

Association of Common Carotid Artery Doppler-Determined Dicrotic Notch Velocity With the Left Ventricular Ejection Fraction

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Objectives—The appearance of the dicrotic notch on blood pressure tracings is associated with impaired cardiac function. Common carotid artery waveforms have similar fiducial markers, yet they have not been related to cardiac function. We studied associations of common carotid artery dicrotic notch velocities with the left ventricular ejection fraction (LVEF) determined by echocardiography.

Methods—We conducted a retrospective study of 37 patients who had cardiac echocardiography and carotid Doppler evaluations within 1 day of each other. The LVEF was determined by the biplane modified Simpson rule. Doppler parameters were measured from tracings of the left common carotid artery 4 cm from the flow divider. Linear regression and stepwise multivariable linear regression models were used to evaluate any association between the LVEF and the following variables: age, sex, peak systolic velocity (PSV), end-diastolic velocity (EDV), dicrotic notch velocity, rise time (EDV to PSV), resistive index, and cardiac cycle length.

Results—The dicrotic notch velocity was the only variable associated with the LVEF ($P = .028$) in a bivariate analyses. A backward selection stepwise multivariable equation predicting the LVEF had the dicrotic notch ($P = .001$) and resistive index ($P = .01$) as significant predictors, whereas the cardiac cycle length ($P = .08$) and PSV ($P = .08$) were borderline not significant. Model goodness of fit was $R^2 = 0.37$ ($P = .004$).

Conclusions—Dicrotic notch velocities measured from common carotid artery Doppler waveforms are associated with the LVEF and might offer some clinical value in selected cases.

Key Words—carotid artery; Doppler sonography; Doppler waveform analysis; echocardiography; ejection fraction; vascular ultrasound

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Abbreviations

CI, confidence interval; EDV, end-diastolic velocity; LV, left ventricular; LVEF, left ventricular ejection fraction; PSV, peak systolic velocity

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There are few studies looking at the specific components of common carotid artery Doppler waveforms in a quantitative fashion. Holdsworth et al¹ studied metrics such as the peak systolic velocity (PSV) and end-diastolic velocity (EDV) and then added dicrotic notch velocities with parameters of acceleration and deceleration in a small group of healthy young volunteers. Prior studies on the coupling between cardiac function and common carotid artery waveform morphologic characteristics have mostly been subjective² and often focused on the effects of aortic valve disease.^{3,4}

As part of our clinical practice, we have observed the occasional presence of a deep dicotic notch in the common carotid Doppler tracings of patients in heart failure, especially heart transplant candidates. A review of the literature on Doppler sonography did not show any formal analysis addressing this issue. Changes in the dicotic wave measured from pressure tracings have been shown to have associations with heart failure.⁵ However, the possible associations between dicotic velocities measured on Doppler waveforms and cardiac function have not been evaluated.

We proposed to investigate whether dicotic velocity measurements made on Doppler velocity tracings of the common carotid artery were associated with the left ventricular ejection fraction (LVEF) and, specifically, whether lower velocities and a deeper notch are seen in patients with decreased left ventricular (LV) systolic function.

Materials and Methods

Patient Population

We conducted a retrospective study of carotid artery Doppler examinations performed within 1 day of echocardiography during an interval of 8 months in a tertiary care institution. The study was performed with local Institutional Review Board review and permission. Participants' written informed consent was not required because of the retrospective nature of the study.

We randomly identified 37 patients who had carotid artery examinations and transthoracic echocardiography performed within 1 day of each other over a 7-month period: 5 with the carotid examinations the day before, 19 with the examinations on the same day, and 13 with the examinations the day after. We recorded patient demographics (age and sex) and the indications for the studies.

