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L-carnitine on myocardial function after coronary artery bypass grafting

L-karnitinin koroner arter baypas greftleme sonrası miyokard fonksiyonlarına etkisi

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ABSTRACT

Background: This study aims to evaluate the effect of L-carnitine on postoperative cardiac performance and morbidity and complications in patients undergoing coronary artery bypass grafting.

Methods: Between April 2005 and June 2008, a total of 60 patients (36 males, 24 females; mean age 60.6 years; range 57 to 65) who were scheduled for coronary artery bypass grafting were prospectively randomized to receive one of three different strategies of myocardial preservation. Group A (n=20) received antegrade crystalloid cardioplegia, Group B (n=20) received antegrade blood cardioplegia, and Group C (n=20) received antegrade blood cardioplegia with carnitine. Samples for lactate dehydrogenase (LDH), creatinine phosphokinase (CPK), creatinine phosphokinasemyocardial band (CK-MB), and Troponin-I were taken from coronary sinus during the operation and from peripheral venous line postoperatively. Blood samples were obtained before CPB, just after CPB and postoperative 1, 6, 12, 24 and 48 hours. Levels of CPK, CK-MB and Troponin-T levels were studied by immunoassay method.

Results: The patients who received carnitine had significantly improved cardiac output, cardiac index, and right and left ventricular stroke work immediately after cardiopulmonary bypass and at the first postoperative hour (p=0.01). Troponin-T levels decreased in all patients after 12 hours postoperatively, and this change was most prominent in Group C (p=0.001).

Conclusion: Intravenous supplementation of carnitine during cardioplegia provides better results on the recovery of cardiac function and metabolic parameters after coronary artery bypass grafting.

Keywords: Cardioplegia; complication; coronary artery bypass grafting; L-carnitine.

ÖZ

Amaç: Bu çalışmada koroner arter baypas greftleme yapılan hastalarda L-karnitinin ameliyat sonrası kardiyak performans, morbidite ve komplikasyonlar üzerindeki etkisi değerlendirildi.

Çalışma planı: Nisan 2005 - Haziran 2008 tarihleri arasında koroner arter baypas greftleme planlanan toplam 60 hasta (36 erkek, 24 kadın; ort. yaş 60.6 yıl; dağılım 57-65 yıl) prospektif olarak üç farklı miyokard koruma stratejisinden birine randomize edildi. Grup A'ya (n=20) antegrad kristaloid kardiyopleji, Grup B'ye (n=20) antegrad kan kardiyoplejisi ve Grup C'ye (n=20) karnitin ile birlikte antegrad kan kardiyoplejisi uygulandı. Laktat dehidrogenaz (LDH), kreatinin fosfokinaz (CPK), kreatinin fosfokinaz-miyokardiyal bant (CK-MB) ve Troponin-I için ameliyat sırasında koroner sinüsten ve postoperatif periferik venöz hattan KPB öncesi, KPB'da ve postoperatif 1, 6, 12, 24 ve 48 saat sonra kan numuneleri alındı. CPK, CK-MB ve Troponin-T seviyelerinin seviyeleri immünoassay yöntemi ile incelendi.

Bulgular: Karnitin verilen hastaların kalp debisi, kardiyak indeksi, sağ ventrikül ve sol ventrikül atım işi kardiyopulmoner baypastan hemen sonra ve ameliyat sonrası birinci saatte anlamlı olarak düzeldi (p=0.01). Troponin-T düzeyleri ameliyattan 12 saat sonra tüm hastalarda azalırken, bu değişim en belirgin Grup C'de idi (p=0.001).

Sonuç: Kardiyopleji sırasında intravenöz karnitin takviyesi, koroner arter baypas greftleme sonrası kardiyak fonksiyon ve metabolik parametrelerin iyileşmesinde daha iyi sonuçlar vermektedir.

Anahtar sözcükler: Kardiyopleji; komplikasyon; koroner arter baypas greftleme; L-karnitin.

