Abnormalities of left ventricular (LV) diastolic filling have often been described in patients with hypertension (1–7), even in the absence of LV hypertrophy (2,5–7). Doppler imaging of the mitral inflow has gained wide acceptance for the evaluation of hypertensive patients, as a simple, noninvasive and easily repeatable method of assessing LV diastolic function (8). Diastolic dysfunction in hypertensive patients is characterized primarily by impaired isovolumic relaxation (6,9). As a consequence, the velocity of early diastolic filling decreases and the late atrioventricular gradient increases, yielding a decreased early/atrial (E/A) velocity ratio (10).

Although they are only approximate and indirect measures of LV diastolic function (8), flow velocity-derived indexes of diastolic filling are widely recommended for the diagnosis of diastolic dysfunction (11), and they provide independent prognostic information in different clinical settings and populations, including congestive heart failure (12), the early phases of myocardial infarction (13,14) and the elderly (15). Hypertension is the most common risk factor for congestive heart failure in the general population (16) and is a frequent precursor of diastolic heart failure (17). However, it is still debated whether an independent prognostic value of LV diastolic dysfunction exists in hypertensive patients. In particular, it is currently unknown whether assessment of the LV inflow velocity pattern adds to the prognostic information provided by LV mass (18,19). In the setting of the Progetto Ipertensione Umbria Monitoraggio Ambulatoriale (PIUMA) study, we had the opportunity to investigate the relationship between abnormalities of LV diastolic function, as detected by Doppler echocardiography, and the subsequent risk of cardiovascular events in patients with essential hypertension.

METHODS

The PIUMA study is a prospective follow-up study of Caucasian adult patients with essential hypertension (20–22). Hypertensive patients were referred to one of three participating centers (Perugia, Città della Pieve and Castiglione del Lago) for baseline evaluation by a group of general practitioners in Umbria, in central Italy. A total of 1,839 subjects enrolled between 1988 and 1996, who had good-quality M-mode and Doppler echocardiographic recordings and complete follow-up data available, were in-
cluded in the present analysis. All patients fulfilled the following criteria: 1) systolic blood pressure (BP) ≥140 mm Hg, diastolic BP ≥90 mm Hg, or both, on three or more office visits at one-week intervals; 2) no previous treatment for hypertension (70%) or withdrawal from antihypertensive drugs four or more weeks before the study; 3) no clinical or laboratory evidence of heart failure, coronary heart disease, atrial fibrillation, previous stroke, valvular defects (stenosis or grade >1 regurgitation) or secondary causes of hypertension, or important concomitant disease; 4) good-quality echocardiographic recordings (see subsequently); and 5) one or more valid BP measurement per hour over 24 h. We excluded from the present analysis all patients whose LV ejection fraction at echocardiography was ≤0.50. All patients gave written or witnessed oral informed consent to participate in the study.

**Baseline measurements.** Office BP was measured with a mercury sphygmomanometer by a physician in the hospital clinic, after the subject sat for ≥10 min. The average of three or more measurements on two or more sessions was considered for the analysis. Heart rate (HR) was measured immediately after the echocardiographic study, by taking the radial pulse for 1 min. Ambulatory BP was recorded with an oscillometric device (Models 90202 and 90207, SpaceLabs, Redmond, Washington) that was set to take a reading every 15 min throughout 24 h. Reading, editing and analysis of data were performed as previously described (20,21).

The M-mode echocardiographic study of the LV was performed under two-dimensional control. Details on reading procedures and reproducibility in our laboratory are reported elsewhere (22). The LV mass was calculated according to Devereux et al. (23) and corrected by height2.7 to account for the effect of obesity (24).

