Effect of left ventricular hypertrophy on long-term survival of patients with coronary artery disease following percutaneous coronary intervention

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Abstract

The impact of left ventricular hypertrophy (LVH) on survival among patients with established coronary artery disease (CAD) is not well understood. We sought to evaluate the effect of LVH on the survival of patients with CAD following percutaneous coronary intervention (PCI). Three hospitals in New York City contributed prospectively defined data on 4284 consecutive patients undergoing PCI. All-cause mortality at a mean follow-up of three years was the primary endpoint. LVH was present in 383 patients (8.9%). LVH patients had a greater prevalence of hypertension (88% vs. 68%, $p<0.001$), vascular disease (21% vs. 6.6%, $p=0.001$), and prior heart failure (10% vs. 5.5%, $p<0.001$). LVH patients presented less often with one-vessel disease (38% vs. 50%, $p=0.040$) and more often with two- (34% vs. 29%, $p=0.014$) or three-vessel (22% vs. 18%, $p=0.044$) disease. Ejection fractions and angiographic success were similar in both groups. In-hospital mortality did not differ between groups. At three-year follow-up, the survival rate for patients with LVH was 86% vs. 91% in patients without LVH (log-rank $p=0.001$). However, after adjustment for differences in baseline characteristics using Cox proportional hazards analysis, LVH was found not to be an independent predictor of mortality (hazard ratio, 0.93; 95% confidence interval, 0.68-1.28; $p=0.67$). We conclude that LVH at the time of PCI is not independently associated with an increase in the hazard of death at three years.

Introduction

It is well documented that left ventricular hypertrophy (LVH) detected by 12-lead electrocardiography or echocardiography is a significant risk factor for cardiovascular morbidity and mortality in cohorts ranging from the general population to those with established cardiovascular disease, including coronary artery disease (CAD).[1-10] However, the impact of LVH on survival among patients with established CAD following revascularization is largely unknown. The current study was designed to evaluate the effect of LVH on long-term outcomes of patients with CAD following revascularization with percutaneous coronary intervention (PCI).

Patients and Methods

Patient population

The study population was a cohort of 4284 consecutive patients undergoing PCI from January 1, 1998 to October 1, 1999 at three hospitals in New York City.

Clinical data

Prospectively defined data elements were contributed to a central coordinating center for analysis. Data elements included information on demographics, comorbidities, procedural details, complications, and in-hospital outcomes. The same data elements are required to be submitted to the Department of Health on every PCI performed in New York State to make up the Coronary Angioplasty Reporting System database.

Definitions

LVH was defined by physician assessment of the pre-PCI ECG or by echocardiography in documented cases of left bundle branch block and/or pacing. Diabetes included treatment with oral hypoglycemic agents or insulin. Intravenous glycoprotein (GP) IIb/IIIa inhibitors were administered when abciximab, eptifibatide, or tirofiban were given during or within three hours following PCI. The diagnosis of peri-procedural myocardial infarction (MI) required new Q-waves and a rise in creatine kinase to at least 2.5 times the upper limit of normal occurring within 24 hours of the PCI. Heparin therapy indicated treatment with intravenous heparin within 48 hours before the PCI. Nitroglycerin treatment indicated therapy with intravenous nitroglycerin within 24 hours of the procedure for ongoing ischemia or left ventricular failure. Ventricular arrhythmias were those that occurred within seven days of the PCI requiring electrical are pharmacological treatment excluding episodes that occurred within the first 24 hours of an MI. Angiographic success was a reduction of the treated lesion by at least 20% with a residual stenosis of less than 50%.

Percutaneous coronary intervention

All procedural decisions, including device selection and adjunctive pharmacotherapy, were made at the discretion of the individual physician performing PCI. All stents were bare metal. Deployment was at high pressure and patients were maintained on aspirin indefinitely, and ticlopidine or clopidrogel for four weeks following their PCI unless contraindicated. Angiographic assessments were made at the individual hospital by visual assessment.