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Carnitine specifically functions for the transport of fatty acids from cell cytosol across the mitochondrial membrane for β-oxidation. Although cardiac metabolism is extensively dependent on the heart, particularly on β-oxidation for energy production, it cannot synthesize carnitine. Myocardial carnitine concentrations are maintained at high levels by an active uptake mechanism from the blood under physiological conditions. In contrary, myocardial carnitine depletion occurs during ischemia, which indicates that whether initiation of carnitine therapy may improve outcomes in candidates for coronary artery bypass grafting (CABG). In the canine myocardium, carnitine treatment has been associated with significant reduction of deposition of long-chain acyl-coenzyme A (CoA) in the mitochondrial space attributed to ischemia.[1,2]

High levels of long-chain acyl-CoA lead to the inhibition of adenosine triphosphate (ATP) transport, and carnitine may display its protective effects on the ischemic heart through its activity on mitochondrial long-chain acyl-CoA levels.[2,3]

In cardiac surgical procedures, the realization of sufficient myocardial preservation against the metabolic derangements occurring during ischemia is crucial. This preservation may be accomplished by restriction of the duration of ischemia and by application of hyperkalemic cardioplegic solutions to allow a time-limited electromechanical quiescent period for the heart. In the recent literature, a number of studies have been conducted for the assessment of therapeutic additives to be used together with cardioplegic solutions. In an experimental rat model, higher myocardial ATP levels and improved mitochondrial morphometric scores were obtained, when carnitine was added to the perfusate during cardioplegia (CP).[1,3] With respect to these experimental data in addition to the good tolerability of L-carnitine in human, L-carnitine was administered intravenously as a supplement to CP.[1,3]

In the present study, we aimed to investigate whether L-carnitine has an effect on postoperative cardiac performance and morbidity and complications in patients undergoing CABG.

PATIENTS AND METHODS

The study protocol was approved by the local Institutional Review Board (LUT 05/39) of Hacettepe University Medicine Faculty. The study was conducted in accordance with the principles of the Declaration of Helsinki. A written informed consent was obtained from each patient.

This prospective, clinical study included a total of 60 patients (36 males, 24 females; mean age 60.6 years; range 57 to 65) at the Department of Cardiovascular Surgery of a tertiary care center. All patients were scheduled for CABG using the same surgical technique by a single surgical team and were prospectively randomized to receive one of three different strategies for myocardial preservation: Group A (n=20) received antegrade crystalloid cardioplegia (CCP), Group B (n=20) received antegrade blood cardioplegia (BCP), and Group C (n=20) received antegrade blood cardioplegia with carnitine (BCCP).

As numerous intraoperative parameters effect on postoperative hemodynamic, biochemical and metabolic parameters, it is very speculative to claim carnitine effects those parameters until all intraoperative parameters were equalized in identical groups. Although this goal was very difficult to achieve, patients with an ejection fraction (EF) of <30%, additional cardiac problems, or history of previous cardiac surgery (i.e., valve disease, aneurysm, and congenital anomalies), intrinsic pulmonary disease, and renal or hepatic failure were excluded from the study.

Operative technique

Induction of anesthesia was performed by the administration of etomidate (Hypnomidate®; Jannsen, Beerse, Belgium) at a dose of 0.3 mg/kg and fentanyl (Fentanyl®, Jannsen, Beerse, Belgium). Maintenance of anesthesia was provided by sevoflurane (Abbott, North Chicago, IL, USA) at an inspirational concentration <2.4% and a 50 to 50% concentration of N_2O and oxygen. A standard median sternotomy incision was used in all patients. The left internal mammary artery and saphenous vein were prepared. Cannulation was conducted for the cardiopulmonary bypass (CPB) in the usual fashion; arterial cannulation to the ascending aorta and venous cannulation with a two-stage cannula to right atrial appendage were performed. Operations were carried out with body temperature of 26° to 28°C, and local hypothermia was provided subsequently. A cardioplegia delivery cannula with separate vent line (DLP Medtronic, Grand Rapids, MI, USA) was inserted into the ascending aorta. A coronary sinus catheter with an auto-inflating silicone cuff (DLP Medtronic, Grand Rapids, MI, USA) was placed through transarterial-closed technique. After cross-clamping of the aorta, CP was applied via the aortic root. As an initial bolus, a 10 to 15 mL/kg CP solution was infused to aortic root with a pressure of 75 mmHg. An additional volume 400 mL of CP was administered every 20 min during cross-clamping in

addition to infusion of a 50 to 100 mL of CP after graft distal anastomosis of each vein. Upon restart of heart beating, an additional dose of 400 mL of CP was given. The rewarming was initiated during the last anastomosis procedure. After completion of all distal anastomoses, the aortic cross-clamp was removed. Proximal anastomoses were performed, while partial occluding clamp was applied. None of the patients received retrograde CP.