Carotid Sonography

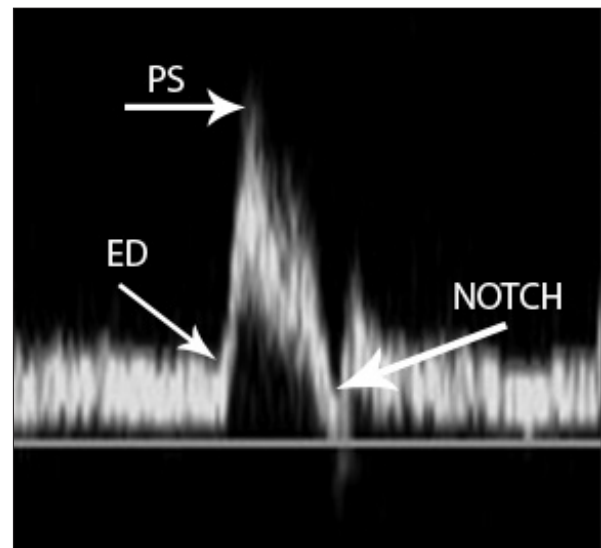
All examinations were performed in an Intersocietal Accreditation Commission Vascular Testing–certified laboratory by experienced sonographers using LOGIQ9 ultrasound scanners and linear array transducers (9L; GE Healthcare, Waukesha, WI). A standard protocol that included sampling of the common carotid, internal carotid, and vertebral arteries was used. We selected the left common carotid artery duplex image for our analyses. In our protocol, this image is acquired with the Doppler gate sampling a point 3 to 4 cm from the common carotid artery bifurcation. The acquired images were transferred as digital files (JPEG). One reader blindly processed the images using ImageJ for the Macintosh (Rasband; National Institutes of Health, Bethesda, MD) measuring the end-diastolic velocity (EDV),

the time to the EDV, the peak systolic velocity (PSV), the time to the PSV, the velocity in the dicotic notch, and the time to the next cardiac cycle (EDV-to-EDV interval). The resistive index was calculated as $(PSV - EDV)/PSV$. Figure 1 shows the sites measured on the common carotid artery waveform.

Thirty of the 37 patients had a regular heart rhythm on the image used for analysis; 5 had ectopic activity; and 2 had an irregular rhythm. The reader picked a representative cardiac cycle for the analysis: nonpotentiated beat, clear spectrum, preceded and followed by a beat with similar morphologic characteristics.

We assessed the intra-reader and inter-reader variability by blinded replicate measurements of the diastolic notch velocities in 14 patients at an interval of 4 months or more. For intra-reader variability, a set of 14 duplex images was blindly reread. The task consisted of selecting one cardiac cycle and then performing the measurements. For inter-reader variability, the same set of 14 duplex images was blindly reread. The task consisted of selecting one cardiac cycle and then performing the measurements. Duplex images of the right common carotid artery were acquired. The right diastolic notch velocities were then blindly measured and compared to the left side ($n = 14$).

Figure 1. Doppler waveform fiducial points used in this study. ED indicates end diastole; NOTCH, dicotic notch; and PS, peak systole. The velocities at PS, ED, and NOTCH are, respectively, the peak systolic, end-diastolic, and notch velocities.



Echocardiography

All 2-dimensional transthoracic echocardiographic examinations were performed in an Intersocietal Accreditation Commission Echocardiography–certified laboratory by certified sonographers. Images were acquired in standard views on iE-33 ultrasound scanners (Philips Healthcare, Andover, MA). The LVEF was determined by using the biplane modified Simpson method from LV cavity tracings that included the papillary muscles and were measured on the ultrasound device. The LVEF was calculated as: $[(LV \text{ end-diastolic volume} - LV \text{ end-systolic volume}) / LV \text{ end-diastolic volume}] \times 100$. The estimated LVEF values were verified by qualitative assessment of the dynamic recordings during clinical interpretation of the studies. The LVEF results used in this study were the original readings as reported in the clinical echocardiography report.

Statistical Methods

We reported the means and standard deviations for continuous variables and the percentages for ordinal variables. We performed a linear regression analysis comparing the various parameters as independent predictors of the LVEF. We then performed a backward stepwise multivariable linear regression analysis with Doppler variables, with all candidate variables setting the threshold for exit at $P > .1$. The model goodness of fit was also estimated as an R^2 value, and the results of the global model F ratio were reported.

