Electrocardiographic Strain Pattern and Prediction of New-Onset Congestive Heart Failure in Hypertensive Patients

The Losartan Intervention for Endpoint Reduction in Hypertension (LIFE) Study

Peter M. Okin, MD; Richard B. Devereux, MD; Markku S. Nieminen, MD; Sverker Jern, MD; Lasse Oikarinen, MD; Matti Viitasalo, MD; Lauri Toivonen, MD; Sverre E. Kjeldsen, MD, PhD; Björn Dahlöf, MD, PhD; for the LIFE Study Investigators

Background—The ECG strain pattern of ST depression and T-wave inversion is strongly associated with left ventricular hypertrophy (LVH) independently of coronary heart disease and with an increased risk of cardiovascular morbidity and mortality in hypertensive patients. However, whether ECG strain is an independent predictor of new-onset congestive heart failure (CHF) in the setting of aggressive antihypertensive therapy is unclear.

Methods and Results—The relationship of ECG strain at study baseline to the development of CHF was examined in 8696 patients with no history of CHF who were enrolled in the Losartan Intervention for Endpoint Reduction in Hypertension (LIFE) study. All patients had ECG LVH by Cornell product and/or Sokolow-Lyon voltage criteria on a screening ECG, were treated in a blinded manner with atenolol- or losartan-based regimens, and were followed up for a mean of 4.7 years. Strain was defined as a downsloping convex ST segment with inverted asymmetrical T-wave opposite the QRS axis in lead V5 or V6. ECG strain was present in 923 patients (10.6%), and new-onset CHF occurred in 265 patients (3.0%), 26 of whom had a CHF-related death. Compared with patients who did not develop CHF, hypertensive patients who developed CHF were older; were more likely to be black, current smokers, and diabetic; were more like to have a history of myocardial infarction, ischemic heart disease, stroke, or peripheral vascular disease; and had greater baseline severity of LVH by Cornell product and Sokolow-Lyon voltage, higher baseline body mass indexes, higher serum glucose levels and albuminuria, similar baseline systolic and diastolic pressures, and reductions in diastolic pressure with treatment but greater reductions in systolic pressure. In univariate Cox analyses, ECG strain was a significant predictor of new-onset CHF (hazard ratio [HR], 3.27; 95% CI, 2.49 to 4.29) and CHF mortality (HR, 4.74; 95% CI, 2.11 to 10.64). In Cox multivariable analyses adjusting for baseline differences between patients with and without new-onset CHF, in-treatment differences in systolic and diastolic pressures, Sokolow-Lyon voltage, and Cornell product, and the impact of treatment with losartan versus atenolol on outcomes, ECG strain remained a significant predictor of incident CHF (HR, 1.80; 95% CI, 1.30 to 2.48) and CHF-related death (HR, 2.78; 95% CI, 1.02 to 7.63).

Conclusions—ECG strain identifies hypertensive patients at increased risk of developing CHF and dying as a result of CHF, even in the setting of aggressive blood pressure lowering. (Circulation. 2006;113:67-73.)

Key Words: blood pressure ■ electrocardiography ■ heart failure ■ hypertension ■ hypertrophy

The classic strain pattern of ST depression and T-wave inversion on the ECG is a well-recognized marker of the presence and severity of anatomic left ventricular hypertrophy (LVH).1-7 The association between lateral repolarization abnormalities and anatomic LVH is independent of the possible relationship of this repolarization abnormality to underlying coronary heart disease,7,8 and incorporation of ECG strain into scores that include standard voltage criteria improves ECG detection of LVH.2,6 ECG strain also has been associated with adverse prognosis in a variety of populations,9-15 including hypertensive patients,9-11 and has been implicated as the primary marker of untoward outcomes when ECG LVH criteria have been used for risk stratification.9,10,12 In the Losartan Intervention for Endpoint Reduction in Hypertension (LIFE) study,11 the presence of strain on the baseline ECG identified hypertensive patients at increased

Clinical Perspective p 73

Received June 16, 2005; revision received October 25, 2005; accepted October 31, 2005.

