Article Review

Author / Title / Journal / Year	Type of Study	Outcomes Studied	Patient Characteristics	Results	HCFA Comments
Ahmad S, Robertson T, Golper T, Wolfson M et al / Multicenter trial of l-carnitine in maintenance hemodialysis patients . II. Clinical and biochemical effects / Kidney International / 1990	Randomized controlled trial (multicenter)	Albumin Protein intake Body weight Phosphorous Creatinine Skin fold anthropometrics Clinical status measurement Cramps Hypotension Asthenia Maximum exercise capacity Maximum oxygen consumption L-carnitine 20mg/kg given IV after each HD session OR placebo	97 patients enrolled. 82 completed 5 months of the study. 38 experimental 44 control Inclusion criteria: Maintenance HD patients (> 9 months) Clinically stable Exclusion criteria: Diabetes Prior/current carnitine treatment Lipid lowering agents Class IV angina Malignant hypertension Liver failure Endocrinopathies Malignancy Unreliable behavior patterns	Experimental group Baseline 6 mos Albumin 4.1 4.1 Prot intake 65 74 Body wt 67.5 67.3 Phosph 6.6 5.2 * Creatinine 16.46 14.6** * p< 0.009 ** p < 0.002 Decreased episodes of hypotension, muscle cramps, asthenia. Small increase in mid-arm circumference and mid-arm muscle mass. No change in maximum exercise capacity. Improved maximum oxygen consumption. 50% of patients had clinical status improvement. Control group Baseline 6 mos Albumin 4.1 4.1 Prot intake 64 67 Body wt 69.7 69.6 Phosph 6.0 6.4 Creatinine 16.9 17.38 No change in hypotension, muscle cramps. Decreased episodes of asthenia. Small increase in mid-arm	Clinical assessment scale was subjective and not a standard tool. Anthropometric measurements difficult to standardize and reproduce. Baseline symptoms were higher in the carnitine treatment group than the placebo group. All patients at each center could not participate in every phase of the study. Intent-to-treat analysis not performed.

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				circumference and mid-arm fat area. No change in maximum exercise capacity, or maximum oxygen consumption 18% of patients had clinical status improvement.	
Bellinghieri G, Savica V, Mallamace A, DiStefano C, et al / Correlation between increased serum an tissue l-carnitine levels and improved muscle symptoms in hemodialyzed patients / American Journal of Clinical Nutrition / 1983	Prospective clinical trial (cross over double blind trial)	Free carnitine Acetyl carnitine Asthenia scores Morphology of muscle fragments Symptoms (asthenia, cramps) Group 1: 7 patients received l-carnitine 1 gm orally BID for 2 months then placebo for 2 months. Group 2: 7 patients received placebo for 2 months, then l-carnitine for 2 months	14 healthy controls 10 males Age: 39 years 4 females Age: 42 years 14 patients on HD Study conducted in Italy.	Group 1 Baseline 2 mos 4 mos free car 28 88* 19 acetly car 8 24* 12 muscle car10 20 p< 0.005 Asthenia symptoms reduced during active treatment Group 2 Baseline 2 mos 4mos free car 33 25 41 acetyl car 11 8 13 muscle car 9 14 Asthenia symptoms somewhat reduced during active treatment. Morphological examination of the muscle of 13 of 14 patients did not reveal any pre- or post-treatment pathologic changes.	Authors did not report on all the symptoms collected Group 2 had no significant increases in free carnitine after treatment.

Bertoli M, Battistella PA, Vergani L, Naso A, et al / Carnitine deficiency induced during hemodialysis and hyperlipidemia: effect of replacement therapy / American Journal of Clinical Nutrition / 1981	Prospective clinical trial	Plasma carnitine Muscle carnitine Chol TG 10 patients (of the 14 HD patients) had hypertriglyceridemia received IV carnitine (50mg/kg) for 2 months.	3 groups of patient studied: 1. 4 male patients (27-64 years) with ESRD not yet on HD 2. 14 patients (24-60 years) on HD 3. 27 healthy controls (20-50 years) Study conducted in Italy.	Baseline 60 days Plasma carn 36.5 201 * Muscle carn 1.24 2.52 Chol 209 196 * TG 550 57 ** * p< 0.005 ** p < 0.001 Muscle carnitine levels 3.0 in uremic patients, 2.0 in normal controls. (P< 0.005)	At end of 2 months, TG reduced, and muscle carnitine increased. Side effects noted in 2 patients (asthenia, ptosis, decreased mastication). Symptoms disappeared after reducing carnitine dosage.

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Brass EP, Adler S, Sietsema KE, Hiatt WR, et al / Intravenous l-carnitine increases plasma carnitine, reduces fatigue, and may preserve exercise capacity in hemodialysis patients / American Journal of Kidney Diseases / 2001	Randomized controlled trial (multicenter)	Exercise capacity (VO 2 max) Quality of Life (QOL) questionnaire (KDQ) Carnitine Acylcarnitine Lipid profile Study A: L-carnitine 20 mg/kg IV or placebo x 24 weeks Study B: L-carnitine 10 mg/kg, 20 mg/kg, 40 mg/kg, or placebo.	Study A: 60 patients, 30 control Mean age: 45 years (23-64) 30 experimental Mean age: 42 years (19-76) 43% female Study B: Control Mean age: 43 years (24-67) 10 mg group Mean age: 48 years (27-76) 20 mg group Mean age: 48 years 27-76) 40 mg group Mean age: 46 (25-79) Inclusion criteria: HD for at least 6 months Age > 18 years Medical suitability to undergo graded ergometer exercise testing. Exclusion criteria: Claudication	Study A VO2max Baseline Week 24 Control 18.5 19.2 Exper 20.0 20.7 Study B VO2max Baseline Week 24 Control 18.7 18.1 10 mg 18.1 17.9 20 mg 20.1 19.6 40 mg 17.6 14.2 QOL Experimental group Baseline Week 24 Tot score 4.83 5.27 Fatigue 4.65 5.09 p=0.03 Control group Baseline Week 24 Tot score 5.0 5.29 Fatigue 4.9 5.14 No changes on Hgb or Hct.	Intention-to-treat analysis performed. (7 patients withdrew)

