2. Swanton RH, Thomas ML, Coltarte DJ, Jenkins BS, Webb-Peploe MM, Williams BT. Coronary artery ectasia, a variant of occlusive coronary arteriosclerosis. *Br Heart J* 1978;40:393–400.
3. Markis JE, Joffe CD, Cohn PF, Feen DJ, Herman MV, Gorlin R. Clinical significance of coronary artery ectasia. *Am J Cardiol* 1976;37:217–222.
4. Gabay C, Kushner I. Acute phase proteins and other systemic responses to inflammation. *N Engl J Med* 1999;340:448–454.
5. Biasucci L, Colizzi C, Rizzello V, Vitrella G, Crea F, Liuzzo G. Role of inflammation in the pathogenesis of unstable coronary artery disease. *Scand J Clin Lab Invest* 2000;59:12–22.
6. Koch AE, Haines GK, Rizzo RJ, Radosevich JA, Pope RM, Robinson PG, Pearce WH. Human abdominal aortic aneurysms. Immunophenotypic analysis suggesting an immune-mediated response. *Am J Pathol* 1990;137:1199–1213.
7. Falsetti HL, Carroll RJ. Coronary artery aneurysm. *Chest* 1976;69:630–636.
8. Williams MJA, Stewart RAH. Coronary artery ectasia: local pathology or diffuse disease? *Cathet Cardiovasc Diag* 1994;33:116–119.
9. Morrow DA, Ridker PM. C-reactive protein, inflammation, and coronary risk. *Med Clin North Am* 2000;84:149–161.
10. Tracy RP. Inflammation markers and coronary heart disease. *Curr Opin Lipidol* 1999;10:435–551.
11. Brophy CM, Reilly JM, Smith GJ, Tilson MD. The role of inflammation in nonspecific abdominal aortic aneurysm disease. *Ann Vasc Surg* 1991;5:229–233.
12. Patel MI, Hardman DT, Fisher CM, Appleberg M. Current views of the pathogenesis of abdominal aortic aneurysms. *J Am Coll Surg* 1995;181:371–382.
13. Powell JT, Muller BR, Greenhalgh RM. Acute phase proteins in patients with abdominal aortic aneurysms. *J Cardiovasc Surg (Torino)* 1987;28:528–530.
14. Azar RR, Aoun G, Fram DB, Waters DD, Wu AH, Kiernan FJ. Relation of C-reactive protein to extent and severity of coronary narrowing in patients with stable angina pectoris or abnormal exercise tests. *Am J Cardiol* 2000;86:205–207.
15. Arroyo-Espliguero R, Avanzas P, Cosín-Sales J, Aldama G, Pizzi C, Kaski JC. C-reactive protein elevation and disease activity in patients with coronary artery disease. *Eur Heart J* 2004;25:401–408.

Effect of *Atorvastatin* on Left Ventricular Diastolic Function and Ability of Coenzyme Q_{10} to Reverse That Dysfunction

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This study evaluated left ventricular diastolic function with Doppler echocardiography before and after statin therapy. Statin therapy worsened diastolic parameters in most patients; coenzyme Q_{10} supplementation in patients with worsening diastolic function with statin therapy improved parameters of diastolic function. ©2004 by Excerpta Medica, Inc.
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On the basis of the known nonselective inhibition of cholesterol synthesis by statins, previously reported data, and the widespread use of statin therapy, we hypothesized that atorvastatin might have its greatest initial impact on sensitive measures of left ventricular (LV) diastolic heart performance. We therefore prospectively studied 14 asymptomatic patients who were to begin atorvastatin therapy, with baseline and follow-up measurements of clinical status, LV diastolic parameters on Doppler echocardiography, and plasma coenzyme Q_{10} (CoQ_{10}) levels. Ten of the 14 patients (71%) had worsening of $\geq$1 marker of LV diastolic function. Eight of the 9 patients who received CoQ_{10} supplementation with atorvastatin had reversal of $\geq$1 diastolic abnormality.