From the Greenberg Division of Cardiology, Weill Medical College of Cornell University, New York, NY (P.M.O., R.B.D.); Division of Cardiology, Department of Medicine, Helsinki University Central Hospital, Helsinki, Finland (M.S.N., L.O., M.V., L.T.); Sahlgrenska University Hospital/Ostra, Göteborg, Sweden (S.J., B.D.); and Ulleval University Hospital, Oslo, Norway, and University of Michigan Medical Center, Ann Arbor (S.E.K.).

Correspondence to Peter M. Okin, MD, Weill Medical College of Cornell University, 525 E 68th St, New York, NY 10021. E-mail pokin@med.cornell.edu

© 2006 American Heart Association, Inc.

Circulation is available at http://www.circulationaha.org

DOI: 10.1161/CIRCULATIONAHA.105.569491
risk of cardiovascular (CV) morbidity and mortality in the setting of antihypertensive therapy associated with large decreases in systolic and diastolic pressures independently of baseline severity of ECG LVH and of treatment type.

Increased LV mass and LVH on the echocardiogram are predictors of new CHF and of the development of a decreased LV ejection fraction. ECG criteria for LVH, including the Romhilt-Estes point score and Framingham criteria, both of which incorporate some measure of ECG strain into their determination, have also been demonstrated to predict the development of new-onset CHF. In the LIFE study, ECG strain was associated with a history of CHF at baseline and, in the prespecified echocardiographic sub-study of LIFE, with greater LV mass, a higher prevalence of LVH, and depressed LV function, suggesting that ECG LVH.

Methods

Subjects

The LIFE trial enrolled hypertensive patients with ECG LVH by Cornell voltage-duration product and/or Sokolow-Lyon voltage criteria on a screening ECG in a prospective, double-blind study large enough (n=9193) to demonstrate that an appreciable reduction in mortality and morbidity events is associated with the use of losartan as opposed to atenolol. Eligible patients for LIFE were men and women 55 to 80 years of age with previously untreated or treated essential hypertension with mean seated blood pressure in the range of 160 to 200/95 to 115 mm Hg after 1 and 2 weeks on placebo. A total of 8696 patients with no history of CHF had baseline ECGs on which the strain pattern could be determined. There were 4687 women and 4009 men whose mean age was 67±7 years.

Electrocardiography

Hard-copy ECGs, recorded at either 25- or 50-mm/s paper speeds, were interpreted at the Core Laboratory at Sahlgrenska University Hospital/Östra in Göteborg, Sweden, by experienced investigators blinded to clinical information as previously reported in detail. Using calipers, they measured QRS duration to the nearest 4 ms in all 12 leads; R-wave amplitudes in leads aVL, V1, and V6; and S-wave amplitudes in leads V5 and V6 to the nearest 0.5 mm (0.05 mV). The product of QRS duration times the Cornell voltage combination (R45+S90, with 6 mm [0.6 mV] added in women) was used to identify ECG LVH.

Determination of the presence or absence of ECG strain as a dichotomous variable was visually assessed at Helsinki University Central Hospital as previously described. Repolarization abnormalities in leads V1 and/or V6 were considered consistent with the presence of typical strain when there was a downsloping convex ST segment with an inverted asymmetrical T wave with polarity opposite the main QRS deflection. No specific magnitude of ST-segment depression was required for diagnosis of ECG strain.

End-Point Determination

Hospitalization for CHF was a prespecified secondary end point in LIFE, with the diagnosis of CHF based on clinical and diagnostic findings. Each case was reviewed and verified by End Point Committee members who were blinded to ECG strain results when classifying possible morbid events.

Statistical Methods

Data management and analysis were performed with SPSS version 12.0 software. Data are presented as mean±SD for continuous variables and proportions for categorical variables. Differences in prevalences between groups were compared through χ² analyses, and mean values of continuous variables were compared by 2-sample t tests. To test the hypothesis that ECG strain at baseline was associated with an increased risk of CHF and CHF mortality, the relation of strain to the risk of developing these events was analyzed on the intention-to-treat principle: All randomized patients were followed up for end points for the duration of the study, regardless of protocol violations or adherence to study medication.