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Caruso U, Cravotto E, Tisone G, Elli M, et al / Long-term treatment with l-carnitine in uremic patients undergoing chronic hemodialysis: effects on the lipid pattern / Current Therapeutic Research / 1983	Prospective clinical trial	Cholesterol TG HDL Group A: l-carnitine 1 gm IV after HD for 40 days then placebo for 6 weeks OR Group B: Placebo for 40 days then l-carnitine 1 gm IV after HD for 6 weeks	27 patients 14 males 13 females Average age: 41 years Study conducted in Italy.	Group A: Baseline 40 days 80 days TG 178 164 190 Chol 195 202 225 HDL 50 58 56 Group B: Baseline 40 days 80 days TG 158 118 104 Chol 145 185 178 HDL 54 48 58	Although patients were randomly assigned to Group A or Group B, comparisons were made only in a before-after fashion within each group, not between groups. Increase in HDL levels appear to be statistically significant, although the comparisons are a bit unclear. TG and chol levels did not change significantly as a result of carnitine therapy. The effects disappeared with discontinuation of carnitine treatment.

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Caruso U, Leone L, Cravotto E, Nava D. / Effects of L-carnitine on anemia in aged hemodialysis patients treated with recombitant human erythropoietin: a pilot study. / Dialysis and Transplantation / 1998	Randomized controlled trial	rHuEPO dose Hct RBC Total carnitine Free carnitine Patients randomized to receive either 1 gm L-carnitine IV post-HD for 6months, or placebo. After randomization, 3 months of no treatment	31 patients 16 males 15 females Age range: 41-95 years Experimental group: 11 males 4 females Mean age: 67.6 years Control group: 5 males 11 females Mean age: 65.7 years Inclusion criteria: rHuEPO therapy >9 mos Age > 40 years Dialytic age > 1 year Hct 30-35 Normal iron status Exclusion criteria: Anemia other than that due to uremia Carnitine treatment in last 2 months PTH > 150 Aluminum intoxication Uncontrolled HTN Severe liver disease Other severe illnesses Pregnancy Study conducted in Rome.	Experim Control rhUEPO dose Baseline 4833 5875 Month 6 5167 5875 Followup 6364 7125* * p < 0.05 Hct Baseline 33 32.8 Month 6 33.3 30.8 Followup 33 29.9 RBC Baseline 3.33 3.29 Month 6 3.57 3.28 Followup 3.50 3.16 Beneficial effects disappeared when L-carnitine was discontinued. For patients > 65 years, Hct was significantly lower than baseline.	Benefits most pronounced in patients > 65 years, specifically reduction in rHuEPO needs. 3 patients dropped out. Control and experimental groups were not well-balanced in terms of gender. Most data not presented for patients > 65 years of age although authors state data is statistically significant.

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Casciani C, Caruso U, Votto E, Corsi M, et al / Beneficial effects of l-carnitine in post-dialysis syndrome / Current Therapeutic Research / 1982	Prospective clinical trial (double blind, cross-over)	Carnitine Asthenia Cramp Intradialysis hypotension Dyspnea after exertion Precordial pain Cardiopalmus Insomnia Epigastric pain Nausea Vomiting Altered appetite Group 1: L-carnitine 990 mg orally for 60 days, 10 days washout, and then placebo for 60 days, OR Group 2: placebo for 60 days, then 10 days washout, and then l-carnitine 990 mg orally for 60 days	18 patients 11 males 7 females Age range: 20-45 years	Group 1: Baseline 60d 130d Asthenia 2.5 0.5* 2.5** Cramps 2.4 0.4* 1.8*** Hypoten 2.3 0.4* 1.4+ Dyspnea 1.8 0.1* 1.5 * p< 0.001 ** p< 0.01 *** p< 0.02 + p< 0.05 Group2: Baseline 60d 130d Asthenia 2.4 2.0 0.6* Cramps 2 .0 2.0 1.0** Hypotens 1.5 1.5 0.2* Dyspnea 1.8 1.6 0.4* * p< 0.01 ** p < 0.05	Asthenia, cramp, intradialysis hypotension, dyspnea after exertion showed an inverse relationship to serum carnitine levels. Symptom assessment may not have been standardized. Data presented in histograms.

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Chan MK, Persaud J, Varghese Z, Baillod R, et al / Response patterns to DL-carnitine in patients on maintenance hemodialysis / Nephron / 1982	Prospective clinical trial	Chol TG HDL FFA DL-carnitine 300 mg BID for 8 weeks then 600 mg BID for 12 weeks, Drug given orally	10 hypertriglyceridemic HD patients 5 males 5 females Mean age: 43.8 years Exclusion criteria: Thyroid disease Patients taking estrogens, androgens, or beta blockers.	Baseline Week 8 Week 12 Chol 6.24 6.62 6.23 TG 3.62 3.10 3.92 HDL 0.67 0.70 0.60 FFA 270 176 166* * p<0.05	Authors note that there were "responders" and non responders" but do not give split data; overall results are not significant. It would be interesting to know the characteristics of the responders. There was a rise in TG with the high-dose carnitine. Two patients have sever neuromuscular symptoms (myasthenia-like).
Elisaf M, Bairaktari E, Katopodis K, Pappas M, et al / Effect of L-carnitine supplementation on lipid parameters in hemodialysis patients / American Journal of Nephrology / 1998	Prospective clinical trial	Carnitine TG Chol HDL Lp(a) Apo A Apo B L-carnitine 5 mg/kg IV post HD	28 Greek dialysis patients 16 males 12 females Mean age: 43 years (21-61) Patients used either acetate or bicarbonate dialysate. Exclusion criteria: DM with glucose > 140 or treated with oral hypoglycemic agents or insulin Primary hyperlipidemia Secondary dyslipidemia Previous/current carnitine treatment Liver failure	Baseline 6 mos Chol 200 195 TG 225 201* HDL 36 36 LDL 120 122 Apo A 126 122 Apo B 128 133 Lp(a) 18.3 18.0 *p=0.03 No differences between acetate and bicarbonate.	Unclear why authors hypothesized differences based on dialysate buffer. No control group