Sensitivity analysis consisted of using the echocardiographically determined stroke volume as the dependent variable instead of the LVEF. We also evaluated the effect of measuring the notch velocity as the negative peak versus the negative upper base of the diastolic notch in 2 cases. We performed a sensitivity analysis looking at the estimated stroke volume (LV end-diastolic volume – LV end-systolic volume) as the dependent variable.

All analyses were performed with JMP version 9.0 software (SAS Institute Inc, Cary, NC). Significance levels were set at $P < .05$ (2 sided). The degree of significance was based on F ratios for the models and t ratios for individual parameter estimates.

Results

The mean age of the patients was 67.1 (SD, 12.9) years, with men composing 64.9% (24 of 37) of the cohort (Table 1). The mean LVEF was 37.6% (SD 18.6%), with a range of 5%–65% (Figure 2). The indications for the studies were preoperative coronary artery bypass surgery in 54.0%, preoperative evaluation for other surgery (16.2%), workup of patients with neurologic symptoms or suspected

carotid stenosis (10.8%), preoperative evaluation of possible cardiac transplant recipients (16.2%), and aortic valve replacement (2.7%). The mean LVEFs were different ($P = .01$) based on the indication, with mean values of 38.5% (SD, 13.9%) in the preoperative bypass surgery group, 18.3% (SD, 13.9%) in the preoperative transplant workup group, 49.2% (SD, 22.2%) in the general preoperative workup group, 48.3% (SD, 24.7%) in the neurologic workup group, and 15% for the aortic valve replacement patient. Two of the 37 patients had negative notch velocities (Figure 3).

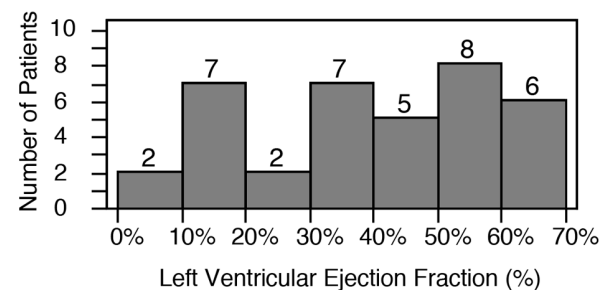
The correlation coefficients between replicate readings of notch velocities were 0.92 ($P < .0001$; 95% confidence interval [CI], 0.76–0.97) for intra-reader variability and 0.95 ($P < .0001$; 95% CI, 0.86–0.99) for inter-reader variability. The right and left diastolic notch velocities were correlated with each other ($n = 14$), giving a correlation coefficient of 0.68 ($P = .007$; 95% CI, 0.24–0.89).

Table 1. Demographics, Common Carotid Artery Doppler-Derived Velocity Parameters, and LVEF by Transthoracic Echocardiography for 37 Patients

Variable	Value
Age, y	67.1 (12.9)
Sex (male)	24 (64.9)
Indication	
Preoperative bypass surgery	20 (54.0)
Neurologic	4 (10.8)
Preoperative (general)	6 (16.2)
Transplant evaluation	6 (16.2)
Aortic valve replacement	1 (2.7)
PSV, cm/s	73.0 (25.2)
EDV, cm/s	18.2 (5.9)
Notch velocity, cm/s	18.1 (9.71)
Rise time, ms	69.2 (18.5)
Cardiac cycle length, ms	889.2 (133.0)
Resistive index	0.74 (0.07)
LVEF, %	37.6 (18.6)

Numbers in parentheses represent SD values for continuous variables and percentages for ordinal variables.

Figure 2. Distribution of LVEF values in the patients studied.



Bivariate associations between key variables and the LVEF are shown in Table 2. Notch velocities ($P = .028$) were significantly associated with the LVEF (Figures 3 and 4A). The other variables were not. The correlation coefficient between notch velocities and the LVEF was 0.36.

A full linear regression multivariable model (Table 3 and Figure 4B) showed that the notch velocity was the only variable positively associated with the LVEF ($P = .021$). Model goodness of fit was $R^2 = 0.46$ ($P = .015$).