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The protocol and consent process were approved by the institutional review board for the Protection of Human Subjects of the Advocate Health Care System, and all patients gave informed consent. All patients met the National Cholesterol Education Program's recommendations for initiating pharmacologic therapy. The decision to initiate therapy was made by the primary physician. Patients who began statin therapy as outpatients were eligible for the trial. Patients were excluded if they had poor acoustic windows, were $<$50 years old, had a history of heart failure or previous myocardial infarctions with ejection fractions of $<$40%, had unstable angina pectoris, or were currently receiving statin or CoQ_{10} therapy. Baseline measurements of plasma CoQ_{10}, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triglycerides were made. Standard M-mode, 2-dimensional, and Doppler echocardiograms were performed. The 2-dimensional images were acquired in parasternal long-axis, short-axis, and apical 2-, 4-, and 5-chamber views. Doppler spectral recordings were obtained in the apical 4-chamber view, with the sample volume positioned at the tip of the mitral leaflets. The transmitral pulse Doppler velocity recordings (peak E, peak A, E/A ratio), deceleration time (DT), and isovolumetric relaxation time (IVRT) were averaged from 3 cardiac cycles. The IVRT was obtained in the 5-chamber view with a continuous-wave cursor or a pulse Doppler sample positioned to obtain signals from aortic valve closure and the mitral valve opening. The LV ejection fraction was calculated using the 2-dimensional biplane disk method. After the baseline echocardiogram, patients were initiated on atorvastatin (Lipitor, Pfizer Inc., New York, New York) 20 mg/day for 3 to 6 months. All baseline measurements; plasma CoQ_{10} levels, and standard M-mode, 2-dimensional, and Doppler echocardiography were repeated after 3 to 6 months of statin therapy. Those patients demonstrating $\geq$1 measurement of diastolic LV function that worsened during the 3 to 6 months of statin therapy were supplemented with

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TABLE 1 Demographics, Clinical Characteristics, Cholesterol, and CoQ_{10} Levels of Study Patients (n = 14) Who Were Initiated on Statin Therapy for Hyperlipidemia

Sl No.	Age/Sex	Co-morbidity	Medications	Total Cholesterol Baseline	LDL Baseline	CoQ_{10} Baseline	Total Cholesterol after Statin	LDL after Statin	CoQ_{10} after Statin	CoQ_{10} Supplementation
1	51 Male	DM	OH	203.0	142	0.40	126.0	87	0.4	0.6
2	52 Male	HTN	HCTZ, CCB	247.0	162	1.10	168.0	88	1.2	NS
3	56 Male	HTN	HCTZ, ACEI	256.0	176	0.80	171.0	104	0.8	2.5
4	56 Female	HTN, DM	HCTZ, CCB, ACEI, ARB, OH	210.0	130	1.60	219.0	132	1.7	NS
5	56 Male	HTN, DM	ACEI, OH	233.0	146	1.20	149.0	76	1.5	4.6
6	61 Female	HTN, DM	BB, insulin, OH	218.0	130	0.80	N/A	N/A	1.1	1.1
7	62 Female	HTN	HCTZ	276.0	171	1.00	N/A	N/A	0.8	NS
9	63 Female	HTN, PVD, CVA	HCTZ	228.0	125	1.10	N/A	N/A	0.9	NS
10	70 Female	HTN, DM	BB, ACEI, CCB	267.0	174	0.70	185.0	101	0.7	N/A
11	71 Female	HTN, DM	HCTZ, ACEI, insulin	214.0	144	1.00	N/A	N/A	0.9	1.2
12	77 Female	HTN	CCB	311.0	222	0.90	189.0	124	0.6	1
13	77 Female	HTN	CCB	312.0	243	1.20	243.0	153	1.8	NS
14	79 Female	HTN	BB, ACEI, CCB	230.0	121	1.10	157.0	65	0.9	2.2

ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; BB = β blocker; CCB = calcium channel blocker; CVA = cardiovascular accident; DM = diabetes mellitus; HCTZ = hydrochlorothiazide; HTN = hypertension; LDL = low-density lipoprotein cholesterol; OH = oral hypoglycemic agents; NS = not supplemented.