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Fagher B, Cederblad G, Eriksson M, Monti M, et al / L-carnitine and haemodialysis: double blind study on muscle function and metabolism and peripheral nerve function / Scandinavian Journal of Clinical Laboratory Investigation / 1985	Randomized controlled trial	Serum carnitine Muscle carnitine Muscle function and metabolism Dialysis symptoms 2 gm IV l-carnitine 3x/week for 6 weeks OR placebo	28 HD patients Experimental group: 9 males 5 females Mean age: 48 years (28-65) Control group: 8 males 6 females Mean age: 42 years (24-62) Exclusion criteria: Patients on any drug treatment, or had concomitant metabolic disease.	No effect on symptoms such as fatigue, paresthesias, itching, headache, muscle cramps, general condition, dialysis tolerance, appetite, muscular strength. Carnitine administration increased muscle carnitine levels. Carnitine administration only increased serum levels for female patients. No change in muscle strength and endurance by the end of the study. No change in muscle heat production. No changes in peripheral nerve function, except for some small improvements in temperature sensitivity of the hand and foot in the carnitine group.	Short study period. Only female patients showed increased in serum carnitine; this finding has not been observed in other studies, and could be a result of lower initial carnitine levels. Authors detected no evidence that carnitine deficiency led to muscle and nerve dysfunction for HD patients. Study could have been underpowered.

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Fagher B, Cederblad G, Monti M, Olsson L et al / Carnitine and left ventricular function in hemodialysis patients / Scandinavian Journal of Clinical Laboratory Investigation / 1985	Randomized controlled trial	Cardiac function EF LVED diameter Systolic time intervals Plasma carnitine Muscle carnitine L-carnitine 2 gm IV 3x/week for 6 weeks OR placebo	28 HD patients 17 males 11 females Mean age: 45 years (24-65)	Experimental group: Baseline / 6 weeks (change) Qs2I 557 / 1 PEPI 145 / 1 LVETI 415 / 0 A:H ratio 11.2 / 3.1 EF 62 / -0.6 HV 475 / 22 Control group: Baseline / 6 weeks (change) Qs2I 537 / -2 PEPI 139 / -1 LVETI 399 / -1 A:H ratio 10.5 / -0.8 EF 62 / 1 HV 455 / -8 No deficiency in muscle carnitine found. Carnitine concentrations did not correlate with cardiac function.	Carnitine administration increased muscle and carnitine levels, but had no effect on cardiac function.

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Giovenali P, Fenocchip D, Montanari G, Cancellotti C, et al / Selective trophic effect of l-carnitine in type I and II a skeletal muscle fibers. / Kidney International / 1994	Prospective clinical trial	Trophic effect on type I and II a skeletal muscle fibers, as measured by biopsy Muscle strength Muscle carnitine Plasma carnitine General clinical symptoms Group 1: 0.0725 mM/liter carnitine for dialytic solution Group 2: 2 gm l-carnitine orally Group 3: L-carnitine 2 gm IV post dialysis Study lasted 24 weeks	26 patients Exclusion criteria: Malignancies Liver failure Severe hypertension Concomitant diseases affecting the skeletal muscle function Treatment with anabolistic compounds Previous treatment with carnitine during previous 6 months Group 1: 7 males, 4 females Mean age: 55.5 years Group 2: 4 males, 2 females Mean age: 50.9 years Group 3: 6 males, 3 females Mean age: 54.8 years	Both serum and muscle carnitine levels increased in all 3 groups, which was statistically significant. There was no statistical difference in the proportion of single types of muscle fibers before and after treatment. Mean diameter values after treatment were significantly greater in both sexes than pre-therapy values in type I and II a , but not in type II b fibers. Percentage of atrophic fibers (type I and II a) fell after therapy while no changes noted in type II b fibers. Improved muscle strength in Group 1 and 3.	Effects noted on Type I and II a fibers, possibly related to the use of carnitine for fatty acid oxidation to produce energy. No changes in Type II b fibers, which depend on glycolysis. Muscular atrophy seems not to be associated with carnitine deficiency.

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Golper TA, Wolfson M, Ahmad S, Hirschberg R, et al / Multicenter trial of l-carnitine in maintenance hemodialysis patients. I. Carnitine concentrations and lipid effects. / Kidney International / 1990	Randomized controlled trial (multicenter)	Total carnitine Free carnitine LDL Chol HDL TG Apo A Apo B Apo E Patients randomized to either: L-carnitine 20 mg/kg IV after HD for 6 months OR placebo	Experimental group 38 patients 24 males 24 females Mean age: 47.5 years Control group 44 patients 27 males 17 females Mean age: 48 years Inclusion criteria: Maintenance HD patients (> 9 months) Clinically stable Exclusion criteria: Diabetes Prior/current carnitine treatment Lipid lowering agents Class IV angina Malignant hypertension Liver failure Endocrinopathies Malignancy Unreliable behavior patterns	Experimental group: Baseline Month 6 Tot car 61 466 p<0.001 LDL 107 99 Chol 188 189 HDL 35 36 TG 198 170 Apo A 124 120 Apo B 99 98 Apo E 5.7 5.6 Control group: Baseline Month 6 Tot car 62 58 LDL 112 109 Chol 188 181 HDL 37 36 TG 166 170 Apo A 123 124 Apo B 101 98 Apo E 5.5 5.5	15 patients dropped out of study. Unclear if intent-to-treat analysis was performed.