Results of the backward selection stepwise linear regression multivariable model are shown in Table 4 and Figure 4C. The notch velocity ($P = .0011$) remained a significant predictor of the LVEF with the resistive index ($P = .01$), whereas the cardiac cycle length ($P = .08$) and PSV ($P = .08$) were not. Overall model goodness of fit was $R^2 = 0.37$ ($P = .004$).

We performed sensitivity analyses correlating demographics and the Doppler-derived indices with stroke volume. There were no significant associations with the Doppler indices, whereas men tended to have a greater stroke volume than women ($P = .046$). The mean stroke volume was 58.8 (SD, 26.5) mL in 31 patients with available measurements. The mean stroke volume for men ($n = 20$) was 65.8 (SD, 22.7) mL versus 46.1 (SD, 29.2) mL for women ($n = 11$). Use of either the base of the dirotic notch or the negative peak seen in 2 cases (Figure 3C) did not substantially alter the results.

Discussion

We found that the dirotic notch velocity evaluated on Doppler tracings of the left common carotid artery was significantly associated with the LVEF. This association is maintained over a broad range of ejection fraction values.

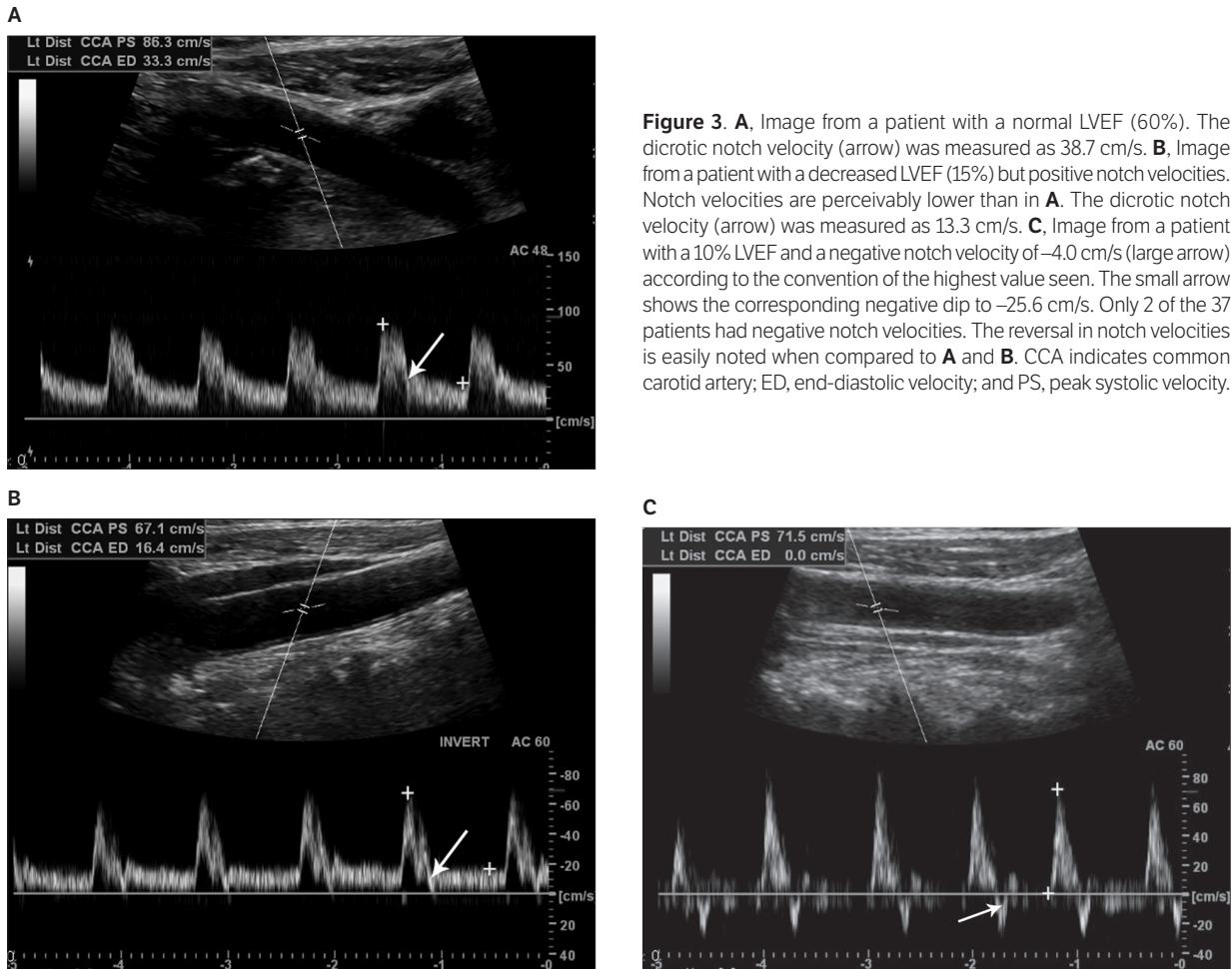


Figure 3. **A**, Image from a patient with a normal LVEF (60%). The dirotic notch velocity (arrow) was measured as 38.7 cm/s. **B**, Image from a patient with a decreased LVEF (15%) but positive notch velocities. Notch velocities are perceptibly lower than in **A**. The dirotic notch velocity (arrow) was measured as 13.3 cm/s. **C**, Image from a patient with a 10% LVEF and a negative