Endpoints

The primary endpoint was all-cause mortality following discharge from the hospital for the index PCI as determined from the Social Security Death Index. This index has been shown to be highly specific and unbiased.[11,12] Follow-up was for a mean of three years.

Statistical analysis

Categorical variables were compared by χ^2-analyses. Continuous variables are presented as mean ± SD and were compared using the Student's t-test. All probability values are two-tailed. Statistical significance was defined as $p<0.05$ or confidence intervals that did not include 1.0. Survival curves were constructed by the Kaplan-Meier method with differences in survival assessed with the log-rank test. LVH was related to all-cause mortality using multivariable Cox proportional hazard regression analyses to adjust for differences in baseline characteristics. Potential confounders were entered into models if they were clinically relevant or showed univariable differences between groups with a $p<0.10$. All analyses were performed using the SPSS (Chicago, IL, USA) statistical analysis program.

Results

Baseline characteristics

LVH was identified in 383 (8.9%) of 4284 patients who underwent PCI for CAD. Baseline characteristics of patients are presented in Table 1. Patients with LVH were older (66 vs. 63 years, $p=0.001$) and less often characterized as white (66% vs. 79%, $p<0.001$). LVH patients had a lower prevalence of smoking (9.4% vs. 14%, $p=0.019$) but greater prevalence of hypertension (88% vs. 68%, $p<0.001$), diabetes (31% vs. 26%, $p=0.041$), vascular disease (21% vs. 6.6%, $p<0.001$), creatinine of >2.5 mg/dL, (3.7% vs. 1.7%, $p=0.009$), dialysis (3.9% vs. 1.5%, $p<0.001$), and prior heart failure (10% vs. 5.5%, $p<0.001$).

Procedural characteristics

Angiographic and procedural characteristics are depicted in Table 2. LVH patients presented less often with one-vessel disease (38% vs. 50%, $p=0.04$) and more often with two-vessel (34% vs. 29%, $p=0.01$) and three-vessel disease (22% vs. 18%, $p=0.04$). Mean ejection fraction was lower in LVH patients (49% vs. 51%, $p=0.01$). Stent placement did not differ in either group. Angiographic success was similar in both groups (98% vs. 97%, $p=0.27$).

Outcomes

Adverse outcomes following PCI are depicted in Table 3. In-hospital adverse outcomes including death, post-PCI MI, and stent thrombosis were not different between groups. There was a greater rate of emergency bypass surgery in the LVH group (0.5% vs. 0.1%, $p=0.004$). The mortality at a mean follow-up of three years for patients with LVH was 14% vs. 8.9% in patients without LVH (Figure 1) (log-rank $p<0.001$). The independent predictors of long-term mor-

tality as determined by Cox proportional hazards analysis are presented in Table 4. LVH was not independently associated with an increase in the hazard of long-term mortality (hazard ratio, 0.93; 95% confidence interval, 0.68-1.28; $p=0.67$). Clinical characteristics associated with an increased hazard for long-term mortality were age, prior history of heart failure, vascular disease, diabetes, creatinine of >2.5 mg/dL, and dialysis.

Discussion

The significant findings of this retrospective, observational study are two-fold. First, in an unselected population of patients undergoing PCI for CAD, LVH was associated with an increase in unadjusted three-year mortality. Second, after adjustment for differences in baseline characteristics, LVH was no longer

Table 1. Baseline characteristics.

	LVH (N=383)	No LVH (N=3901)	p
Demographics			
Mean age ± SD (years)	66.6±11.4	63.1±11.9	<0.001
Age > 75 years (%)	27	18	<0.001
Female (%)	35	31	0.06
White (%)	66	79	<0.001
Body mass index ± SD	28.1±5.8	28.6±6.0	0.13
Clinical history (%)			
Obesity	30	33	0.14
Smoking	9.4	14	0.02
Hypertension	88	68	<0.001
Diabetes	31	26	0.04
Stroke	0.3	0.1	0.51
Vascular disease	21	6.6	<0.001
Creatinine >2.5 mg/dL	3.7	1.7	0.009
Dialysis	3.9	1.5	<0.001
Cardiac history (%)			
Previous CHF	10	6	<0.001
Prior MI	37	35	0.45
Previous cardiac surgery	18	17	0.74
Previous PCI	25	26	0.84
Clinical presentation (%)			
CHF	12	4.3	<0.001
MI <6 hours	2.6	4	0.17
MI <24 hours	4.2	6.5	0.08
Unstable angina	45	42	0.27
Heparin <48 hours	31	29	0.46
Nitroglycerin <24 hours	16	13	0.09
Ventricular arrhythmia	2.1	1.9	0.82
Thrombolysis <6 hours	0.3	0.7	0.32
Thrombolysis >6 hours	0.8	3.4	0.005
Shock	2.6	2.5	0.88