Event rates were calculated and plotted according to the Kaplan-Meier product limit method. The relation of strain to the risk of clinical end points was assessed with Cox proportional-hazards models. Hazard ratios for the incidence of CHF and CHF mortality were computed as the antilog of the estimated coefficient. The 95% CI of each hazard ratio was calculated from the estimated coefficients and standard errors, and Wald χ² statistics and probability values were calculated. Because of the previously demonstrated strong association of ECG strain with clinical and demographic variables that are also potential risk markers for CHF, a propensity score for ECG strain was calculated with logistic regression analysis in which ECG strain was the dependent variable and the variables listed in Table 1 and the baseline variables in Table 2 were the independent variables. Propensity analysis provides an additional means of accounting for baseline confounding, with the propensity score indicating the likelihood that any individual patient would have ECG strain given all other known variables other than the outcome variable. To test the independence of ECG strain as a predictor of new-onset CHF, ECG strain was entered into a multivariable Cox model that also included as covariates the propensity score for ECG strain, age, gender, treatment group, race, diabetes, history of ischemic heart disease, myocardial infarction, stroke, peripheral vascular disease or smoking, baseline urinary albumin-to-creatinine ratio, total and HDL cholesterol, and body mass index as standard covariates; baseline and in-treatment values of systolic and diastolic pressure, Cornell product, and Sokolow-Lyon voltage were time-varying covariates. Because of the limited number of CHF deaths (n=26), multivariable Cox models for the prediction of CHF mortality considered only ECG strain, the propensity score, and treatment group or also included baseline and in-treatment blood pressure and ECG LVH variables entered as time-varying covariates.

Analyses were repeated with the population stratified by sex, age, race, treatment group, history of ischemic heart disease or myocardial infarction, prevalent diabetes and microalbuminuria, and presence or absence of LVH by Cornell product and Sokolow-Lyon voltage on the baseline ECG. Interaction between strain and these variables was formally tested by adding cross-product terms of strain and these variables into the models of the total population. For all tests, a 2-tailed value of P<0.05 was required for statistical significance.

Results

Patient Characteristics in Relation to the Development of CHF

ECG strain was present in 923 patients (10.6%); after a mean follow-up of 4.7±1.1 years, new-onset CHF developed in 265 patients (3.0%), and death resulting from CHF occurred in 26 patients (0.3%). Clinical and demographic characteristics of patients in relationship to the development of CHF are shown in Table 1. Compared with patients who did not develop CHF, patients who developed CHF were older; were more likely to be black; were more likely to have diabetes and a prior history of ischemic heart disease, myocardial infarc-
tion, stroke, and peripheral vascular disease; had higher body mass indexes, higher urine albumin-to-creatinine ratios, and lower total and HDL cholesterol levels; were more likely to be current smokers and to have the strain pattern on their baseline ECG; but were similar with respect to gender and randomized assignment to losartan or atenolol treatment arms.

Blood pressure and ECG LVH measurements at baseline and changes in these measurements between baseline and last in-study determination in relation to the development of CHF are shown in Table 2. Patients who developed CHF had similar baseline systolic pressures, lower baseline diastolic pressures, and greater reductions in systolic pressure but similar changes in diastolic pressure. Development of CHF was associated with greater baseline severity of Cornell product and Sokolow-Lyon voltage LVH and with higher baseline prevalences of ECG LVH using both Cornell product (73.2% versus 65.2%; \( P = 0.009 \)) and Sokolow-Lyon voltage criteria (27.8% versus 21.6%; \( P = 0.022 \)).

Despite similar reductions in diastolic pressure and a greater decrease in systolic pressure, Cornell product LVH on average became more severe over the course of treatment in patients who developed CHF compared with a significant reduction in Cornell product LVH between baseline and last in-study measurement in patients who did not develop CHF. In contrast, there was no difference in the degree of regression of Sokolow-Lyon voltage LVH in relation to development of CHF.