notch velocity of -4.0 cm/s (large arrow) according to the convention of the highest value seen. The small arrow shows the corresponding negative dip to -25.6 cm/s. Only 2 of the 37 patients had negative notch velocities. The reversal in notch velocities is easily noted when compared to **A** and **B**. CCA indicates common carotid artery; ED, end-diastolic velocity; and PS, peak systolic velocity.

We decided to evaluate the dicrotic notch velocities as possibly being associated with the LVEF based on the subjective observation that worsening heart failure was associated with deepening of the dicrotic notch and an

increasing dicrotic wave on blood pressure tracings.⁵ To our knowledge, the correlation between the deepening of this notch and the LVEF had not been previously studied.

Table 2. Bivariate Associations for Various Common Carotid Artery Doppler Variables and Demographics With the LVEF as Determined by Transthoracic Echocardiography

Variable	β	P
Age, y	0.28	.24
Sex (male)	2.02	.54
PSV, cm/s	0.09	.46
EDV, cm/s	-0.05	.92
Notch velocity, cm/s	0.69	.028
Rise time, ms	-0.26	.13
Cardiac cycle length, ms	0.04	.11
Resistive index	70.7	.12

Table 3. Results of a Multivariable Linear Regression Model Predicting the LVEF With All Candidate Variables Entered

Variable	β	SE	t Ratio	P
Age, y	0.29	0.23	1.26	.21
Sex (women)	1.39	3.05	0.46	.65
PSV, cm/s	-0.53	0.33	-1.60	.12
EDV, cm/s	1.65	1.41	1.17	.25
Notch velocity, cm/s	0.86	0.35	2.45	.021
Rise time, ms	-0.20	0.15	-1.31	.20
Cardiac cycle length, ms	0.042	0.021	2.02	.053
Resistive index	221.4	109.9	2.01	.054

Model goodness of fit: $R^2 = 0.46$ ($P = .015$).