TABLE 2 Doppler Diastolic Parameters at Baseline and After Statin Therapy from All 14 Patients

Patients	E/A Baseline	E/A After Statin	Change in E/A	Percent Change	DT Baseline	DT After Statin	Change in DT	Percent Change	IVRT Baseline	IVRT After Statin	Change in IVRT	Percent Change
1	1.36	1.05	−0.31	−22.70	204	266	62	30	64	79	15	23.4
2	1.21	1.45	0.24	19.80	194	175	−19	−10	85	85	0	0.0
3	1.36	1.21	−0.15	−11.00	169	190	21	12	114	82	−32	−28.0
4	1.28	1.05	−0.23	−17.00	221	232	11	5	80	83	3	4.0
5	1.70	1.17	−0.53	−31.00	155	179	24	15	83	93	10	12.0
6	0.99	1.16	0.17	17.10	152	260	108	45	101	81	−20	−19.8
7	0.74	0.93	0.19	25.60	230	245	15	6	97	100	3	3.0
8	0.95	0.85	−0.10	−10.50	236	249	13	6	81	92	11	13.5
9	0.87	1.04	0.17	19.50	224	210	−14	−6	106	90	−16	−15.0
10	1.38	1.08	−0.30	−21.70	190	259	69	36	70	112	42	60.0
11	1.47	1.52	0.05	3.00	202	226	24	12	55	81	26	47.0
12	1.34	0.93	−0.41	−30.50	264	300	36	14	80	103	23	28.7
13	0.66	0.67	0.01	1.50	278	265	−13	−5	117	101	−16	−13.6
14	1.45	1.10	−0.35	−24.10	156	250	94	60	118	144	26	22.0

CoQ_{10} 300 mg/day (100 mg orally 3 times daily) for an additional 3 months while continuing to take atorvastatin 20 mg/day. Worsening diastolic function at follow-up was defined as a 10% decrease in the E/A ratio, a 10% increase in E-wave DT, or a 10% increase in the IVRT. Patients who had worsening diastolic parameters on echocardiography and completed supplementation with CoQ_{10} underwent repeat measurements of their plasma CoQ_{10} levels and M-mode, 2-dimensional, and Doppler echocardiographic parameters for systolic and diastolic function after 3 months. The plasma CoQ_{10} levels were measured by liquid chromatography by Richard Willis, PhD, Division of Nutritional Sciences, University of Texas, Austin, Texas.

Initially, 17 patients who began statin therapy as outpatients were enrolled in the trial. Four patients did not complete all phases of the trial; 3 discontinued the study after initial enrollment because of their personal preferences. One patient discontinued statin therapy after 3 months because of myalgia. She had no liver function or creatinine phosphokinase abnormalities but did develop abnormalities in diastolic function. This patient was not supplemented with CoQ_{10}, but her baseline and follow-up echocardiograms were included in the data analysis. The 14 patients included 10 women and 4 men, aged 51 to 79 years (mean 62) who completed 3 to 6 months of statin therapy and completed follow-up. Thirteen patients had associated systemic hypertension, and 6 had diabetes mellitus (Table 1). After statin therapy, patients had significant reductions in total cholesterol (from 246 to 178 mg/dl, $p < 0.005$) and low-density lipoprotein cholesterol (from 160 to 102 mg/dl, $p = 0.005$). The baseline and supplemented CoQ_{10} levels are listed in Table 1.

No patients developed signs or symptoms of heart failure during the study period. No significant changes were seen at 3 to 6 months in left atrial dimension, LV

TABLE 3 Change in Doppler Diastolic Parameters After Supplementation With CoQ_{10}