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Guarnieri GF, Ranieri F, Togio G, Vasile A, et al / Lipid-lowering effect of carnitine in chronically uremic patients treated with maintenance hemodialysis / American Journal of Clinical Nutrition / 1980	Randomized controlled trial (single center)	Carnitine levels TG Cholesterol (obtained before dialysis, after an overnight fast, before treatment, and after 6 and 14 weeks, 1 month after end of treatment) Patients were given l-carnitine IV 500 mg after HD 3x/week for 8 weeks, followed by 1gm for 6 weeks.	16 patients Mean age: 47 years (range 24-66) Randomly assigned to treatment with carnitine or placebo (8pts each arm) Baseline characteristics: Control group: carnitine 40 TG 329 chol 192 Experimental group: Carnitine 39 TG 336 Chol 283 Inclusion criteria: Trigylcerides > 200 mg/dl Exclusion criteria: Diabetes Patients were encouraged not to modify their eating habits, nor did they receive any drug affecting lipid metabolism. Study conducted in Italy	Baseline 6wks 14wks Experimental Carn 39 106 96 p<0.05 TG 336 345 244 p<0.05 Chol 283 249 229 p NS Control Carn 40 37 51 TG 329 382 444 Chol 192 201 202 Student's t-test for paired data and linear regression used.	Short term study. Limited statistical analysis provided. Unclear of the clinical significance of the outcome measures.

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Kletzmayr J, Mayer G, Legenstein E, Heinz-Peer G, et al / Anemia and carnitine supplementation in hemodialyzed patients / Kidney International / 1999	Randomized clinical trial (single center)	Total carnitine Free carnitine Acyl carnitine Hgb EPO EPO resistance index A. L-carnitine IV (15 pts 5 mg/kg; 5 pts 25 mg/kg) for 8 months B. placebo for 8 months	40 patients 37 patients evaluated at T4; 28 patients finished the study. Experimental: Mean age: 54.3 years 8 females 12 males Control: Mean age: 51.3 years 11 females 9 males Inclusion criteria: Stable HD Stable EPO requirement Stable Hgb (9-12 g/dl) Exclusion criteria: Blood loss Transfusion in past 6 months All patients had IV iron for 4 months. Study conducted in Austria.	Experimental: Baseline 4mos 8 mos Tot car 53 72 80 * Free car 31 43 42* Acyl car 22 30* 39* Hgb 10.6 EPO 172 152 * p< 0.05 Control: Baseline 4mos 8 mos Tot car 57 55 60 Free car 32 31 33 Acyl car 25 24 28 Hgb 10.7 EPO 144 158	After withdrawal of iron therapy, EPO requirements increased in both groups. More than 50% of patients showed no benefit. Follow-up values for Hgb not provided. Unclear if an intent-to-treat analysis performed. Subgroup analyses if responders did not incorporate a Bonferonui adjustment to the p-value. Authors comment that "further studies to identify those HD patients who might have a benefit of carnitine supplementation, as well as studies concerning the optimal dosage, duration, and way of administration of carnitine supplementation and its mechanism of action are required."

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Labonia WD / L-carnitine effects on anemia in hemodialyzed patients treated with erythropoietin / American Journal of Kidney Diseases / 1995	Randomized controlled trial (single-center)	Total carnitine Free carnitine Hct RBC osmotic fragility Endogenous EPO secretion Lipids Iron status L-carnitine 1000 g given IV after each HD session, 3x weekly, for 6 months	24 patients randomly assigned 13 experimental group (6 male, 7 female) Mean age: 41.8 years (25-71) 11 control group (5 male, 6 female) Mean age: 62.5 years (54-76) Inclusion criteria: Chronic HD > 1 yr Epo use > 6 months Hct 28-33% Normal iron status Exclusion criteria: Prior carnitine treatment in last 6 months Severe hyperparathyroidism Blood transfusion in last 6 months Study conducted in Argentina	Experimental group Baseline 6mos Tot car 70 395 * Free car 42 248 * Plasma EPO 33 29 EPO dose/wk 102 63 ** Osm fragility 0.4 0.4 Hct 29.8 29.1 Chol 161 144 HDL 30.7 38.5 TG 123 107 * p <0.02 ** p< 0.001 Control group Baseline 6mos Tot car 63 72 Free car 36 47 Plasma EPO 40 33 EPO dose/wk 79 80 Osm fragility 0.4 0.4 Hct 30 28 *** Chol 174 165 HDL 35 43 TG 122 139 *** p <0.05	In the active treatment group, the changes in EPO dose were driven by 7 patients (responders) while 6 had no response. Authors speculate that L-carnitine deficiency might promote EPO resistance in dialyzed patients, which might be corrected by L-carnitine supplementation, and thereby reduce EPO requirements.

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Lacour B, Chanard J, Haguet M, Basile C, et al / Carnitine improves lipid anomalies in hemodialysis patients / Lancet / 1980	Prospective clinical trial	Chol TG HDL Phospholipids (Taken at weekly intervals) Daily dose of 2.4 g carnitine orally for 30 days	51 HD patients with hypertriglyceridemia. Mean age: 42 years Exclusion criteria: Obesity DM Endocrinopathies Overt GI or hepatic disorders Patients on lipid-lowering medications, or thiazides, steroids, or salicylates.	Baseline 15 day 30 day Chol 5.8 5.8 5.6 TG 3.5 3.0 3.0 * HDL 0.9 1.0 1.4 ** phosphol 4.0 3.76 3.5 ** * p < 0.01 ** p < 0.001	Minimal statistical analysis provided. Data presented in figures, rather than tables, making it difficult to discern precise numbers.