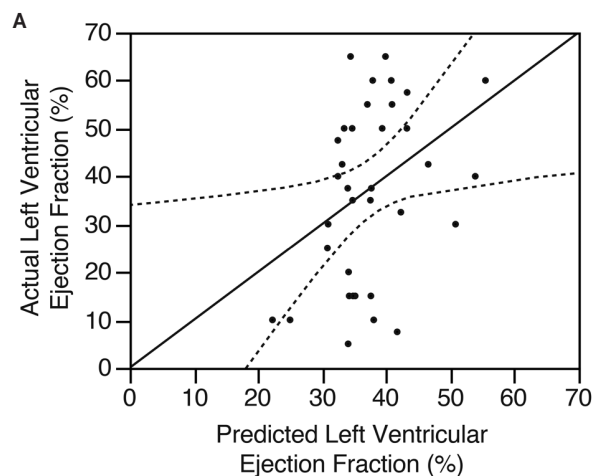
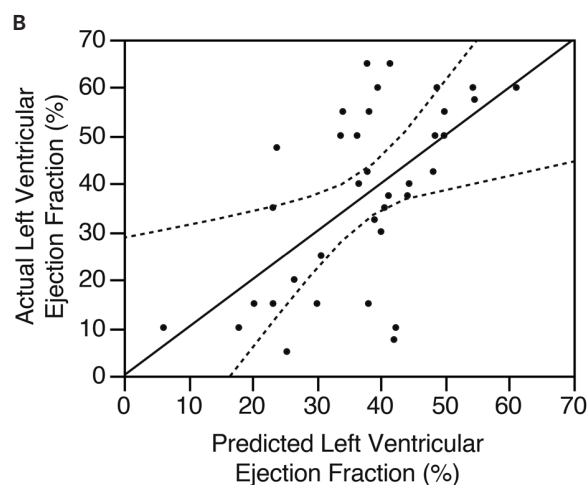
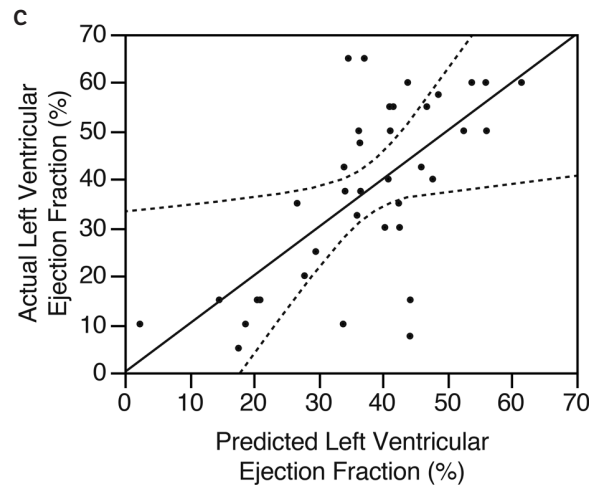


Figure 4. A. Association between notch velocities and the LVEF. The results are plotted as the predicted LVEF (from the regression equation used for Table 2) compared to the actual LVEF determined by echocardiography. Model goodness of fit was $R^2 = 0.13$ ($P = .028$). The regression curve (solid line) and 95% CIs (dashed lines) are shown.



B. Association between notch velocities and the LVEF after adjusting for all variables. The results are plotted as the predicted LVEF (from the regression equation used for Table 3) compared to the actual LVEF determined by echocardiography. Model goodness of fit was $R^2 = 0.46$ ($P = .015$). The regression curve (solid line) and 95% CIs (dashed lines) are shown. **C.** Association between notch velocities and the LVEF after adjusting for variables selected according to a backward selection process. The results are plotted as the predicted LVEF (from the regression equation used for Table 4) compared to the actual LVEF determined by echocardiography. Model goodness of fit was $R^2 = 0.37$ ($P = .004$). The regression curve (solid line) and 95% CIs (dashed lines) are shown.



Holdsworth et al¹ reported a mean notch velocity of 19.4 cm/s in 11 healthy volunteers with a mean age of 28 years. We report a mean notch velocity of 18.1 cm/s, a value slightly lower than that reported by Holdsworth et al.¹ We further looked at a stratified breakdown of notch velocities for LVEF estimates above or below 45%. The mean notch velocity for an LVEF below 45% was 16.5 cm/s compared to 20.4 cm/s for an LVEF of 45% or above. This finding suggests that the range of measurement is narrow; therefore, the measurement may not be robust enough for routine clinical use. The association between the LVEF and dicrotic notch velocity was modest at best (correlation coefficient of 0.36). The statistical models we used showed a range of goodness of fit, with R^2 values ranging from 0.37 to 0.47 for the multivariable models shown in Tables 3 and 4. These values indicate that 37% to 46% of the variability in the LVEF could be explained by the variables in the model. This aspect might be difficult to understand, and it is highly probable that the multivariable model with all variables was “overadjusted” given the number of predictor variables and the number of participants. The parsimonious model may more closely reflect the variability in the LVEF that could be explained by common carotid artery Doppler parameters in these specific individuals. This likelihood in no way guarantees that these results are generalizable. Of interest, the univariate association between the LVEF and notch velocities indicates that 13% of the LVEF variability might be explainable by notch velocities.

