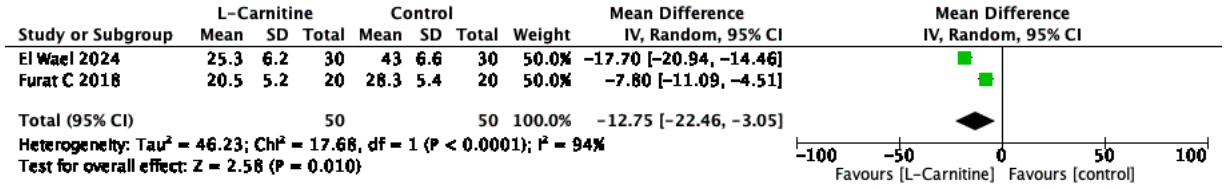


Figure 4.

**Figure 4.** Forest Plot CK-MB

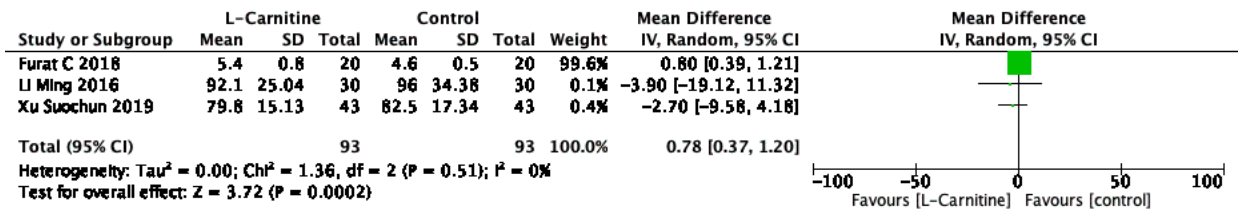


Figure 5.

**Figure 5.** Forest Plot CPB Time

## DISCUSSION

This study aimed to assess the potential benefits of L-Carnitine (LC) supplementation on postoperative cardiac function and serum CK-MB levels in patients undergoing coronary artery bypass grafting (CABG). The findings from this meta-analysis indicate positive and significant effects. Among the five studies analyzed, LC was administered at an average dose of 2-6 g/day 3-4 days after CABG surgery, resulting in a notable increase in left ventricular ejection fraction (LVEF) as demonstrated by the random effects model.

LVEF measurement is vital for assessing the severity of cardiac systolic function decline and guiding the management of various cardiovascular diseases (Bonhorst et al., 2019). The theoretical basis for LC's antioxidative properties relates to its role in transporting fatty acids into the mitochondria, preventing the accumulation of free fatty acids in the cytosol. The observed reduction in left ventricular systolic and diastolic dimensions, along with an increase in LVEF in the LC group, suggests that CABG promotes reverse remodeling through improved energy production by cardiomyocytes. Previous findings indicate that LC supplementation is linked to enhanced creatine concentrations and myocardial strength in CABG patients (Dantas et al., 2015). In another study involving 472 patients, LC was found to reduce left ventricular dilation and lower the incidence of death, congestive heart failure, and ischemic events after acute anterior infarction. These results align with our systematic review, indicating that LC supplementation post-CABG enhances lipid oxidation in cardiac myocytes and supports mitochondrial function, which is essential for optimal cardiac energy metabolism (Li M et al., 2016).

Our results revealed a significant postoperative increase in serum cardiac markers (CK-MB) across both the control and LC groups, although levels decreased notably compared to pre-surgical values ($p < 0.0001$). Troponin I and CK-MB are key diagnostic markers for myocardial injury and were significantly elevated following CABG surgery (Zhao et al., 2020). Notably, the LC group exhibited significantly lower postoperative CK-MB levels compared to the control group, consistent with previous studies that highlighted LC's potential to mitigate myocardial injury. This supports the idea that LC plays a protective role for the heart, aiding recovery after ischemic events.

Analysis of three studies on cardiopulmonary bypass (CPB) duration showed no significant differences between the LC and control groups (Table 5). It is important to recognize that conventional medicine views LC as a supplemental treatment for energy metabolism disorders rather than a replacement for existing therapies (J. Ma et al., 2015).

However, this study has limitations. The high level of heterogeneity observed in LVEF and CK-MB responses suggests variability that may stem from several factors: (1) the limited number of studies available, (2) differences in the dosages of LC used, (3) varying disease states and stages of treatment among participants, and (4) inconsistent reporting of LC manufacturers and specifications across studies. Future research should focus on conducting large-scale, standardized trials with consistent dosing and clear reporting of LC specifications to better understand its impact on cardiac function and recovery following CABG. Additionally, exploring the effects of LC in different patient populations may provide further insights into its therapeutic potential.

## CONCLUSION

In conclusion, the results of this study indicate that intravenous LC supplementation during cardioplegia at an average dose of 2-12 g/day and can be given one month preoperatively or 4 to 60 days postoperatively provides better results in the recovery of cardiac function and serum CK- MB after CABG. However, potential public health implications of LC use in CABG patients are significant. If proven effective, it could lead to reductions in postoperative complications, faster recovery times, and improved long-term cardiac health, all of which could contribute to substantial cost savings for healthcare systems. Its relatively low cost and broad applicability across patient demographics make it an attractive option for improving outcomes in CABG patients and could support healthcare sustainability by lowering the burden of chronic cardiovascular disease. Additionally, by improving quality of life and reducing readmissions, LC has the potential to positively impact both individual patients and the broader healthcare system.

## CONFLICT OF INTEREST

There are no conflicts of interests in this study.

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