### ECG Strain and Prediction of CHF

In univariate Cox analyses, the presence of the strain pattern of lateral repolarization abnormality on the baseline LIFE study ECG was associated with an increased risk of new-onset CHF and CHF mortality (Figures 1 and 2, Table 3). The 923 patients with strain on their baseline ECG had a 3-fold

### TABLE 1. Demographic and Clinical Characteristics in Relation to the Development of New-Onset CHF

<table>
<thead>
<tr>
<th>Variables</th>
<th>No CHF (n=8431)</th>
<th>CHF (n=265)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>66.7±7.0</td>
<td>70.6±6.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sex, % male</td>
<td>45.9</td>
<td>50.9</td>
<td>0.123</td>
</tr>
<tr>
<td>Race, % black</td>
<td>5.6</td>
<td>10.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>12.2</td>
<td>27.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>History of ischemic heart disease, %</td>
<td>14.5</td>
<td>37.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>History of myocardial infarction, %</td>
<td>5.3</td>
<td>19.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>History of stroke, %</td>
<td>4.1</td>
<td>8.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>History of peripheral vascular disease, %</td>
<td>5.3</td>
<td>13.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Treatment with losartan, %</td>
<td>50.2</td>
<td>49.8</td>
<td>0.958</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>28.0±4.7</td>
<td>28.8±5.8</td>
<td>0.022</td>
</tr>
<tr>
<td>Total cholesterol, mmol/L</td>
<td>6.05±1.12</td>
<td>5.79±1.18</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HDL cholesterol, mmol/L</td>
<td>1.50±0.44</td>
<td>1.37±0.45</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Urine albumin-to-creatinine ratio, mg per mmol/L</td>
<td>6.9±32.6</td>
<td>17.7±35.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Smoking status, %</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Never</td>
<td>50.9</td>
<td>40.0</td>
<td></td>
</tr>
<tr>
<td>Previous</td>
<td>33.1</td>
<td>32.0</td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>16.0</td>
<td>28.0</td>
<td></td>
</tr>
<tr>
<td>Strain on baseline ECG, %</td>
<td>10.1</td>
<td>26.4</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

### TABLE 2. Baseline and Change From Baseline to Last In-Study Measurement of Blood Pressure and ECG LVH in Relation to the Development of New-Onset CHF

<table>
<thead>
<tr>
<th>Variables</th>
<th>No CHF (n=8431)</th>
<th>CHF (n=265)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline measurements</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>174.4±14.3</td>
<td>174.9±14.1</td>
<td>0.548</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>97.9±8.7</td>
<td>95.0±10.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cornell voltage-duration product, mm-ms</td>
<td>2803±1019</td>
<td>3174±1324</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sokolow-Lyon voltage, mm</td>
<td>30.0±10.4</td>
<td>33.3±11.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Change from baseline to last measurement</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>−29.5±19.5</td>
<td>−35.1±21.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>−17.1±10.2</td>
<td>−17.8±12.6</td>
<td>0.371</td>
</tr>
<tr>
<td>Cornell voltage-duration product, mm-ms</td>
<td>−226±790</td>
<td>60±1352</td>
<td>0.001</td>
</tr>
<tr>
<td>Sokolow-Lyon voltage, mm</td>
<td>−3.9±7.0</td>
<td>−4.4±9.4</td>
<td>0.494</td>
</tr>
</tbody>
</table>
increased risk of developing CHF, with an actuarial 5-year rate of 8.8% compared with only 2.7% in those without ECG strain. Patients with strain also had an ≈5-fold-increased risk of CHF mortality, with a 5-year CHF mortality of 1.2% compared with only 0.3% in patients without strain.

Because patients who developed CHF differed significantly from those who did not develop CHF with respect to demographic and clinical variables that could affect outcome (Tables 1 and 2), the independent relation of new-onset CHF to the presence or absence of strain was examined after adjustment for the propensity score and the possible effects of treatment with losartan vs atenolol, baseline and in-treatment systolic and diastolic blood pressures, baseline and in-treatment Sokolow-Lyon voltage and Cornell voltage-duration product, and propensity score for ECG strain; CHF mortality was adjusted for the possible effects of treatment with losartan vs atenolol, baseline and in-treatment systolic and diastolic blood pressures, baseline and in-treatment Sokolow-Lyon voltage and Cornell voltage-duration product, and propensity score for ECG strain.

The predictive value of ECG strain for new-onset CHF in relevant subsets of the population is examined in Table 4. The association between strain and new-onset CHF was similar in men and women, in blacks and other races, in both treatment arms of the study, in patients >65 and <65 years of age, among patients with and without a history of ischemic heart disease or myocardial infarction, and among patients with and without LVH on their baseline ECG by either Cornell product or Sokolow-Lyon voltage criteria, with nonsignificant interaction terms for these variables. In contrast, strain did not appear to equally predict the risk of developing CHF in hypertensive patients stratified according to the presence or absence of diabetes and albuminuria. Strain was a strong predictor of new CHF in patients without diabetes but did not significantly stratify risk among patients with diabetes (P=0.004 for the interaction term between strain and diabetes), reflecting the higher incidence of CHF in diabetic patients without strain. In contrast, strain was a predictor of new CHF in both patients with and without microalbuminuria at baseline but was associated with a significantly greater risk of developing CHF in patients without albuminuria.