Patients	E/A After Statin	E/A After CoQ_{10}	Change in E/A With CoQ_{10}	Percent Change	DT After Statin	DT After CoQ_{10}	Change in DT With CoQ_{10}	Percent Change	IVRT After Statin	IVRT After CoQ_{10}	Change in IVRT With CoQ_{10}	Percent Change
1	1.05	0.96	−0.09	−8.5	266	210	−56	−21	79	80	1	1
2	1.45	NS	NS	NS	175	NS	NS	NS	85	NS	NS	NS
3	1.21	1.41	0.2	16.5	190	213	23	12.1	82	79	−3	3.6
4	1.05	Withdrew	Withdrew	Withdrew	232	Withdrew	Withdrew	Withdrew	83	Withdrew	Withdrew	Withdrew
5	1.17	1.39	0.22	18.8	179	151	28	−15.6	93	74	−19	−20.4
6	1.16	1.28	0.12	10.3	260	290	30	11.5	81	71	−10	−12.3
7	0.93	NS	NS	NS	245	NS	NS	NS	100	NS	NS	NS
8	0.85	1.05	0.2	23.5	249	202	−34	−13.6	92	83	−9	−10
9	1.04	NS	NS	NS	210	NS	NS	NS	90	NS	NS	NS
10	1.08	1.37	0.29	26.8	259	280	21	8	112	83	−29	−26
11	1.52	1.4	−0.12	−8	226	220	−6	2.6	81	85	4	5
12	0.93	1.17	0.24	25.8	300	169	−131	−43.6	103	82	−21	−20
13	0.67	NS	NS	NS	265	NS	NS	NS	101	NS	NS	NS
14	1.1	1.26	0.16	14.5	250	150	−100	−40	144	130	−14	−10

NS = not supplemented with CoQ_{10}.

end-diastolic or end-systolic dimensions, LV septal thickness, fractional shortening, or the LV ejection fraction. The diastolic parameters at baseline and with statin therapy are listed in Table 2. Similarly, the comparisons of diastolic parameters before and after CoQ_{10} supplementation are listed in Table 3. Ten of the 14 patients (71%) had worsening of ≥1 marker of LV diastolic performance (E/A ratio, DT, or IVRT), 5 patients (36%) had worsening of all 3 markers, and 3 patients (21%) had worsening of 2 parameters. There was no significant change in systolic blood pressure, diastolic blood pressure, pulse pressure, and mean arterial pressure at baseline and at follow-up echocardiographic examination.

Of the 10 patients who had worsening of LV diastolic function by ≥1 parameter, 9 received supplementation with CoQ_{10} 300 mg/day (100 mg 3 times daily) while continuing atorvastatin; all patients completed echocardiographic evaluation after supplementation with CoQ_{10} therapy. Eight of the 9 patients (89%) had reversal of the ≥1 diastolic abnormality. Four patients (44%) had reversal of all 3 of the diastolic parameters. Two patients (22%) had reversal of 2 parameters. One patient had no change in the parameters (Table 3). Paired Student's *t* test analyses of the E/A ratio, DT, and IVRT before and after CoQ_{10} supplementation are shown in Figures 1 to 3. Of the 9 patients who received CoQ_{10} supplementation, the mean E/A ratio at baseline of 1.33 decreased to 1.11 ($p = 0.02$) after 3 to 6 months of statin therapy. The mean E/A ratio decreased to 1.25 ($p = 0.02$) after 3 months of CoQ_{10} supplementation.

Baseline CoQ_{10} levels varied from 0.4 to 1.6 μg/ml (mean 0.95) in the 14 patients. All 4 patients without worsening of diastolic parameters had levels of CoQ_{10} greater than the mean (range 1.0 to 1.2 μg/ml). After atorvastatin therapy, the plasma CoQ_{10} levels decreased in 5 patients, remained the same in 4 patients, and increased in 5 patients. Of the 9 patients who were supplemented with CoQ_{10}, 8 had their follow-up CoQ_{10} levels drawn. Seven patients had significant increases in their blood levels, and 1 had no change. The mean CoQ_{10} level after CoQ_{10} supplementation was 1.82 ± 1.28 μg/ml compared with the mean CoQ_{10} level before supplementation of 0.84 ± 0.35 μg/ml ($p = 0.03$).

Of our 14 patients initiated on atorvastatin therapy, the mean E/A ratio decreased from 1.2 to 1.09 ($p = 0.12$), the mean DT increased from 205 to 236 ms ($p = 0.01$), and the mean IVRT increased from 89 to 95 ms ($p = 0.35$). Patients who received CoQ_{10} therapy on the basis of their worsening LV diastolic parameters with atorvastatin had significant improvement in their diastolic filling parameters (E/A ratio and IVRT). The reversal of trend was also seen in DT.