Pulsed Doppler measurements of LV diastolic inflow were obtained as reported previously (5). Briefly, the LV diastolic filling pattern was recorded from the apical transducer position in patients in the partial left lateral decubitus position during expiratory apnea, with the sample volume situated between the mitral leaflet tips. The peak velocity of early rapid filling (E velocity) and the peak velocity of atrial filling (A velocity) were recorded, and the E/A ratio was calculated. The time of E velocity deceleration was measured as the interval between the peak E velocity and the point at which the descending segment of E-wave, or its asymptote, crosses the zero-velocity line. Tracings were read by two observers who were unaware of the patients’ clinical data, and the mean value from five or more measurements per observer was computed. Intra-observer between-occasion reproducibility of the Doppler measures was assessed in 20 consecutive hypertensive patients examined twice, 7 days apart. The mean differences ± SD were −0.001 ± 0.049 m/s−1 for peak E velocity, −0.006 ± 0.051 m/s−1 for peak A velocity and 0.019 ± 0.162 for the E/A velocity ratio.

**Follow-up procedures and end-point evaluation.** All patients were followed by their family physicians, in cooperation with the outpatient clinic of the referring hospital, and treated through the implementation of standard lifestyle and pharmacologic measures. Most patients continue to be periodically referred to our institutions for BP control and other diagnostic procedures. At the follow-up visit, 70% of the study patients were taking antihypertensive drugs, and 30% were complying with lifestyle measures only. Diuretics, beta-blockers, angiotensin-converting enzyme inhibitors, Ca2+ channel blockers and alpha2-blockers, alone or in various combinations, were the antihypertensive drugs that were most frequently prescribed. Periodic contact with the family physician and telephone interviews were used to determine the incidence of major cardiovascular complications of hypertension. For patients who developed a cardiovascular morbid event, hospital record forms and other available original-source documents were reviewed by the authors as a group. Cardiovascular events included new-onset coronary artery disease (myocardial infarction, unstable angina with documentation of ischemic electrocardiographic changes, sudden cardiac death or coronary revascularization procedure), congestive heart failure that required hospital admission, stroke, transient cerebral ischemia, symptomatic aorto-iliac occlusive disease verified by angiography and end-stage renal disease. The international standard criteria used to diagnose cardiovascular events in the PIUMA study have been reported previously (20,22).

**Statistical analysis.** Parametric data are reported as the mean value ± SD. Standard descriptive and comparative analyses were undertaken. The incidence of cardiovascular events is presented as the number of events per 100 patient-years, based on the ratio of the number of events observed to the total number of patient-years of exposure, up to the terminating event or censor. For those patients without events, the date of censor was that of the last contact with the patient. For those patients who experienced multiple events, survival analysis was restricted to the first event. Survival curves were estimated by using the Kaplan-Meier product-limit method and compared by using the Mantel (log-rank) test. The effect of prognostic factors on survival was evaluated by using the stepwise Cox semi-parametric regression model (25). The assumption of linearity for the Cox model was tested through visual inspection, and no violation of proportional hazards was found. We tested the variables of age (years), gender, body weight divided by the square of the height (kg/m2), office
and 24-h systolic and diastolic BP (mm Hg), office HR (beats/min$^{-1}$), serum cholesterol (mmol/l), diabetes (present or absent), smoking habits (previous, current or never), LV mass (g/m$^{-2.7}$) and antihypertensive treatment at the time of follow-up contact (e.g., lifestyle measures only, diuretics and beta-blockers alone or combined, angiotensin-converting enzyme inhibitors and Ca$^{2+}$ channel blockers alone or combined, other drug combinations).

It is well-recognized that the E/A ratio decreases markedly with increasing age and HR in both normotensive and hypertensive patients (26). In the present population, we found that the E/A ratio had a strong inverse relationship with age ($r = -0.55$) and HR ($r = -0.13$, both $p < 0.001$). Therefore, analyses were adjusted for age and HR. In a linear regression analysis, the E/A ratio was found to be a dependent variable related to age and HR (multiple $r = 0.63$, $p < 0.0001$). The following is the adjustment of the E/A ratio based on the regression lines:

$$\text{E/A ratio}_{\text{adjusted}} = \text{E/A ratio}_{\text{observed}} + (0.0199 \times [\text{age} - 50]) + (0.0082 \times [\text{heart rate} - 75])$$