Preparation of cardioplegic solution

Crystalloid cardioplegia: Plegisol (Abbott Laboratories, Abbott Park, IL, USA) at 4°C was used in the following composition per 100 mL: 643 mg sodium chloride, magnesium chloride 325.3 mg, potassium chloride 17.6 mg (K^+ concentration of 16±1 mEq/L).

Blood cardioplegia: Blood CP was administered with Dideco D 514 delivery set (Sorin Group, Milan, Italy) which mixes and cools a hyperkalemic crystalloid concentration with oxygenated blood in a 1:3 dilution. To achieve a final potassium concentration similar to that of the crystalloid solution, additional potassium was added.

Blood and carnitine cardioplegia: L-carnitine (free base) was added to cardioplegic solution at a dose of 5 mM/L. None of the patients in three groups received a terminal "hot shot" of warm CP.

Hemodynamic assessment

Hemodynamic parameters including the heart rate (HR), mean arterial blood pressure (MAP), central venous pressure (CVP), mean pulmonary artery pressure (mPAP), pulmonary capillary wedge pressure (PCWP), pulmonary vascular resistance (PVR), cardiac output (CO), cardiac index (CI), left ventricular stroke work index (LVSWI), right ventricular stroke work index (RVSWI), stroke volume index (SVI), systemic vascular resistance (SVR), and ventricular performance score (VPS) were recorded preoperatively and at 1, 6, 12, 24, and 48 hours after CPB. Cardiac output was measured in triplicate using the thermodilution technique. The rate of return to spontaneous sinus rhythm after cardioplegic arrest, need for mechanical support during weaning from CPB, duration of weaning from ventilation (hours), and duration of stay in the intensive care unit (ICU) were evaluated.

Enzyme measurements

Samples for lactate dehydrogenase (LDH), creatine phosphokinase (CPK), creatine phosphokinase myocardial band (CK-MB), and Troponin-I were obtained from the coronary sinus during the operation and from the peripheral venous line postoperatively. Blood samples were obtained before CPB, immediately after CPB, and at postoperative 1, 6, 12, 24, and 48 hours. Levels of CPK, CK-MB and Troponin-T levels were studied by immunoassay method (Roche/Hitachi Elesys-2010 Immunoassay Analyzer, Roche Diagnostics, Indianapolis, IN, USA), whereas CK level was assigned with the Hitachi Modulator (Hitachi 747 Analyzer, Hitachi Chemical Co. Ltd, Chiyoda, Tokyo, Japan). The reference values for CPK, CK-MB, and Troponin-T were as follows: 30-170 U/L, 0.0-5.0 ng/mL, and 0.0-0.1 ng/mL, respectively. An Olympus AU-600 autoanalyzer (ABS Biomedical, Dallas, Texas, USA) was used for the measurement of LDH concentrations.

Lactic acid levels were measured from blood samples received from the coronary sinus preoperatively and

Table 1. Demographic and clinical characteristics of patients

	Group A (n=20)			Group B (n=20)			Group C (n=20)			
	n	%	Mean±SD	n	%	Mean±SD	n	%	Mean±SD	*p*
Age (year)			59.5±3.5			60.7±2.3			61.6±1.3	0.5
Gender										
Male	12	60		11	55		13	65		0.5
Female	8	40		9	45		7	35		0.53
Body surface area (m^2)			1.9±0.1			1.9±0.2			1.9±0.1	0.6
Ejection fraction			59.1±1.9			56.1±1.9			59±1.9	0.73
LVEDP			10.5±2.4			10.1±1.4			10.6±3.1	0.5
VPS			9.7±1.2			9.8±1.1			9.8±1.3	0.47
NYHA score			2.1±0.8			2.0±0.7			2.1±0.9	0.55
Hypertension	9	45		10	50		8	40		0.52
Diabetes mellitus	5	25		6	30		4	20		0.5
Smoking habit	8	40		7	35		7	35		0.5

LVEDP: Left ventricular end diastolic pressure; VPS: Ventricular performance index; NYHA: New York Heart Association.