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Human and animal studies have suggested decreases in plasma levels of CoQ_{10} with the use of statins[1–5] and the ability to replace exogenously diminished plasma levels induced by statin therapy[6]. We did not see significant decreases in all patients. This

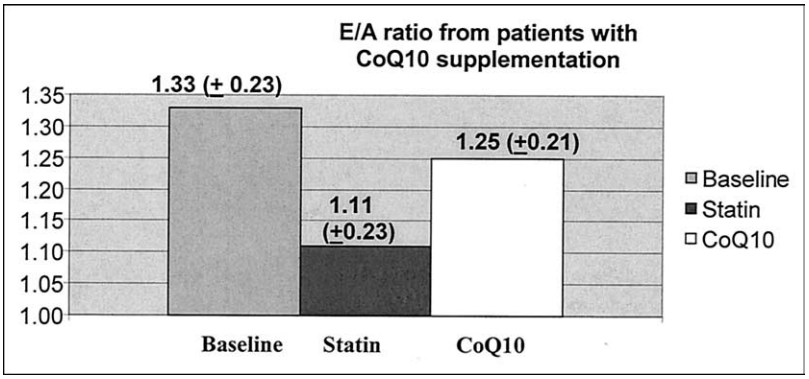

FIGURE 1. Mean E/A ratios (±SDs) at baseline and after statin therapy and CoQ_{10} supplementation in patients who received CoQ_{10} supplementation. Paired Student's *t* test between baseline E/A ratio and after-statin E/A ratio was p = 0.02. Paired Student's *t* test between statin E/A ratio and CoQ_{10} E/A ratio was p = 0.02.

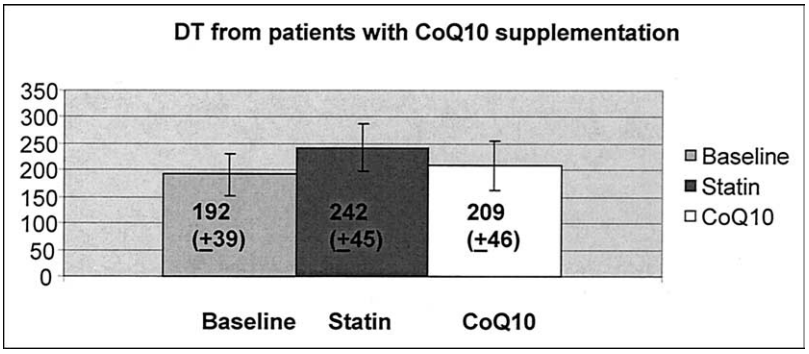

FIGURE 2. Mean DTs (±SDs) at baseline and after statin therapy and CoQ_{10} supplementation from patients who received CoQ_{10} supplementation. Paired Student's *t* test between baseline DT and after-statin DT was p = 0.002. Paired Student's *t* test between statin DT and CoQ_{10} DT was p = 0.12.

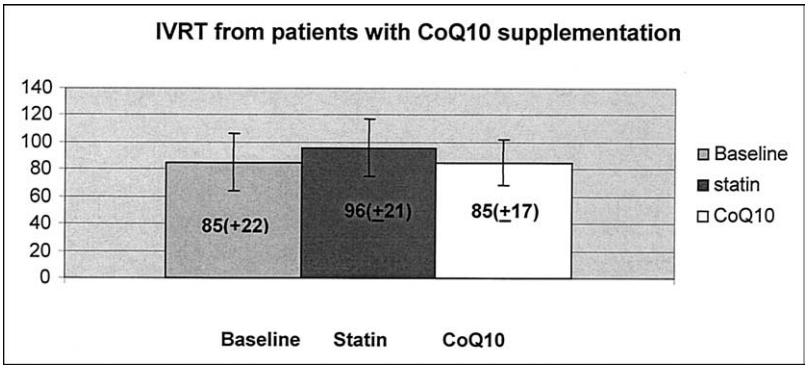

FIGURE 3. Mean IVRTs (±SDs) at baseline and after statin therapy and CoQ_{10} supplementation from patients who received CoQ_{10} supplementation. Paired Student's *t* test between baseline IVRT and after-statin IVRT was p = 0.18. Paired Student's *t* test between statin IVRT and CoQ_{10} IVRT was p = 0.01.