where the observed ratio is normalized for an individual’s age (years) and HR (beats/min$^{-1}$) using the slopes of the age- and HR-related regression lines. Using this formula, the individual value of E/A ratio is normalized for an age of 50 years and HR of 75 beats/min. For the purpose of survival analysis, the age- and HR-normalized E/A mitral flow velocity ratio was modeled as either a binary or continuous variable. Patients were categorized according to whether their adjusted E/A ratio was below (n = 919) or above (n = 920) the median value ($-0.036$). We also tested the independent prognostic value of the adjusted E/A ratio as a continuous variable, as well as of the E-wave and A-wave velocities taken separately. To explore whether the relationship between the adjusted E/A ratio and the outcome variable was better fitted by a J- or U-shape, we also included in the model the square term of the adjusted E/A ratio. The SPSS statistical package, release 8.0 (SPSS Inc., Chicago, Illinois), was used to perform the analyses. A $p$ value of $< 0.05$ was considered as statistically significant.

**RESULTS**

Follow-up data were available in 1,839 (99%) of 1,856 patients, and only 1% of the patients were lost to follow-up. We classified the study group into two subgroups with an unadjusted E/A mitral velocity ratio below or above 0.98, which is the median value of the population. As expected from the inverse relationships depicted in Figure 1, patients with a low E/A ratio were older ($56 \pm 10$ years vs. $45 \pm 10$ years) and had a higher HR ($76 \pm 10$ beats/min vs. $74 \pm 10$ beats/min), 24-h systolic/diastolic BP ($140 \pm 16/88 \pm 11$ mm Hg vs. $134 \pm 14/86 \pm 10$ mm Hg) and LV mass ($52 \pm 14$ g/m$^{-2.7}$ vs. $47 \pm 13$ g/m$^{-2.7}$).

Table 1 reports the main clinical and echocardiographic characteristics of the study patients with an age- and
HR-normalized E/A mitral velocity ratio lower or higher than the median value. The two groups did not differ in terms of age, gender distribution, smoking habits, diabetes, serum cholesterol, duration of hypertension or left atrial diameter. Patients with a low E/A velocity ratio had a greater body mass index and higher office-visit and average 24-h systolic and diastolic BP values. In addition, the LV mass was higher and the LV ejection fraction was lower in patients with a low age- and HR-normalized E/A velocity ratio.

During an average follow-up period of 4.4 ± 2 years (range: 1.0 to 10.8 years), there were 164 new cardiovascular morbid events (2.04 events per 100 patient-years) and 55 all-cause deaths (0.66 deaths per 100 patient-years). Specifically, there were 31 patients with myocardial infarction, 4 who had a sudden cardiac death, 1 who had a cardiac death from other causes, 21 with unstable angina, 11 with coronary revascularization, 13 with heart failure that required hospital admission, 48 with stroke, 20 with transient cerebral ischemia, 11 with new-onset aorto-iliac occlusive disease and 4 with end-stage renal failure. We also registered a total of 87 new cardiac morbid events (1.06 events per 100 patient-years), including 7 additional cardiac events that occurred after a noncardiac event (3 myocardial infarctions, 2 sudden cardiac deaths, 1 cardiac death from other causes, 1 unstable angina).

Overall, there were 98 and 66 cardiovascular events in the groups with a low (n = 919) and high (n = 920) age- and HR-adjusted E/A mitral velocity ratio, respectively. The incidence of cardiovascular events in the two groups was 2.47 and 1.65 per 100 patient-years, respectively, and the cardiovascular event-free survival curves differed significantly (p < 0.005 by the log-rank test) (Fig. 2, lower panel).

When the analysis was restricted to cardiac morbid events, the event rate was significantly higher in the group with a low versus high adjusted E/A mitral velocity ratio (1.33 vs. 0.73 per 100 patient-years; p < 0.01 by the log-rank test). The event-free survival curves in patients with an unadjusted E/A velocity ratio below or above the median value are reported in Figure 2, upper panel.