Table 2. Distribution of perioperative variables among three groups

	Group A (n=20)			Group B (n=20)			Group C (n=20)			
	n	%	Mean±SD	n	%	Mean±SD	n	%	Mean±SD	*p*
CPB (min)			83.9±15.6			82.1±4.3			96.0±13.5	0.2
AKZ (min)			55.6±8.3			50.5±5.4			62.3±12.8	0.1
Number of bypass procedures			3.2±0.8			3.0±0.3			3.7±0.8	0.5
Normal sinus rhythm	12	60		14	70		18	90		0.001
Spontaneous defibrillation	10	50		7	35		3	15		0.001
Postoperative atrial fibrillation	5	25		3	15		2	10		0.08
AV block	0	0		0	0		0	0		
Low output syndrome	2	10		1	5		0	0		0.1
Medical inotropic treatment	2	10		1	5		0	0		0.1
IABP	0	0		0	0		0	0		
Duration of ventilator support (hour)			8.2±2.3			9.0±1.3			6.3±1.0	0.1
ICU stay (day)			2.1±0.3			1.9±0.2			1.8±0.1	0.1
Duration of hospitalization (day)			7.3±0.8			7.2±0.7			7.1±1.2	0.1

CPB: Cardiopulmonary bypass time (minute); ACT: Aortic cross-clamp time (minute); AV: Atrioventricular; IABP: Intra-aortic blood pressure monitorization; ICU: Intensive care unit.

immediately after cross-clamp using a Radiometer Copenhagen ABL-4 device (Radiometer Medical, Bronshoj, Denmark).

Statistical analysis

Statistical analysis was performed using the SPSS version 11.0 software (SPSS Inc., Chicago, IL, USA). Descriptive statistics are expressed as numbers and percentages for categorical variables and as means, standard deviations, medians, and minimum-maximum ranges for numerical variables. The Student's t-test was used to compare hemodynamic parameters among the groups. Logistic regression analysis was used to evaluate categorical variables. The equality of variances was investigated using the Levene test and the results of the Student's t-test were analyzed on the equality of variances. Clinical parameters were tested using the Mann-Whitney U test. A p value of <0.05 was considered statistically significant.

RESULTS

As shown in Table 1, there was no significant difference among the groups in terms of demographic and preoperative clinical parameters. Intraoperative and early postoperative findings were also similar among three groups, except for the rate of recovery for return normal sinus rhythm spontaneously and frequency of need for defibrillation. Group C had a significantly higher rate of recovery to normal sinus rhythm and lower need for defibrillation than groups A and B (p=0.001) (Table 2).

Hemodynamic parameters

All groups demonstrated improved scores for CI, LVSWI, and RVSWI immediately after CPB and at the first postoperative hour, compared to postoperative 1, 6, 12, 24, and 48 hours. In addition, the patients who received carnitine had significantly improved CO, CI, LVSWI, and RVSWI immediately after CPB and at the first postoperative hour (p=0.01). However, there was no significant difference in the hemodynamic variables between Group A and B (Table 3).

Biochemical parameters

There were no significant differences in the perioperative Troponin-T, CK, CK-MB, and LDH levels among the groups (Table 4). Postoperatively, an increase was noted in Troponin-T, CK, CK-MB and LDH in three groups.

Troponin-T levels tended to decrease in all patients after 12 hours postoperatively, and this change was most prominent in Group C (p=0.001). Similarly, CK and CK-MB levels showed a notable decrease in all groups, although it was most evident in Group C, compared to other two groups (p=0.001). Twelve hours after the operation, increased LDH levels seemed to decrease, and this was mostly evident in Group C (p=0.001) (Table 4).

Metabolic parameters

Carnitine: Carnitine levels before and after cross-clamp revealed that Group C had significantly higher levels of carnitine (p=0.001).