Author / Title / Journal / Year	Type of Study	Outcomes Studied	Patient Characteristics	Results	HCFA Comments
Maebashi M, Imamura A, Yoshinaga K, Sato T, et al / Carnitine depletion as a probable cause of hyperlipidemia in uremic patients on maintenance hemodialysis / Tohoku Journal of Experimental Medicine / 1983	Prospective clinical trial	Carnitine TG Chol HDL LDL A. 25 patients received no intervention as were followed observationally (split into HD < 6 months, and > 24 months) B. 18 patients placed on amino acid supplements and followed observationally C. 15 patients received carnitine treatment 6 patients IV DL-carnitine 3 gm with HD x 6 treatments 9 patients 1.2 gm DL-carnitine orally for 4 weeks (daily)	58 patients Ages 25-50 years Exclusion criteria: Patients with diabetes or lipid disorders. Study conducted in Japan.	Group A The serum concentration of carnitine in the long-term dialysis patients was significantly lower than that in the short-term dialysis. There was a slight increase in TG Group B TG remained within normal range. No differences in carnitine levels. Group C Without carnitine, TG increased; with carnitine treatment, TG remained unchanged. No change in HDL.	Limited data provided. The group receiving oral carnitine had a much higher TG level than the other groups. IV carnitine did not lower TG or cholesterol levels.

Author / Title / Journal / Year	Type of Study	Outcomes Studied	Patient Characteristics	Results	HCFA Comments
Matsumura M, Hatakeyama S, Koni I, Mabuchi H, et al / Correlation between serum carnitine levels and erythrocyte osmotic fragility in hemodialysis patients / Nephron / 1996	Case series	Total carnitine Free carnitine Acyl-carnitine Erythrocyte osmotic fragility Mean hemolysis end point (HEP) Hemolysis maximum point (HMP) Hemolysis start point (HSP)	26 patients 10 male 16 female Mean age: 57.3 years (27-84) Exclusion criteria: Iron deficiency Uncontrolled hyperparathyroidism Infection Aluminum toxicity Inflammatory disease ESRD not from DM Study conducted in Japan.	Significant negative correlations were found in the following comparisons: serum TC levels versus HEP and HMP, serum FC levels versus HMP, serum AC levels versus HEP, serum TC levels versus rhEPO dose, serum FC levels versus rhEPO dose. No correlation between any hemolysis point and reticulocyte counts.	Limited data provided. Authors conclude that carnitine may contribute to the metabolism of erythrocyte membrane and have an impact on the efficacy of rhEPO in correcting renal anemia.

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Nilsson-Ehle P, Cederblad G, Fagher B, Monti M, et al / Plasma lipoproteins, liver function and glucose metabolism in haemodialysis patients: lack of effect of l-carnitine supplementation / Scandinavian Journal of Clinical Laboratory Investigation / 1985	Randomized controlled trial	TG Cholesterol HDL LDL Insulin Glucose Galactose TSH Hgb L-carnitine 2 gm IV 3x/week for 6 weeks OR placebo	28 HD patients Age range: 24-65 years Experimental group: 9 males 5 females Mean age: 48 years (28-65) Control group: 8 males 6 females Mean age: 42 years (24-62) Exclusion criteria: Patients on any drug treatment, or had concomitant metabolic disease.	Experimental group Baseline 6 weeks (% change) TG 2.5 0.12 Cholesterol 6.2 0.05 HDL 1.1 0.06 LDL 4.0 0.01 Insulin 9.9 - 0.9 Glucose 4.7 -0.2 Galactose 13.0 1.4 TSH 3.0 -0.6 Hgb 84 0.6 Control group Baseline 6 weeks (% change) TG 3.1 -0.4 Cholesterol 6.6 0.09 HDL 1.3 0.01 LDL 3.9 0.08 Insulin 16.2 -2.2 Glucose 4.5 0.1 Galactose 13.0 0.8 TSH 3.0 0.2 Hgb 85 0.1	Short study period Data reported in terms of delta as opposed to actual numbers. No effect on any variables noted. No differences in subpopulations.

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Rocchi L, Feola I, Calvani M, D'Iddio S, et al / Effects of carnitine administration in patients with chronic renal failure undergoing periodic dialysis, evaluated by computerized electromyography / Drugs Experimental Clinical Research / 1986	Prospective clinical trial	EMG activity All patients treated with placebo for 1 month, followed by l-carnitine 3 gm IV for 7 months.	20 patients 14 males 6 females Mean age: 46.6 years (31-63)	After carnitine treatment: Increase in the total power of the surface EMG activity ($p<0.001$) Spectral array showed a progressive shift towards lower frequencies in the 8 cases who had shown higher values. Reduction in number of polyphasic action potentials in 5 cases. Normalization of maximal MCV occurred in 2 patients. Normalization of minimal MCV occurred in 3 patients.	Need to better discern the clinical relevance of these effects.
Sakurauchi Y, Matsumoto Y, Shinzato T, Takai I, et al / Effects of l-carnitine supplementation on muscular symptoms in hemodialyzed patients / American Journal of Kidney Disease / 1998	Prospective clinical trial	Muscle symptoms (evaluated at week 2, 4,8, and 12) Plasma carnitine fractions Lipid profiles Patients received 500 mg oral carnitine daily for 12 weeks or placebo	30 patients with muscular weakness, fatigue, or cramps/aches. 12 male 18 female Mean age: 62 years (34-78) 21 patients with no muscle symptoms 9 men 11 women Mean age: 57.8 years (26-66)	Carnitine levels were lower in the group with muscle symptoms. 2/3 of patients had some improvement in muscle symptoms. No change in lipid profiles.	Unclear assessment method for determining muscle weakness. The scores were subjective and not compared to the control group. Little data provided for control group. Most data was shown in figures, making abstraction of data points imprecise.