could be related to lower baseline levels in older patients or to the observation that plasma levels do not always reflect tissue levels. In the recently published Anglo-Scandinavian Cardiac Outcomes Trial,[7] there was trend toward more heart failure admissions in patients randomized to the atorvastatin arm. The details of these admissions are not known but could be secondary to worsening LV diastolic function. The much smaller Greek Atorvastatin and Coronary-heart-disease Evaluation study showed decreased heart failure admissions in patients treated with atorvastatin.[8] A recent tissue Doppler study of patients with hypercholesterolemia without heart disease or diabetes mellitus on atorvastatin suggested a favorable effect of atorvastatin on contractile reserve.[9]

The present study's limitations are several, including the small sample size and the lack of a control arm, but the patients did serve as suitable contemporary controls for themselves. We defined worsening LV diastolic function as a 10% change in the E/A ratio, DT, and IVRT, which would be true only in patients with normal LV diastolic function at baseline, and some patients may have had baseline abnormalities with subsequent pseudonormalization. In patients with pseudonormalization or restrictive filling, increases in IVRT and DT may be an improvement in their diastolic parameters. Tissue Doppler, which is an alternative marker of LV diastolic function, was not used. Patients were asymptomatic, and therefore, there were no clinical end points during the short follow-up. This, however, represents the initiation phase of statin therapy and hence an early part of the natural history of the potential for statin-induced cardiomyopathy. For more than a decade, there has been a suggestion of impairment of diastolic function after the administration of statins,[10,11] and our findings suggest that this may be a common event and potentially a precursor to symptoms associated with ventricular dysfunction. Because baseline levels of CoQ_{10} do not predict dysfunction, routine concomitant CoQ_{10} administration, especially in patients at risk, seems prudent.[2]

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1. Langsjoen PH, Langsjoen AM. The clinical use of HMG CoA-reductase inhibitors and the associated depletion of coenzyme Q10. A review of animal and human publications. *BioFactors* 2003;18:101–111.
2. Rundek T, Naini A, Sacco R, Coates K, DiMauro S. Atorvastatin decreases the conenzyme Q 10 level in the blood of patients at risk for cardiovascular disease and stroke. *Arch Neurol* 2004;61:889–892.
3. Krum H, McMurray JJ. Statins and chronic heart failure: do we need a large-scale outcome trial? *J Am Coll Cardiol* 2002;39:1567–1573.
4. Ghirlanda G, Oradei A, Manto A, Lippa S, Uccioli L, Caputo S, Greco AV, Littarru GP. Evidence of plasma CoQ10 lowering effect by HMG-CoA reductase inhibitors: double blind placebo controlled study. *J Clin Pharmacol* 1993;33:226–229.
5. Mortensen SA, Leth A, Agner E, Rohde M. Dose related decrease of serum coenzyme Q10 during treatment with HMG-CoA reductase inhibitors. *Mol Aspects Med* 1997;18(suppl):S137–S144.
6. Bargossi AM, Battino M, Gaddi A, Fiorella PL, Grossi G, Barozzi G, Di Giulio R, Descovich G, Sassi S, Genova ML. Exogenous CoQ10 preserves plasma ubiquinone levels inpatients treated with 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors. *Int J Clin Lab Res* 1994;24:171–176.
7. Sever PS, Dahlof B, Poulter NR, Wedel H, Beevers G, Caulfield M, Collins R, Kjeldsen SE, Kristinsson A, McInnes GT, et al, ASCOT Investigators. Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial–Lipid Lowering Arm (ASCOT-LLA): a multicentre randomised controlled trial. *Lancet* 2003;361:1149–1158.
8. Athyros VG, Papageorgiou AA, Mercouris BR, Athyrou VV, Symeonidis AN, Basayannis EO, Demitriadis DS, Kontopoulos AG. Treatment with atorvastatin to the National Cholesterol Educational Program goal versus "usual" care in secondary coronary heart disease prevention. The GREek Atorvastatin and Coronary-heart-disease Evaluation (GREACE) study. *Curr Med Res Opin* 2002;18:220–228.
9. Bountioukos M, Rizzello V, Krenning BJ, Bax JJ, Kertai MD, Vourvouri EC, Schinkel AF, Biagini E, Boersma E, Roelandt JR, et al. Effect of atorvastatin on myocardial contractile reserve assessed by tissue Doppler imaging in moderately hypercholesterolemic patients without heart disease. *Am J Cardiol* 2003;92:613–616.
10. Langsjoen PH, Langsjoen PH, Folkers K. Isolated diastolic dysfunction of the myocardium and its response to CoQ10 treatment. *Clin Invest* 1993;71(suppl):S140–S144.
11. Oda T. Recovery of load-induced left ventricular diastolic dysfunction by coenzyme Q10: echocardiographic study. *Mol Aspects Med* 1994;15(suppl):S149–S154.