**Discussion**

This study demonstrates that the presence of typical strain on the ECG in hypertensive patients with ECG LVH by Cornell product and/or Sokolow-Lyon voltage identifies patients at increased risk of developing CHF and of dying as a result of CHF in the setting of antihypertensive therapy associated with substantial decreases in both systolic and diastolic blood pressure.
pressures. The increased risk of new-onset CHF and CHF mortality associated with ECG strain was independent of the improved prognosis with losartan therapy in LIFE and persisted after adjustment for the greater baseline severity and prevalence of ECG LVH and the higher prevalence of other CV disorders in patients who develop subsequent CHF. These findings suggest that more aggressive therapy may be warranted in hypertensive patients with ECG strain to reduce the risk of CHF and CHF mortality.

ECG Strain and the Prediction of CHF

Previous studies have examined the predictive value of ECG LVH criteria for the development of CHF, including criteria that incorporate some measure of ECG strain into their determination. Among participants in the Framingham Heart Study, the presence of the combination of voltage criteria for LVH and ST depression and T-wave flattening or inversion was associated with a >7-fold-increased risk of developing CHF in both men and women after adjustment for age, systolic pressure, cholesterol, glucose, and smoking. However, this population-based study used a less-specific definition of strain than in the present study, had much lower prevalences of repolarization abnormalities than the LIFE study, did not adjust for baseline severity of ECG LVH, and did not examine the predictive value of strain alone. Similarly, studies of Romhilt-Estes point score criteria, which depend heavily on the presence of ECG strain, demonstrated a significant association of LVH by these criteria with new-onset CHF in the elderly and in patients presenting to the emergency department with suspected acute coronary syndrome, but they did not address the predictive value of strain alone. A serial analysis of the ECG in a subset of the Framingham study, a population-based study of elderly men, and the Copenhagen City Heart Study examined the predictive value of ECG strain alone for CV outcomes but unfortunately did not report CHF outcomes. Similarly, previous studies of the predictive value of ECG strain...
among hypertensive patients did not examine the relationship of strain to developing CHF.

In contrast, the present study demonstrates that typical strain on the baseline ECG of hypertensive patients with ECG LVH by Cornell product or Sokolow-Lyon voltage criteria was a significant predictor of new-onset CHF and CHF mortality. The predictive value of strain in LIFE was independent of the possible impact of standard CV risk factors, baseline and in-treatment severity of ECG LVH by both criteria, baseline and in-treatment systolic and diastolic pressures, baseline demographic differences, and the known impact of treatment with losartan versus antenol on these outcomes in LIFE. In addition, the association between strain and new CHF was similar in all relevant subsets of the LIFE study population except patients with and without diabetes and microalbuminuria (Table 4). Of note, the decrease in statistical power of ECG strain between the univariate and multivariable Cox models (Table 3) reflects a strong association between ECG strain and clinical and demographic variables that are also potential risk markers for CHF.

Although the precise mechanisms linking ECG strain to the development of CHF are not known, the strong association of strain with abnormalities of CV structure and function may explain in part the adverse prognosis associated with strain. In a heterogeneous population of 161 patients with echocardiographic or autopsy measures of LV mass, ECG strain was associated with increased LV mass and reduced ejection fraction. In the echocardiographic substudy of LIFE, ECG strain was strongly related to the presence of coronary heart disease, increased LV mass, and echocardiographic LVH that was more likely to be concentric, factors that predispose to the development of CHF. In addition, ECG strain was associated with higher estimated myocardial oxygen demand, lower myocardial contractility as estimated by stress-corrected midwall shortening, and a 2.5-fold greater prevalence of abnormal myocardial contractility, evidence linking strain on the ECG to LV functional abnormalities that can predispose to CHF. The lack of association between ECG strain and echocardiographic parameters of diastolic dysfunction provides further support that the predictive value of strain for new CHF may be mediated by abnormalities of LV systolic function. The additive prognostic value of ST depression and echocardiographic LV mass measurements for CV mortality in a separate population suggests that strain and LV mass may provide complementary risk information for the development of CHF as well, although the low number of new CHF events in the echocardiographic subset of LIFE precludes meaningful analyses of the predictive value of strain after adjustment for echocardiographic LV mass.