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Semeniuk J, Shalansky KF, Taylor N, Jastrzebski J, et al / Evaluation of the effect of intravenous l-carnitine on quality of life in chronic hemodialysis patients / Clinical Nephrology / 2000	Randomized controlled trial (crossover design)	QOL (as measured by the Kidney Dialysis Questionnaire) Heart rate Blood pressure Hgb Serum electrolytes Iron indices L-carnitine (20 mg/kg) or placebo IV after each HD session for 12 weeks, followed by a 6 week washout period, then the crossover therapy for 12 weeks.	30 patients initially screened; 12 refused, 2 were withdrawn in first 3 weeks of trial. 16 patients 5 males 11 females Mean age: 66.9 years Inclusion criteria: HD > 1 yr Two of the following symptoms: Intradialytic hypotension Muscle cramping Lack of energy Muscle weakness/myopathy Cardiomyopathy Lack of response to EPO Exclusion criteria: Mentally incompetent to complete a QOL questionnaire.	No significant effect of l-carnitine on QOL irrespective of treatment order. No differences in any secondary outcomes, including incidence of muscle cramping, intradialytic hypotension, EPO requirements, or hemoglobin.	Authors failed to demonstrate a benefit of QOL in their patient population. Study might have been underpowered to detect any differences.

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Siami G, Clinton ME, Mrak R, Griffis J, et al / Evaluation of the effect of intravenous l-carnitine therapy on function, structure, and fatty acid metabolism of skeletal muscle in patients receiving chronic hemodialysis / Nephron / 1991	Randomized controlled trial (single center)	Plasma carnitine Muscle carnitine Muscle strength Fatty acid oxidation 2 gm carnitine given IV after HD 3/week for 6 months, then 1 month washout, then 10 months of 1 gm IV post HD Double blind manner with placebo.	14 male patients receiving HD, who were stable medically, and had presence of muscle weakness.	Experimental group Baseline 6 mos Muscle carnitine 17.2 52.6 Patient activity score 3.4 2.0 Control group Baseline 6 mos Muscle carnitine 18.3 22.0 Patient activity score 3.5 3.1 Plasma carnitine levels were increased by IV carnitine supplementation. 4/7 experimental patients had clear improvement in muscle activity while 3/7 control patients had clear improvement.	Unclear as to the validity of the muscle strength rating scale; all assessments were made by the author.

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Sloan RS, Kastan B, Rice SI, Sallee CW, et al / Quality of life during and between hemodialysis treatments: role of l-carnitine supplementation / American Journal of Kidney Diseases / 1998	Randomized controlled trial Cross-over study (placebo-control)	SF -36 measured at baseline, and 1.5 month intervals Intradialytic symptoms Kt/V urea Level of nutrition Patients randomized to 2 groups: A. 1000 mg oral carnitine before and after HD, or placebo for 6 months B. Cross over 3 months placebo, then 3 months carnitine OR 3 months carnitine, then 3 months placebo	101 patients, clinically stable on HD. 60% men 38% diabetic Mean age 52.2 years (23-82) Stratified by age and DM. Inclusion criteria: Stable HD patients Exclusion criteria: Prior carnitine treatment	For Group A, at 1.5 months, carnitine treatment had increased scores for physical functioning and general health, but over 6 months, the sloe for these dropped greater than for the placebo group. For Group B, at 1.5 months, carnitine treatment had increased scores for vitality, and general health; there was no change in slope compared to placebo. For physical role, there was no change at 1.5 months, but over 6 months, the slope increased for the carnitine treatment group. For all patients on carnitine for 6 months, there was a negative effect on perception of general health, mental health, and vitality. There were no changes in intradialytic symptoms.	Results were counter to the investigator's premise that carnitine supplementation improves quality of life for ESRD patients. Carnitine treatment had an early positive effect on some measures, however, it is not sustained beyond 3 months, and by 6 months, the scores were actually lower than baseline. Of note, serum albumin concentration was directly correlated to how patients perceived their quality of life.

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Spagnoli LG, Palmieri G, Mauriello A, Vacha G, et al / Morphometric evidence of the trophic effect of l-carnitine on human skeletal muscle / Nephron / 1990	Prospective clinical trial	Morphometric parameters Serum carnitine Muscle carnitine Muscle biopsies taken at 12 months, then 16 months, then 20 months TG Albumin 2 gm l-carnitine given IV post-HD for 12 months. Carnitine treatment then withheld for 4 months, then carnitine added to dialysis fluid for 4 months.	22 patients 12 males 10 females Mean age: 66 years	Diameter of Type I fibers First biopsy 78.2 Second biopsy 75.7 Third biopsy 57.3 P < 0.0002 Total carnitine M=muscle S=serum First biopsy 51.9 M 1297 S Second biopsy 25.2 M 101.2 S Third biopsy 19.2 M 121.1 S p< 0.01 Proximal muscle weakness and cramps did not reappear when l-carnitine therapy was withdrawn. Serum TG increased from 190 to 287 after end of treatment with l-carnitine (p<0.01) By third biopsy, type I fibers had reduction in diameter, while type 2 fibers remained unchanged.	Study may have been too short to appreciate all possible effects.

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Srivastava DK, Kumar S, Misra AP / Reversal of haemodialysis induced hypertriacylglycerolemia by l-carnitine / Indian Journal of Clinical Biochemistry / 1992	Prospective clinical trial	Triacylglycerol Cholesterol HDL Patients followed for 24 weeks. At end of 24 weeks, 8 patients from each group were randomly picked to be the control group. Rest of patients received 5mg/kg l-carnitine orally BID for 3 weeks.	25 HD patients on biweekly treatment, 16 ESRD patients not getting HD Exclusion criteria: Endocrine abnormalities	ESRD group on no dialysis Baseline 24 wk 27wk (% increase) Triacyl 2.56 7.2 - 5.1 * Chol 7.25 5.3 3.2 HDL 1.18 0.6 1.3 *p<0.01 HD patients Baseline 24 wk 27 wk (% increase) Triacyl 2.49 23.0 - 21.6** Chol 6.99 5.8 1.9 HDL 1.21 1.6 1.7 ** p< 0.001	Limited data provided. Results shown in % changes, rather than absolute numbers. Lack of clarity in data reporting. Carnitine may have reversed a trend toward increasing TAG levels No change in lipid profile.
Suzuki Y, Narita M, Yamazaki N. / Effects of l-carnitine on arrhythmias during hemodialysis / Japan Heart Journal / 1982	Prospective clinical trial	Carnitine FFA TG Electrolytes Heart abnormalities measured by ECG 2 gm l-carnitine orally administered 2 hours before each dialysis session x 4-8 weeks	17 patients 9 males 8 females Mean age: 52 years (28-72) All patients had sporadic ventricular or supraventricular beats, or ST-T abnormalities.	L-carnitine decreased arrythmias after 4 and 8 weeks of treatment. There was > 90% reduction in premature beats, and in severity of ventricular premature beats.	Authors speculate that carnitine is effective in treating arrythmias by restoring impaired oxidation of free fatty acids. Data units not always apparent. Most data presented in terms of changes during the course of dialysis, as opposed to the length of the trial, although results concerning arrythmias are presented as changes from baseline to completion of study.

