# Usefulness of Electrocardiographic Strain to Predict Survival After Surgical Aortic Valve Replacement for Aortic Stenosis

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**Electrocardiographic (ECG) strain has been reported as a specific marker of midwall left ventricular (LV) myocardial fibrosis, predictive of adverse clinical outcomes in aortic stenosis (AS), but its prognostic impact after aortic valve replacement (AVR) is unknown. We aimed to assess the impact of ECG strain on long-term mortality after surgical AVR for AS. From January 2005 to January 2014, patients with interpretable preoperative ECG who underwent isolated AVR for AS were included. ECG strain was defined as ≥1-mm concave downslopping ST-segment depression with asymmetrical T-wave inversion in lateral leads. Mortality was assessed over a follow-up period of 4.8 ± 2.7 years. Among the 390 patients included, 110 had ECG strain (28%). They had significantly lower body mass index, higher mean transaortic pressure gradient and Cornell-product ECG LV hypertrophy than in those without ECG strain. There was also a trend for lower LV ejection fraction in patients with ECG strain as compared with those without. Patients with ECG strain had significantly lower 8-year survival than those without. ECG strain remained associated with reduced survival both in patients with and without LV hypertrophy (p <0.0001 for both). After adjustment, ECG strain remained a strong and independent determinant of long-term survival (hazard ratio 4.4, p <0.0001). Similar results were found in patients with LV hypertrophy or without LV hypertrophy. In the multivariate model, the addition of ECG strain provided incremental prognostic value (p <0.0001). In conclusion, in patients with AS, ECG strain is associated with 4-fold increased risk of long-term mortality after isolated AVR, regardless of preoperative LV hypertrophy.**  **(Am J Cardiol 2017;120:1359–1365)**

Recently, an "old" electrocardiographic (ECG) parameter, that is, ECG strain, defined as ST-segment depression with asymmetrical T-wave inversion in the lateral leads (Figure 1), has been brought up to date in patients with aortic stenosis (AS). Indeed, patients with AS and ECG strain generally have more severe AS, associated with left ventricular (LV) hypertrophy, and have worse cardiovascular risk.[1] Furthermore, in patients with AS, ECG strain is not simply reflecting LV hypertrophy but is also an accurate marker of LV midwall fibrosis,[2] associated with advanced LV myocardial structural changes injury. Consistently, several studies demonstrated the prognostic significance of ECG strain in asymptomatic patients,[2–5] regardless of LV hypertrophy or LV mass. Later in the course of the disease, after aortic valve replacement (AVR), when aortic valve-related LV pressure overload is released and LV reverse remodeling may occur, there are no data on the impact of preoperative ECG strain on outcome. Therefore, we aimed to assess the postoperative prognostic value of ECG strain in patients with severe AS who underwent surgical AVR (SAVR). We hypothesized that preoperative ECG strain is a predictor of poorer long-term survival after valve replacement for AS, independent of the presence of LV hypertrophy.

## Methods

From January 2005 to January 2014, 575 consecutive patients with severe AS underwent isolated SAVR (i.e., without concomitant other valve intervention or coronary artery bypass graft) in our institution. Severe AS was defined as aortic valve area ≤1 $cm^2$ or indexed aortic valve area ≤0.6 $cm^2/m^2$ and/or mean transaortic pressure gradient >40 mmHg. All patients with other concomitant significant valve disease (i.e., ≥grade 2 mitral regurgitation, or ≥grade 2 aortic regurgitation, or any mitral stenosis), previous cardiac surgery, or valve endocarditis were excluded from the study. Patients with noninterpretable ECG or with left or right bundle-branch block or concurrent digoxin use (i.e., precluding ECG strain analysis) were also excluded. Baseline preoperative demographic and