Results of the multivariate survival analysis are reported in Table 2. The E/A mitral velocity ratio maintained an association with cardiovascular morbidity after adjustment for the confounding effects of age, gender, smoking, diabetes, cholesterol level, LV mass and average 24-h systolic BP. Treatment status, 24-h diastolic BP, office-visit BP, HR, body mass index and a family history of early-onset coronary artery disease were included in the model, but failed to enter the final equation. Patients with a low age- and HR-adjusted E/A ratio had a 57% higher risk of cardiovascular events (95% confidence interval [CI] +11% to +118%; p < 0.02). When the age- and HR-adjusted E/A mitral velocity ratio was included in the multivariate model as a continuous variable, a 21% higher risk of cardiovascular events was found for each 0.3 decrease in the adjusted E/A mitral velocity ratio (95% CI +2% to +43%; p = 0.03). The prognostic impact of the E/A velocity ratio remained significant when the multivariate analysis was restricted to cardiac morbid events. The higher risk of cardiac events associated with the presence of a low age- and HR-adjusted E/A ratio was 68% (95% CI +6% to +167%; p = 0.03). The incidence of all-cause deaths was 0.73 and 0.58 per 100 patient-years in the groups with a normalized E/A ratio below and above the median value, respectively (p = 0.48 by the log-rank test). The prognostic impact of the E/A ratio was not significant in Cox regression analysis (p = 0.23).

### Table 1. Clinical Characteristics of Study Subjects With an Age- and Heart Rate-Adjusted Mitral E/A Velocity Ratio Below or Above the Median Value

<table>
<thead>
<tr>
<th>Variables</th>
<th>Total (n = 1,839)</th>
<th>E/A &gt; Median (n = 920)</th>
<th>E/A &lt; Median (n = 919)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>50.3 ± 12</td>
<td>50.3 ± 13</td>
<td>50.2 ± 11</td>
<td>0.86</td>
</tr>
<tr>
<td>Male gender (%)</td>
<td>53</td>
<td>53</td>
<td>53</td>
<td>0.77</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>26.7 ± 4</td>
<td>26.2 ± 4</td>
<td>27.1 ± 4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Current smokers (%)</td>
<td>23</td>
<td>24</td>
<td>23</td>
<td>0.86</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>5</td>
<td>6</td>
<td>5</td>
<td>0.27</td>
</tr>
<tr>
<td>Duration of hypertension (yrs)</td>
<td>4.2 ± 6</td>
<td>4.0 ± 6</td>
<td>4.3 ± 6</td>
<td>0.24</td>
</tr>
<tr>
<td>Office-visit systolic BP (mm Hg)</td>
<td>156 ± 19</td>
<td>155 ± 18</td>
<td>157 ± 19</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Office-visit diastolic BP (mm Hg)</td>
<td>98 ± 10</td>
<td>96 ± 9</td>
<td>99 ± 10</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>24-h systolic BP (mm Hg)</td>
<td>137 ± 15</td>
<td>135 ± 14</td>
<td>139 ± 15</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>24-h diastolic BP (mm Hg)</td>
<td>87 ± 10</td>
<td>85 ± 9</td>
<td>89 ± 10</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cholesterol (mmol/l)</td>
<td>5.53 ± 1.1</td>
<td>5.50 ± 1.0</td>
<td>5.56 ± 1.1</td>
<td>0.23</td>
</tr>
<tr>
<td>LV diameter (mm)</td>
<td>49.4 ± 5</td>
<td>49.1 ± 5</td>
<td>49.6 ± 5</td>
<td>&lt;0.03</td>
</tr>
<tr>
<td>LV mass (g/m²)</td>
<td>49.3 ± 14</td>
<td>47.5 ± 14</td>
<td>50.9 ± 14</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV ejection fraction</td>
<td>0.66 ± 0.09</td>
<td>0.67 ± 0.09</td>
<td>0.66 ± 0.08</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Left atrial diameter (mm)</td>
<td>35.6 ± 6</td>
<td>35.3 ± 6</td>
<td>35.8 ± 6</td>
<td>0.11</td>
</tr>
<tr>
<td>Peak E-wave velocity (m/s²)</td>
<td>0.63 ± 0.17</td>
<td>0.72 ± 0.15</td>
<td>0.56 ± 0.14</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peak A-wave velocity (m/s²)</td>
<td>0.65 ± 0.18</td>
<td>0.58 ± 0.17</td>
<td>0.71 ± 0.16</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peak E/A velocity ratio</td>
<td>1.04 ± 0.40</td>
<td>1.31 ± 0.40</td>
<td>0.82 ± 0.23</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>E-wave velocity deceleration time (ms)</td>
<td>198 ± 58</td>
<td>183 ± 51</td>
<td>210 ± 61</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Data are presented as the mean value ± SD or percentage of subjects.
BP = blood pressure; E/A = early/atrial; LV = left ventricular.
Diastolic Dysfunction and Prognosis in Hypertension