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Thomas S, Fischer FP, Mettang T, Pauli-Magnus C, et al / Effects of l-carnitine on leukocyte function and viability in hemodialysis patients: a double-blind randomized trial / American Journal of Kidney Disease / 1999	Randomized controlled trial (single center)	Leukocyte oxidative metabolism Phagocytic function Morbidity Anemia BUN Creatinine Total carnitine Free carnitine Acyl carnitine WBC Self-assessment -- frequency of angina, intensity of muscle cramps, muscle strength, pruritus, and general well-being (measured on a visual analogue scale L-carnitine 10 mg/kg IV after HD for 4 months OR Placebo	17 patients 8 experimental 5 women 3 men Mean age: 59.5 years 9 control 6 women 3 men Mean age: 64.6 years Exclusion criteria: Diabetes Cancer Immunosuppressive therapy Prior carnitine treatment Study conducted in Germany.	Experimental group: Baseline 4 months Tot car 34 137 p<0.05 Free car 23 91 p<0.05 Acyl car 12 46 p<0.05 WBC 7.4 7.5 Hct 31 32 Control group: Baseline 4 months Tot car 41 31 Free car 24 19 Acyl car 16 13 WBC 5.4 5.1 Hct 33 36 No changes in self-assessment measures; no changes in phagocytic activity.	No beneficial effects demonstrated. 2 patients withdrew from study; unclear if an intent-to-treat analysis was performed.

Author / Title / Journal / Year	Type of Study	Outcomes Studied	Patient Characteristics	Results	HCFA Comments
Trovato G, Ginardi V, Di Marco V, Dell'aira A, et al / Long-term L-carnitine treatment of chronic anaemia of patients with end-stage renal failure / Current Therapeutic Research / 1982	Randomized controlled trial	Hgb Hct Red cell count MCV Reticulocyte Iron Transferrin L-carnitine 1.6 gm oral daily for 12 months OR placebo	26 HD patients 13 males 13 females Average age: 47.5 years (22-68)	Control group Baseline / 12 months Hgb 8.3 / 2.46 Hct 24 / 22 MCV 89.8 / 90.3 Retic 0.51 / 0.53 Iron 45.6 / 53.2 Transferrin 284 / 264 Experimental group Baseline / 12 months Hgb 7 / 12.25** Hct 25 / 37*** MCV 91 / 88 Retic 0.44 / 0.48 Iron 50 / 57 Transferrin 258 / 256 ** p<0.01 *** p<0.001	Improvement started at 3 months. Further increases in successive months. No side effects observed. 2 patients in placebo group excluded since they required a blood transfusion.

Author / Title / Journal / Year	Type of Study	Outcomes Studied	Patient Characteristics	Results	HCFA Comments
Vacha GM, Giorcelli G, DiIddio S, Valentini G, et al / L-carnitine addition to dialysis fluid: a therapeutic alternative to hemodialysis patients. / Nephron / 1989	Prospective clinical trial	Serum carnitine Muscle carnitine Lipid profile Serum chemistry Serum hematology 2 gm IV L-carnitine post-HD for 12 months. Treatment with L-carnitine discontinued for 4 months. Then patients divided into 2 groups. Received 1 gm IV l-carnitine post-HD for 1 month. Then l-carnitine was added to the dialysate (2gm group 1, 4 gm group 2) for 3 months.	22 HD patients Group 1 7 males 4 females Mean age: 66 years Group 2 5 males 6 females Mean age: 61 years	Group 1 Baseline 4 mos 5 mos 8 mos Free car 542 41* 187* 71* TG 199 274** 240 198 Chol 170 181 90*** 201 HDL 40 38 40 48* Apo A 190 170* 188 200 * p< 0.001 ** p<0.05 *** p< 0.02 Group 2 Baseline 4 mos 5 mos 8 mos Free car 576 61* 214* 98* TG 180 299* 200 160 Chol 165 195* 200* 190** HDL 35 32 35 48* Apo A 190 160** 180 192 * p< 0.001 ** p< 0.05 Muscle biopsies demonstrated "supernormal" muscle concentrations of free carnitine with long-term IV l-carnitine therapy. No significant differences were observed between the 2 gm and 4 gm doses of l-carnitine added to the dialysate.	Authors conclude that the therapeutic objectives in the supplementation of hemodialysis patients with l-carnitine may be best achieved with short-term IV administration followed by long-term administration through the dialysate.

Author / Title / Journal / Year	Type of Study	Outcomes Studied	Patient Characteristics	Results	HCFA Comments
Vacha GM, Giorcelli G, Siliprandi N, Corsi M. / Favorable effects of l-carnitine treatment on hypertriglyceridemia in hemodialysis patients: decisive role of low levels of high-density lipoprotein-cholesterol / American Journal of Clinical Nutrition / 1983	Prospective clinical trial	Cholesterol TG HDL LDL Apo A Hct L-carnitine (20 mg/kg) IV post-HD for 120 days, then placebo for 120 days At end of trial, l-carnitine dosage was increased to 60 mg/kg IV in four patients of the group of nonresponders.	29 HD patients with hypertriglyceridemia 16 males 13 females Mean age: 49 years (21-78) Group A: 12 patients TG > 300 chol < 250 HDL < 40 Group B: 17 patients TG > 300 chol < 250 HDL > 40	A reduction in TG was observed only in 12 patients with high TG, low HDL, and normal Apo A. L-carnitine did not change lipid parameters in patients with high TG, normal HDL, and normal Apo A. Hct values increased in all 29 patients.	Authors speculate that l-carnitine can be especially effective in managing hypertriglyceridemia when patients have low HDL. No side effects observed.