LVH, left ventricular hypertrophy; CHF, congestive heart failure; MI, myocardial infarction; PCI, percutaneous coronary intervention.

Table 2. Angiographic and procedural characteristics.

	LVH (N=383)	No LVH (N=3901)	p
Mean ejection fraction ± SD (%)	51	51	0.70
One-vessel CAD (%)	38	50	<0.001
Two-vessel CAD (%)	34	29	0.02
Three-vessel CAD (%)	22	18	0.04
IABP (%)	1.8	1.3	0.43
Stent (%)	74	77	0.13
GP IIb/IIIa inhibitor (%)	21	24	0.23
Angiographic success (%)	98	97	0.27
Atherectomy (%)	15	13	0.41

LVH, left ventricular hypertrophy; SD, standard deviation; CAD, coronary artery disease; IABP, intra-aortic balloon pump; GP, glycoprotein.

associated with an increased hazard of death.

LVH has long been associated with an increased risk of cardiovascular mortality.[1-8] However, there is a paucity of data regarding its impact in patients with CAD and even less information on the effect of LVH on prognosis of patients with CAD following percutaneous revascularization. East and colleagues found echocardiographic LVH to be associated independently with a 56% increase in risk of three-year mortality among patients with CAD.[13] However, only 37% of LVH patients underwent revascularization compared to 51% of patients without LVH despite more three-vessel disease in the LVH group. Likewise the Heart and Soul Study found that increased LV mass index determined by echocardiography in patients with CAD increased the risk for both all-cause mortality and sudden or arrhythmic death.[9] Again in this study, although all patients had CAD, only 62% with LVH had been revascularized.

LVH may be associated with increased mortality by a number of mechanisms. Activation of the renin-angiotensin system not only leads to LVH but also may promote the progression of atherosclerosis by the effects of angiotensin II on vasomotor tone, coagulation, and vascular smooth muscle cell proliferation.[14-17] Additionally, LVH may predispose to arrhythmic death. Myocardial fibrosis occurs in LVH and may provide the substrate for reentrant ventricular arrhythmias.[18-21]

It is unclear why the current study found no detrimental effect of LVH on three-year adjusted mortality. One potential explanation is methodological. This database uses primarily the ECG for diagnosis of LVH, which is less sensitive for the detection of LVH than echocardiography.[22,23] Thus, if the ECG were insensitive, patients with LVH would be incorrectly assigned to the group without LVH. In such a scenario, if LVH were truly an independent risk factor for mortality, assigning patients with LVH to the no-LVH group would minimize or eliminate any true differences in mortality. Alternatively, it is possible that certain elements of the medical therapy for secondary prevention following PCI, such as β-blockers and angiotensin converting enzyme inhibitors,[24] induced regression of LVH, which has been shown to reduce mortality.[25] Finally, it is possible that in the setting of CAD, the adverse effect of LVH on survival is magnified in the presence of untreated or unrecognized ischemia. In this scenario, revascularization would eliminate or reduce ischemia and thereby decrease the impact of LVH on mortality to an undetectable level in a cohort of this size.

Several limitations must be borne in mind when analyzing these findings. First, because of its nonrandomized retrospective nature, there may be unrecognized differences

Table 3. Adverse outcomes following percutaneous coronary intervention.