Table 2. Independent Predictors of Cardiovascular Events (Cox Model)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Adjusted Hazards Ratio (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (10 yrs)</td>
<td>1.77 (1.49–2.11)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes (yes or no)</td>
<td>2.52 (1.65–3.85)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gender (men or women)</td>
<td>1.75 (1.24–2.49)</td>
<td>&lt;0.002</td>
</tr>
<tr>
<td>Cigarette smoking (yes or no)</td>
<td>1.64 (1.16–2.31)</td>
<td>&lt;0.006</td>
</tr>
<tr>
<td>24-h systolic BP (10 mm Hg)</td>
<td>1.22 (1.05–1.41)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Adjusted E/A ratio (below or above median value)</td>
<td>1.57 (1.11–2.18)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Left ventricular mass (10 g/m²)</td>
<td>1.13 (1.02–1.24)</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>Serum cholesterol (mmol/l)</td>
<td>1.15 (1.00–1.33)</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Family history of premature cardiovascular disease, office-visit blood pressure (BP), 24-h diastolic BP, heart rate, body mass index and treatment status failed to enter the final equation.

CI = confidence interval; E/A = early/atrial.

was no longer significant in a fully adjusted multivariable model (hazards ratio 0.91 for each 50-ms increase, 95% CI 0.80 to 1.05, p = 0.20).

**DISCUSSION**

The new finding of the present study is that the E/A transmitral flow velocity ratio, a Doppler-derived index of LV diastolic function, was predictive of subsequent cardiovascular morbid events in initially untreated and uncomplicated patients with essential hypertension. The relationship between a low age- and HR-adjusted E/A mitral ratio and future cardiovascular morbidity was statistically significant and persisted after correction for the influence of several traditional risk factors, including age, gender, diabetes, cigarette smoking, LV mass, serum cholesterol level and 24-h ambulatory and office-visit BP.

**Previous studies.** Among the elderly participants in the Cardiovascular Health Study, the E/A ratio represented an independent risk factor for congestive heart failure (17). In that study, both high and low Doppler E/A ratios were predictive of incident heart failure, indicating that participants at either extreme of the velocity profile spectrum were at increased risk of heart failure. However, those results were obtained in a population whose age was >65 years and in which the prevalence of hypertension was only 29% (17). Among 3,107 patients undergoing cardiac catheterization, the small subgroup (1.7%) with diastolic dysfunction, defined as those with high LV end-diastolic pressure and no systolic dysfunction, coronary heart disease or LV dilation had a high risk of future cardiac morbid events (27), but no comparison with the remaining patients was made in that study. A transmitral flow pattern characterized by a short isovolumic relaxation time and E-wave velocity deceleration time and an increase in the E/A velocity ratio is a marker of severely impaired LV compliance and elevated end-diastolic filling pressures in patients with congestive heart failure (28). This “restrictive” pattern of mitral inflow has been recognized as a strong predictor of mortality in acute myocardial infarction and congestive heart failure (12–15). Taken together, the available studies do not provide an...
answer to the question regarding the prognostic impact of LV diastolic filling abnormalities in hypertensive patients, which are mostly characterized by abnormally prolonged relaxation (6,9).

**Present study.** This is the first report of an association between impaired early diastolic relaxation of the LV and subsequent cardiovascular morbidity events in a large, initially untreated hypertensive population without prevalent cardiovascular disease at the baseline evaluation. The association held after adjustment for several independent risk markers, including age, male gender, smoking, diabetes and serum cholesterol level. These findings were also independent of echocardiographic LV mass, an established independent predictor of cardiac morbidity and mortality in hypertension (18,19), and average 24-h BP, which is a better risk marker than office-visit BP in hypertensive patients (29).