Table 3. Comparison of hemodynamic parameters among three groups

	CO (L/min)	CI (L/min/m²)	SVI (mL/beat/m²)	SVR (dyne/sec/cm-5)	PVR (dyne/sec/cm-5)	LVSW (gxm)	RVSW (gxm)
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD
Group A (n=20)							
Before CPB	3.9±0.6	2.2±0.2	23.4±0.6	1827.4±135.6	156.8±21.5	39.5±3.5	5.8±0.6
After CPB	4.6±0.5	2.9±0.1*	27.6±0.3	1435.8±115.5	215.7±15.7	54.3±3.2*	11.7±0.5*
Postoperative 1st hour	4.7±0.3	2.8±0.2*	28.2±0.4	1365.7±108.2	231.6±14.9	54.6±3.8*	11.5±0.8*
Postoperative 6th hour	4.9±0.1	2.7±0.1	29.1±0.5	1314.3±113.5	214.5±15.6	52.5±3.1	10.3±0.9
Postoperative 12th hour	5.0±0.3	2.7±0.2	29.3±0.4	1295.3±112.3	207.9±13.8	51.8±3.5	10.0±0.7
Postoperative 24th hour	5.0±0.2	2.6±0.6	29.4±0.5	1280.7±104.7	204.1±15.5	52.0±3.2	9.1±0.5
Postoperative 48th hour	5.1±0.1	2.5±0.3	29.5±0.5	1230.7±118.5	202.1±12.4	52.3±4.2	9.3±0.5
Group B (n=20)							
Before CPB	4.2±0.6	2.5±0.1	24.6±0.6	1617.4±120.2	160.8±12.8	45.6±0.6	8.0±0.8
After CPB	5.1±0.8	2.9±0.1*	29.7±0.4	1307.8±119.9	214.3±14.3	55.0±1.3*	12.2±0.5*
Postoperative 1st hour	4.9±0.1	2.9±0.1*	29.3±0.5	1301.7±117.2	222.6±15.3	55.1±1.0*	12.5±0.9*
Postoperative 6th hour	5.0±0.1	2.7±0.1	29.3±0.4	1282.3±116.3	210.1±15.3	53.4±3.1	10.9±0.9
Postoperative 12th hour	5.1±0.1	2.7±0.2	29.3±0.5	1284.6±102.5	205.9±16.3	53.8±23.5	10.5±0.7
Postoperative 24th hour	5.1±0.1	2.7±0.8	29.3±0.5	1272.7±113.6	206.1±16.2	53.7±3.2	10.3±0.5
Postoperative 48th hour	5.2±0.1	2.6±0.2	29.5±0.5	1216.7±115.9	212.1±13.5	53.6±4.3	10.1±0.6
Group C (n=20)							
Before CPB	4.1±0.5	2.4±0.1	24.3±0.6	1637.2±92.3	163.3±14.5	45.4±2.3	8.0±.04
After CPB	5.4±0.8†	3.2±0.1*†	29.4±0.4	1283.0±112.4	209.9±18.6	56.5±2.3*†	12.9±0.6*†
Postoperative 1st hour	5.3±0.4†	3.0±0.9*†	29.6±0.3	1269.4±123.8	218.1±14.3	56.4±2.4*†	12.8±0.9 *†
Postoperative 6th hour	4.9±0.6	2.8±0.2	26.5±0.4	1276.5±123.6	203.6±10.9	54.4±2.5	10.9±0.7
Postoperative 12th hour	5.0±0.5	2.7±0.1	29.5±0.4	1263.8±105.6	218.8±17.1	54.2±2.0	10.8±0.7
Postoperative 24th hour	5.0±0.4	2.7±0.1	29.4±0.0	1303.9±120.6	213.4±20.6	54.1±4.2	10.6±0.6
Postoperative 48th hour	4.9±1.0	2.8±0.1	29.4±0.4	1269.3±121.1	211.9±10.3	54.3±4.5	10.4±0.6

CO: Cardiac output; CI: Cardiac index; SVI: Stroke volume index; SVR: Systemic vascular resistance; PVR: Pulmonary vascular resistance; LVSW: Left ventricular stroke work; RVSW: Right ventricular stroke work; SD: Standard deviation; CPB: Cardiopulmonary bypass; * p=0.01; Statistically significant for both preoperative and postoperative 1st, 6th, 12th, 24th and 48th hours; † p=0.01; statistically significant difference in terms of postoperative hemodynamic values.

Lactate: Lactate levels were higher after aortic cross-clamp in all groups (p=0.001). There was no significant difference before cross-clamp, whereas the most evident increase in lactate levels was observed in Group C (p=0.001).