Impact of Nonprescriptive Factors on Low-Density Lipoprotein Cholesterol Reduction With Statins

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Nonprescriptive factors, including patient adherence, can affect the fluctuations in low-density lipoprotein (LDL) cholesterol observed in the clinical setting. In 241 statin-treated patients, although drugs and doses remained fixed, 57% of patients initially successful in reaching LDL cholesterol targets showed subsequent increases in LDL cholesterol. Conversely, 60% of patients who initially failed to reach targets had subsequent reductions in LDL cholesterol, with nearly 1/3 eventually attaining their LDL cholesterol goals. ©2004 by Excerpta Medica, Inc.

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Despite the widespread dissemination of the National Cholesterol Education Program Adult Treatment Panel III (ATP III) guidelines and the availability of the potent 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors (statins), many patients are not attaining recommended lipid targets.[1,2] The cause of this "treatment gap" is multifactorial. Often, patients are not treated at all,[3] are offered inadequate medication doses to attain lipid goals,[3,4] or experience low-density lipoprotein (LDL) cholesterol reductions significantly different from those expected from projections in package inserts.[5] Clinically, it is difficult to isolate the relative contributions of these multiple influences on lipid outcomes. However, in patients whose drugs and doses remain constant regardless of their initial responses to therapy, subsequent lipid changes can be more safely ascribed to nonprescriptive factors, including noncompliance.

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Patients from a preventive cardiology practice were identified from January 1996 to March 2003 and were included if they met the following criteria: (1) not on lipid-reducing agents; (2) placed on atorvastatin, simvastatin, or pravastatin at their initial visits; (3) kept on the same agent and dose throughout the study period; (4) baseline LDL cholesterol greater than ATP III target values (i.e., coronary heart disease or equivalent LDL <100 mg/dl; no coronary heart disease with ≥ 2 risk factors and LDL <130 mg/dl; and no coronary heart disease with 0 to 1 risk factors LDL <160 mg/dl); and (5) ≥ 2 follow-up visits (n = 241). Data collection methods have been previously described.[6] ATP III target status was assessed at the first follow-up visit and patients were split into 2 groups (group 1, patients who reached their ATP III LDL cholesterol targets, n = 138; and group 2, patients who did not reach their ATP III LDL cholesterol targets, n = 103).

The attainment of ATP III LDL cholesterol goals was calculated at each follow-up visit. Comparisons of baseline characteristics were made according to the attainment of ATP III goals (i.e., group 1 vs group 2) by unpaired Student's *t* and chi-square tests. LDL cholesterol changes within groups were evaluated by comparing the first and second follow-up visit LDL cholesterol values with baseline LDL cholesterol with paired Student's *t* tests. Change in LDL cholesterol is reported as a percentage of baseline, and unpaired Student's *t* tests were used to compare group 1 with group 2. Coefficients of variation were calculated for

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