	LVH (N=383)	No LVH (N=3901)	p
In-hospital death (%)	0.8	0.4	0.34
Emergency bypass surgery (%)	0.5	0.1	0.004
Myocardial infarction (new Q-waves) (%)	0	0.2	0.41
Myocardial infarction (no new Q-waves) (%)	1.6	1.5	0.93
Vascular complication (%)	0.1	0	0.48
Abrupt closure (%)	0.5	0.5	0.93
Stent thrombosis (%)	0.8	0.6	0.69
Out-of-hospital death (%)	14	9	0.002

LVH, left ventricular hypertrophy.

Table 4. Cox proportional hazards model for all-cause mortality.

Variable	Hazard ratio	95 % Confidence intervals Lower	Upper	p
LVH	0.93	0.68	1.28	0.67
Age (per one-year increase)	1.07	1.06	1.08	<0.001
Vascular disease	1.42	1.07	1.89	0.01
Diabetes	1.47	1.18	1.84	0.001
Previous CHF	2.04	1.53	2.73	<0.001
One-vessel CAD	0.58	0.40	0.83	0.003
Two-vessel CAD	0.69	0.48	0.99	0.048
Creatinine of >2.5 mg/dL	3.41	2.38	4.90	<0.001
Dialysis	4.02	2.68	6.02	<0.001
Female	0.74	0.60	0.93	0.008

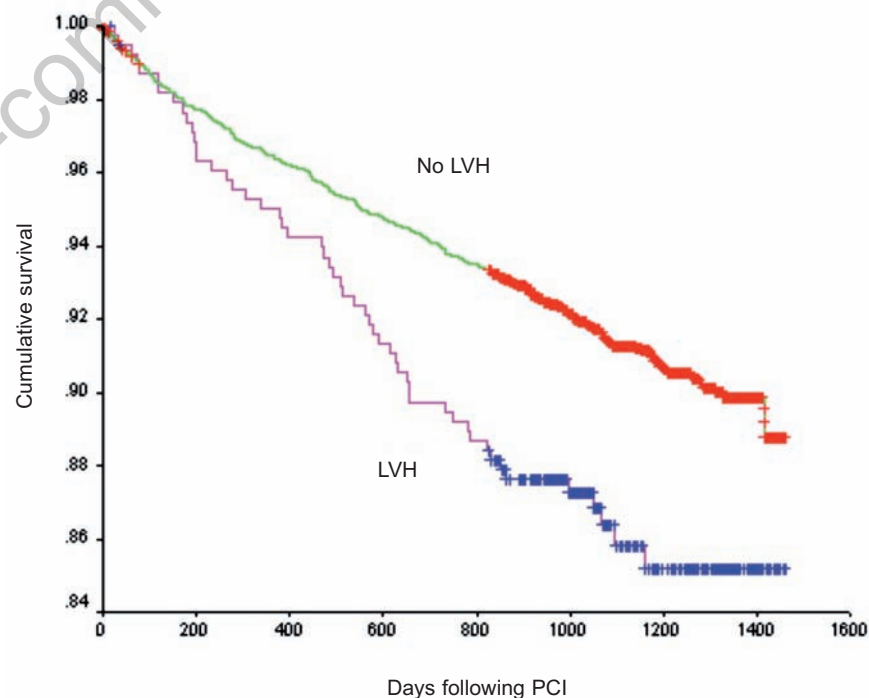LVH, left ventricular hypertrophy; CHF, congestive heart failure; CAD, coronary artery disease.

Figure 1. Kaplan-Meier analysis of survival following percutaneous coronary intervention (log-rank $p<0.001$).

between patients with and without LVH in our study. One possible confounder is medication usage, which was impossible to control for because there were no data on medication use in the database. Second, there were no uniform ECG criteria for the diagnosis of LVH. Thus, different methods of LVH determination probably were used by different practitioners. Finally, this study was performed before the introduction of drug-eluting stents. However, it is unlikely that the exclusive use of bare metal stents would have impacted differentially on patients with and without LVH.

Conclusion

The current study demonstrates that, although LVH is a marker for increased mortality, it does not increase independently the hazard of mortality among patients with CAD following PCI.

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