Strengths of our observations included the close temporal association between the echocardiographic examinations and the carotid Doppler evaluations. We also had a broad distribution of LVEF values showing that the findings apply to a wide range of contractile states of the ventricle (Figure 2).

Limitations included cases in which the dicrotic notch was difficult to identify ($n = 2$) and a lack of a definite definition of where to measure the dicrotic notch when it dips below 0 (Figure 3C). We opted to perform measurements both in the peak (bottom) of the wave-

form as well as the base (closest to the positive velocities). Our results were essentially the same. We were also limited by the mode of acquisition of the Doppler waveforms, since it might not have been optimized to permit clear identification of the dicrotic notch. Better delineation of the dicrotic notch might have been facilitated by the following measures: (1) minimizing the size of the Doppler sample gate; (2) meticulously maintaining the sample gate in the middle of the common carotid lumen; and (3) increasing the time base (pixels per second on the x-axis). Our time base included carotid artery waveforms recorded over a 5-second interval. It is also unclear whether our results will apply to patients with aortic valve disease, given the presence of only 1 individual with this condition in our cohort. Another limitation was the small size of the study. As such, the results could have been affected by an unknown factor or biased by the selection process, which led to these patients having been seen for both echocardiographic and carotid sonographic examinations within a short interval. In addition, the distribution of the LVEF values themselves may have reflected a referral bias.

We selected the left common carotid artery because it is longer than the right artery and therefore offers a greater chance for the blood flow pattern to return to a quasilaminar pattern than for the right side.^{6,7} It is known that in healthy individuals, velocity parameters are similar for the right and left sides.¹ We found a strong correlation between right and left common carotid artery notch velocities, with no significant difference (bias) between sides (paired difference, 6.1 cm/s; $P = .08$). Holdsworth et al¹ also noted a slight difference between sides but did not consider it substantive.

To make our findings generalizable, we did not seek adjustments for sex, cardiovascular risk factors, and medications. Differences between men and women appear minimal based on bivariate associations (Table 2). Lack of adjustment for risk factors and medications leaves open the possibility of residual confounding in our regression model. However, given our sample size, our analytic strategy decreased the chances of overadjusting our model.

We performed a sensitivity analysis by using the LV stroke volume as the dependent variable. None of the Doppler-derived indices were associated with the stroke volume. The LVEF is known to be a better metric of LV contractile function than the stroke volume, which suggests that our measurements of the dicrotic notch velocities are a better index of overall LV contractile strength than the ejected blood volume.

Table 4. Results of a Parsimonious Multivariable Linear Regression Model Using Backward Selection to Identify the Variables Predictive of the LVEF

Variable	β	P
Notch velocity, cm/s	1.13	.0011
Cardiac cycle length, ms	0.037	.08
Resistive index	132.6	.01
PSV, cm/s	-0.25	.08

Model goodness of fit: $R^2 = 0.37$ ($P = .004$).

Although our results were consistent with a form of ventricular-arterial coupling, our study was not directed at investigating possible associations between local arterial compliance and the LVEF, although carotid artery compliance is decreased in patients with heart failure.⁸ We have not found a pertinent reference supporting the existence of a direct association between local carotid artery compliance and Doppler waveform fiducial markers. A prospective experimental protocol would ideally have required local tonometry and a more sophisticated approach to measuring carotid artery compliance.

In conclusion, we have shown a correlation between the LVEF and dicrotic notch velocities. This finding might offer some clinical utility, especially in cases in which the notch velocity is depressed or reversed (Figure 3). Further studies are needed to confirm the robustness of our finding.

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