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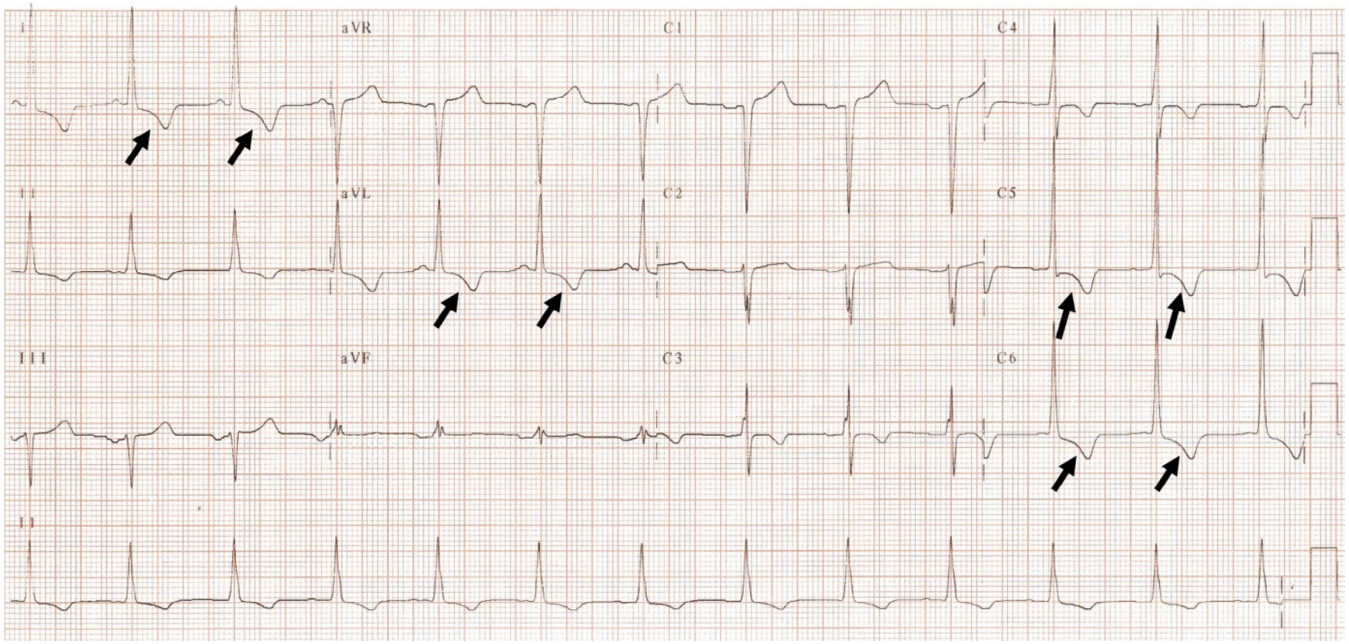


Figure 1. ECG of patients with aortic stenosis demonstrating left ventricular hypertrophy sign and typical signs of electrocardiographic strain *(black arrows)*: ST-segment depression and asymmetrical T-wave inversion in lateral leads.

clinical data, risk factors, and co-morbidities were collected. The EuroScore II was calculated for each patient.

All patients underwent a baseline preoperative 12-lead ECG recorded at 25 mm/s and 1 mV/cm. One investigator (BG) blinded to the outcome data performed the ECG interpretation. Heart rate, QT and QRS intervals, and R wave in a VL lead were measured. The Sokolow-Lyon Index was calculated as amplitude of leads SV1 + RV5 or RV6. The Cornell voltage-duration product was derived from the following equation: [RaVL + SV3 + (6 mV in women)] × QRS duration. The electrical LV hypertrophy was defined as Cornell voltage-duration product ≥2440 mV·ms. The ECG strain was defined as ≥1 mm concave downsloping ST-segment depression with asymmetrical T-wave inversion in the lateral leads (I, aVL, V5, V6, Figure 1). The presence of ECG strain was also assessed in a subgroup of patients with an interpretable ECG at 1 year of follow-up after SAVR (n = 110).

The primary end point of the study was the postoperative all-cause mortality during the follow-up. Mortality data were obtained from death certificates, family physician phone contacts, or hospital records. The mortality data were collected between January 2016 and July 2016.

Continuous data were expressed as mean ± SD and were compared using Student's *t* test or analysis of variance with Tukey post hoc test. Categorical data were given as numbers and percentages and were compared using the chi-square test or Fisher exact test, as appropriate. A p value <0.05 was considered as statistically significant. The independent associated factors of ECG strain were identified using stepwise backward logistic regression. All variables with a p value <0.20 regarding difference between ECG strain and no ECG strain groups in the univariate analysis were entered into the logistic regression. In the case of variables showing collinearity (e.g., systolic blood pressure and hypertension), the variable with the lowest p value in the univariate analysis was selected. Overall survival was calculated from the time of SAVR to the date of last follow-up available or until the date of death. The cumulative probability of death was estimated by the Kaplan-Meier method, and the results presented at 2, 4, and 8 years. The survival between groups was compared using the log-rank test. The impact of ECG strain on survival was assessed using both univariate and multivariate Cox proportional hazard model. Variables with a univariate p <0.20 were considered for subsequent multivariate models. The results are presented as hazard ratios (HR) with corresponding 95% confidence interval (CI). All statistical analyses were performed with a commercially available software package SPSS Version 23 (SPSS Inc., IBM Corp., Armonk, New York).

## Results

Among the 575 patients who underwent SAVR, included during the period, 390 were selected for the present study (Figure 2), among whom 110 (28%) had ECG strain. The baseline preoperative characteristics of the population are reported in Table 1. Only 11% of patients had reduced (i.e., <50%) LV ejection fraction.

The comparison between patients with ECG strain and those without ECG strain is reported in Table 1. Patients with ECG strain had significantly larger body mass index, higher creatinine level, more severe AS according to mean transaortic pressure gradient, and more frequent electrocardiographic LV hypertrophy than patients without ECG strain. There was a trend for lower LV ejection fraction in patients with ECG strain, with higher rate of reduced LV ejection fraction (16% vs 9.5% in the absence of ECG strain, p = 0.082). There was no significant difference between the 2 groups regarding other baseline preoperative characteristics.

In the logistic regression model, the independent factors associated with ECG strain, were New York Heart Association