Because a low E/A mitral velocity ratio is likely to be associated with prolonged LV relaxation (6,8,9), our data suggest that impaired LV relaxation is an independent marker of an adverse prognosis in patients with hypertension. From a pathophysiologic standpoint, it is widely established that the transmitral Doppler flow velocity pattern is influenced by several conditions unrelated to ventricular diastolic function, such as LV filling pressure, HR and age, and that the simple assessment of the E/A flow velocity ratio may not allow for separation of the effects of relaxation and compliance on LV filling (30). Under certain circumstances, an increased or even normal E/A velocity ratio may indicate decreased LV compliance (pseudonormal or restrictive filling pattern). These patterns cannot be easily distinguished from a normal filling pattern without taking into account other variables, such as pulmonary vein flow or mitral inflow responses to a preload reduction (8), which require a more technically demanding and time-consuming echocardiographic investigation that can rarely be sustained in epidemiologic studies, such as PIUMA. Age and HR are unlikely to have influenced our results, however, because in the present study, the E/A velocity ratio was calculated after taking into account the effect of age and HR. Furthermore, our findings were obtained in a population without heart disease and with a normal LV ejection fraction. A restrictive LV filling pattern is a very uncommon finding in patients without heart disease (31) and in hypertensive patients with LV hypertrophy (32), representing <4% of the whole population in those studies. Moreover, an E/A ratio >2 and a deceleration time <150 ms, which have been proposed as partition values for identifying patients with increased left atrial pressure (33), were present in only 1.2% of our population. Therefore, restrictive physiology is unlikely to explain, to a significant extent, the normal to high E/A ratio pattern observed in the present study. Moreover, we were unable to show a J- or U-shaped relationship between the E/A mitral ratio and subsequent cardiovascular events. Because our hypertensive patients were asymptomatic and unmedicated at the time of the initial echocardiographic assessment, there was nothing to suggest that any of them had extremely high or low preload. When significant changes in loading conditions are not expected, as in this study, the transmitral flow velocity pattern is useful to assess gross LV diastolic performance (30).

The potential mechanisms underlying the association between impaired LV relaxation and cardiovascular risk remain hypothetical. The LV mass, a strong independent risk marker in hypertension (18,19), was greater in patients with a low adjusted E/A ratio (50.9 ± 14 g/m² vs. 47.5 ± 14 g/m²; p < 0.001), but the adverse prognostic value of the E/A ratio was consistently independent of LV mass in a multivariate analysis (Table 2). The dependence on the E/A ratio from cardiac loading conditions is well known and cannot be completely accounted for in cross-sectional studies. One possibility is that the E/A ratio and, for extension, early diastolic relaxation might be very sensitive to the whole load imposed on the LV, which cannot be fully measured using BP recordings, not even on a 24-h basis. It has been demonstrated that patients with diastolic heart failure have a reduced aortic distensibility (34). Characteristic aortic input impedance and arterial compliance have not been considered in this study, but are likely to be impaired in patients at higher risk of future cardiovascular events.

**Study limitations.** Because our data were obtained in initially untreated Caucasian patients, the results may not be extended to different ethnic groups or to patients receiving antihypertensive treatment at the time of the qualifying examination. The PIUMA database does not include information on BP control during follow-up in the whole population; this information was available in ∼30% of the study patients. Another limitation, inherent to observational cohort studies, is the lack of control over occasional changes in the antihypertensive regimen over time.

**Conclusions.** Our findings suggest an independent relationship between the baseline E/A mitral flow velocity ratio and the risk of cardiovascular events in initially untreated patients with essential hypertension. In these patients, assessment of LV relaxation by transmitral Doppler echocardiography may help to refine cardiovascular risk stratification. A more aggressive therapeutic management may be advisable for individuals with a low age- and HR-corrected E/A velocity ratio. Future outcome studies should investigate whether preventing or halting diastolic dysfunction through antihypertensive treatment may lead to an improved prognosis in hypertensive patients, independent of an improvement in other markers of preclinical disease.

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