Oxygenation: Oxygen consumption of the heart per min in the cardioplegic period was measured. To obtain comparable values for changes in the oxygen consumption per min, the value during hot shot CP to increase the myocardial oxygen consumption was divided by the initial value at the onset of CP.

While there was no significant difference between Group A and B, Group C had significantly higher levels of oxygen consumption ratio (p=0.001).

DISCUSSION

This study was designed to investigate possible beneficial effects of carnitine supplementation on postoperative cardiac function and metabolism in patients undergoing CABG.

The theoretical basis for carnitine's capability for improving the clinical outcomes after cardiac surgeries has been well-established. During cardiac ischemia, accumulation of intramitochondrial long chain acyl-CoA concentrations inhibits ATP transport, thereby, leading to deterioration of the cellular metabolism and viability. During ischemic period, L-carnitine considerably impedes the deposition of these long-chain acyl-CoA and improves the mitochondrial function and β-oxidation of free fatty acids. Therefore, a protective role of L-carnitine on the ischemic supporting the administration of L-carnitine in patients with the ischemic heart disease can be mentioned.[2,4]

A multi-center study including 472 patients yielded that L-carnitine reduced left ventricular dilatation and incidences of mortality, congestive heart failure, and ischemic events after acute anterior infarction.[5]

Similar to our results, carnitine supplementation before CABG provides higher ATP concentrations.[6] Not only a better-preserved ultrastructure of myocytes can be observed microscopically,[1] but also stroke volumes after weaning from the extracorporeal circulation have been shown to improve in patients receiving carnitine supplementation.[6]

Table 4. Comparison of biochemical parameters among three groups

	CK (U/L)	CK-MB (U/L)	LDH (IU/L)	Tn T (μg/L)	
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	*p*
Group A (n=20)					
Before CPB	35.7±7.8*	5.2±2.5*	160.4±22.5*	0±0*	0.001
After CPB	107.4±32.3	28.3±5.4	343.5±26.2	0.3±0.1	>0.05
Postoperative 1st hour	584.1±46.4	55.6±7.3	418.4±27.3	0.8±0.1	>0.05
Postoperative 6th hour	876.7±83.6	68.8±12.3	484.3±18.5	1.0±0.2	>0.05
Postoperative 12th hour	760.4±69.7	60.2±12.1	585.4±21.8	0.8±0.1	>0.05
Postoperative 24th hour	684.5±76.3	52.3±12.1	525.1±23.7	0.7±0.1	>0.05
Postoperative 48th hour	632.1±56.8	37.1±6.7	443.6±19.4	0.6±0.1	>0.05
Group B (n=20)					
Before CPB	30.2±7.8*	6.2±1.6*	153.5±12.7*	0±0*	0.001
After CPB	115.4±34.1	24.4±4.5	318.3±15.5	0.2±0.1	>0.05
Postoperative 1st hour	512.1±52.9	48.6±6.4	398.4±19.8	0.7±0.2	>0.05
Postoperative 6th hour	858.7±79.7	55.3±10.9	454.3±13.5	0.8±0.1	>0.05
Postoperative 12th hour	755.4±88.7	51.7±11.8	532.4±17.5	0.8±0.1	>0.05
Postoperative 24th hour	620.9±87.7	44.6±11.5	486.1±16.2	0.6±0.1	>0.05
Postoperative 48th hour	528.5±74.3	29.3±5.7	456.5±18.5	0.5±0.1	>0.05
Group C (n=20)					
Before CPB	38.7±11.2*	5.6±3.5*	155.3±17.5*	0±0*	0.001
After CPB	97.4±28.7	20.5±5.2	295.3±16.8	0.2±0.1	>0.05
Postoperative 1st hour	496.4±48.5	41.8±7.6	367.3±18.3	0.6±0.1	>0.05
Postoperative 6th hour	753.5±42.9	50.8±11.2	432.3±14.5	0.7±0.2	>0.05
Postoperative 12th hour	678.6±94.8†	45.7±11.5†	496.5±15.3†	0.6±0.2†	0.001
Postoperative 24th hour	646.9±78.6†	38.6±9.7†	426.1±15.7†	0.5±0.2†	0.001
Postoperative 48th hour	457.3±34.9†	22.7±4.5†	380.3±16.5†	0.3±0.1†	0.001

CK: Creatine kinase; CK-MB: Creatine kinase myocardial band; LDH: Lactate dehydrogenase; Tn T: Troponin T; SD: Standard deviation; CPB: Cardiopulmonary bypass; * p=0.001; statistically significant compared to all other intervals; † p=0.001; Statistically significant difference in terms of postoperative enzyme levels in other groups.