Study Limitations and Perspectives

The independent relation of strain to increased risk of developing CHF in LIFE despite aggressive blood pressure reduction suggests that strain on the baseline ECG may be used to identify hypertensive patients with ECG LVH who require more aggressive antihypertensive therapy aimed at further reducing risk in these patients. However, the inferences that may be drawn from the present study are potentially limited by the lack of information on the serial behavior of the strain pattern over time in the entire LIFE study population, by the absence of quantitative data assessing the degree of ST depression in this population, and by the small number of CHF deaths. Although serial assessment of the presence or absence of strain provides additional prognostic information in a subset of the Framingham population, whether evaluation of the time course of strain on the ECG provides additional risk information with respect to the development of CHF requires further study. The present findings, taken in context of the strong association of strain with LVH and observations from the echocardiographic substudy of LIFE that decreasing LV mass in response to antihypertensive therapy was associated with improvement in LV performance, suggest that regression of LVH in this population may be associated with a decreased risk of developing CHF. Further study is necessary to address this important question.

Acknowledgment

This work was supported in part by grant COZ-368 from Merck & Co, Inc, West Point, Penn.

Disclosures

Dr. Okin, Devereux, Nieminen, Jern, Kjeldsen, and Dahlöf received grant support from Merck & Co, Inc. Drs. Devereux, Kjeldsen, and Dahlöf have received honoraria from Merck & Co, Inc. Dr. Kjeldsen has also received research support from the Norwegian Council for Cardiovascular Diseases and has served on the speakers’ bureaus of and/or received honoraria from AstraZeneca, Bayer, Novartis, and Pfizer. Dr. Dahlöf has also received research grants from Pfizer, Novartis, and Boehringer Ingelheim; served on the speakers’ bureaus of and/or received honoraria from Servier, Novartis, Boehringer Ingelheim, and Pfizer; and served as a consultant to or on the advisory boards of Novartis, Merck, and Boehringer Ingelheim.

References


**CLINICAL PERSPECTIVE**

This study demonstrates that the presence of typical strain on the ECG in hypertensive patients with ECG LVH by Cornell voltage-duration product and/or Sokolow-Lyon voltage identifies patients at increased risk of developing CHF and of dying as a result of CHF in the setting of antihypertensive therapy associated with substantial decreases in both systolic and diastolic pressures. Importantly, the increased risk of new-onset CHF and CHF mortality associated with ECG strain was independent of the improved prognosis with losartan therapy in the LIFE study and persisted after adjustment for the greater baseline severity and prevalence of ECG LVH and the higher prevalence of other CV disorders in hypertensive patients who develop subsequent CHF. These findings suggest that more aggressive therapy may be warranted in hypertensive patients with ECG strain to reduce the risk of CHF and CHF mortality. In addition, the present findings, taken in context of the strong association of strain with LVH and observations from the echocardiographic substudy of LIFE that decreasing LV mass in response to antihypertensive therapy was associated with improvement in LV performance, suggest that regression of LVH in this population may be associated with a decreased risk of developing CHF. Further study is necessary to address this important question.
Electrocardiographic Strain Pattern and Prediction of New-Onset Congestive Heart Failure in Hypertensive Patients: The Losartan Intervention for Endpoint Reduction in Hypertension (LIFE) Study

Peter M. Okin, Richard B. Devereux, Markku S. Nieminen, Sverker Jern, Lasse Oikarinen, Matti Viitasalo, Lauri Toivonen, Sverre E. Kjeldsen and Björn Dahlöf for the LIFE Study Investigators

*Circulation.* 2006;113:67-73; originally published online December 19, 2005;
doi: 10.1161/CIRCULATIONAHA.105.569491
*Circulation* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2005 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/113/1/67

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Circulation* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to *Circulation* is online at:
http://circ.ahajournals.org//subscriptions/