Author / Title / Journal / Year	Type of Study	Outcomes Studied	Patient Characteristics	Results	HCFA Comments
Van Es A, Henny FC, Kooistra MP, Lobatto S, et al / Amelioration of cardiac function by l-carnitine administration in patients on haemodialysis / Contributions Nephrology / 1992	Prospective clinical trial	Total carnitine Free carnitine Ejection fraction L-carnitine 1 gm IV for 3 months	56 patients 16 experimental 40 healthy controls Inclusion criteria: HD > 1 year Bicarbonate dialysis Polysulfone high flux dialyzer HD frequency/time unchanged during the study Hct > 0.30 for more than 3 months, or without EPO No carnitine administration prior to start of study Exclusion criteria: HTN DBP > 95 Fluid overloading History of mi Change in meds during study	EF before tx EF post tx 42 48 Total carnitine Control 42.6 Experimental 50.9 Free carnitine Control 21.5 Experimental 40.2 p < 0.01	Methodology of study not well described. EF not compared between experimental and control group. Overall, no difference except for the "symptomatic" (recurrent hypotensive episodes) group 3 patients lost to followup.

Author / Title / Journal / Year	Type of Study	Outcomes Studied	Patient Characteristics	Results	HCFA Comments
Wanner C, Forstner-Wanner S, Schaeffer G, Schollmeyer P, et al / Serum free carnitine, carnitine esters and lipids in patients on peritoneal dialysis and hemodialysis / American Journal of Nephrology / 1986	Prospective clinical trial (single-center)	Total carnitine Free carnitine Short chain Acyl Long chain Acyl Patients received 1 gm l-carnitine at end of hemodialysis 3/week for 3 months. Labs obtained before dialysis, and at 2,4, 8, and 12 weeks.	41 patients (23 HD, 15 CAPD, 3 IPD) 22 male 19 female Mean age 52 years (26-79) 20 control (medical personal staff) Study conducted in Germany.	HD Group Baseline 4 wks 12 wks Tot car 50 275 * 314* Free car 32 176 * 208* Short acyl17 96 * 100* Long acyl 1.2 6.7* 7.1* * p<0.0001 TG 185 273* 227 Chol 187 190 182 HDL 32 28 30 LDL 139 143 141 * p<0.05 Total carnitine and free carnitine as well as short acyl were higher in female than male patients.	Limited data provided. No information on controls. Little information on the CAPD and IPD patients. This study is essentially on 23 HD patients. Inclusion/exclusion patient criteria not specified. A rise in TG was noted; otherwise there was no effect on lipid profile. Little explanation given for differences in carnitine levels based on gender.

Author / Title / Journal / Year	Type of Study	Outcomes Studied	Patient Characteristics	Results	HCFA Comments
Weschler A, Aviram M, Levin M, Better O, et al / High dose of l-carnitine increases platelet aggregation and plasma trigylceride levels in uremic patients in hemodialysis / Nephron / 1984	Randomized controlled trial (single center)	Lipoprotein levels Platelet aggregation Given 3g/day l-carnitine orally for 5 weeks	10 uremic patients on HD were randomly selected into a control or experimental group. 6 experimental 4 control Average age: 50.8 years (36-66) 8 males 2 females Study conducted in Israel.	Experimental group Baseline 5 weeks TG 180 219 p<0.05 Chol 172 01 Apo A 163 165 Apo B 102 102 Epinephr 51 61 p<0.05 ADP 46 67 p<0.05 Thrombin 72 86 p<0.05 Control group Baseline 5 weeks TG 222 222 Chol 165 190 Apo A 180 156 Apo B 93 99 Epinephr 60 54 ADP 56 59 Thrombin 79 84	Small study size. Inclusion/exclusion criteria not specified. Following carnitine administration, a rise in TG was noted. A significant rise in platelet aggregation also observed. Findings suggested a harmful effect of l-carnitine when given in high doses.

Author / Title / Journal / Year	Type of Study	Outcomes Studied	Patient Characteristics	Results	HCFA Comments
Yderstraede KB, Pedersen FB, Dragsholt C, Trostmann A et al / The effect of l-carnitine on lipid metabolism in patients on chronic haemodialysis / Nephrology Dialysis Transplantation / 1987	Randomized controlled trial (single center)	Carnitine TG HDL LDL apo A apo B Measured at baseline and monthly intervals. Loss of carnitine to dialysis fluid also measured. L-carnitine added to dialysate (100 micromoles/L) for 6 months	21 patients on chronic hemodialysis (median time 35 months) Median age: 49 years (20-72) 16 males 5 females Inclusion criteria: Stable HD at least 6 months Abnormal (high) HDL or LDL Exclusion criteria: Normal lipids Steroid treatment Patients randomized to treatment with either carnitine or placebo; double-blinded. 10 patients studied 1.5 years. Study conducted in Denmark.	Experimental Baseline 6 mos Carnitine 62 96* TG 2.7 2.7 Chol 4.9 5.0 HDL 0.6 0.7 LDL 3.0 3.2 Apo A 1.5 1.3 Apo B 1.0 1.3 *p < 0.001 Control Carnitine 62 56 TG 2.6 2.5 Chol 5.2 5.5 HDL 0.7 0.7 LDL 3.4 3.7 Apo A 1.5 1.4 Apo B 1.1 1.5 There was a significant correlation between the total loss of carnitine and the number of consols used.	Only carnitine levels in the treated group were statistically significant. All other values were not statistically different.