Myocardial ischemia is invariably seen during open heart surgeries with cardioplegic arrest. Sethi et al.[7] reported that pretreatment with L-carnitine was effective in improving all clinical parameters in patients with mitral valve disease. In contrast, Demeyere et al.[3] suggested that an intravenous infusion of 3 or 6 g L-carnitine before the onset of CPB to patients scheduled for elective CABG did not favorably alter the hemodynamic profile.[3] However, Pastoris et al.[1] demonstrated that a multiple dose intravenous therapy with L-carnitine improved the myocardial content of ATP and creatine phosphate.[1] It was also suggested that carnitine enhanced the glucose metabolism while decreasing the relative contribution of β-oxidation of free fatty acids during myocardial ischemia in man.[4] Similarly, a better preservation of the cardiac myocyte was demonstrated in the carnitine-treated patients.[2] Carnitine can preserve the myocardial function by modifying the toxic effects of accumulated free fatty acid intermediates. However, it is an inotropic agent and can increase coronary blood flow other than its primary metabolic effect.[7]

In the present study, with the addition of carnitine into the cardioplegic solution, we saturated the energy stores of myocardium before reperfusion, thereby, accelerating the compensation period and minimizing the reperfusion injury. Stimulation of ATP production in mitochondria by carnitine has been shown to preserve the endothelial and contractile functions in the myocardium.[8]

Despite the limited number of patients in our study, the rate of patients who were in sinus rhythm after weaning from CPB was significantly higher in the carnitine group. These results are consistent with the findings of Nemoto et al.[9] Carnitine was found to improve both systolic and diastolic functions of the left ventricle.[10] Our results also indicate that hemodynamic parameters such as CO, CI, LVSWI, and RVSWI improved in patients receiving carnitine. These findings indicate a more remarkable and generalized beneficial impact of carnitine on cardiac functions. Patients with worse left ventricular functions, previous history of cardiac surgery or long duration of cross-clamp are expected to benefit more significantly from effects of carnitine.[11-19]

Furthermore, the current study showed that elevated levels of CK, CK-MB, and Troponin-T decreased earlier and more obviously in patients receiving carnitine. This finding suggests that myocardium protected by carnitine starts to recover before the other groups. A non-significant increase in the CI in the early postoperative period can be attributed to the rapid recovery rate with carnitine. In consistent with the reports in the literature, we found no significant difference in the morbidity and mortality rates among the groups.

Based on the expectation that oxidative metabolism can be accelerated and formation of free oxygen radicals can be inhibited,[20-22] we also found that oxygen consumption significantly increased in the patients receiving carnitine.

On the other hand, the main limitation of our study is its small sample size and single-center nature. In addition, there are three major limitations. First, it is very difficult to equalize two study groups with different coronary heart disease anatomies and revascularization procedures via CABG. Numerous intraoperative parameters such as sequential or individual grafting, quality of grafts, distribution of diseased coronary arteries among groups, kind of grafts, quality of coronary arteries, and flow rate of grafts may affect postoperative hemodynamic, biochemical, and metabolic parameters. Therefore, it is very speculative to claim that carnitine would affect those parameters until all intraoperative parameters were equalized in identical groups. The second limitation is the absence of preoperative supplementation with carnitine. Third, we were only able to use antegrade CP. Myocardium sites of totally occluded coronary arteries would receive less carnitine, compared to the stenotic ones. A patient with two occluded target vessels would receive a limited benefit, compared to those with stenotic vessels (not totally occluded two vessel disease).

In conclusion, our study results suggest that intravenous supplementation of carnitine during cardioplegia provides better results on the recovery of cardiac function and metabolic parameters after coronary artery bypass grafting. However, the short-term prominence of this beneficial effect indicates that patients with low ejection fraction, those requiring prolonged duration of cross-clamp, or candidates of complex surgeries or re-do surgeries are rather more likely to benefit from carnitine.

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