# Cardiac Function In Renovascular Hypertensive Patients With and Without Renal Dysfunction

Kirandeep K. Khangura,[1] Alfonso Eirin,[1] Garvan C. Kane,[2] Sanjay Misra,[3] Stephen C. Textor,[1] Amir Lerman,[2] and Lilach O. Lerman[1,2]

**BACKGROUND**
Hypertension impairs left ventricular (LV) diastolic and systolic function, which might be aggravated by inflammation or neurohumoral activation. We hypothesized that LV diastolic dysfunction is more common in patients with renovascular hypertension (RVHT) compared with essential hypertension (EHT).

**METHODS**
Hypertensive patients who underwent both renal imaging to exclude RVHT and cardiac echocardiography within a 3-year period were identified retrospectively. Patients with significant renovascular disease were included in the RVHT group (n = 75); those without significant renovascular disease were included in the EHT group (n = 69). Cardiac function and structure were compared.

**RESULTS**
Baseline renal function was preserved (serum creatinine ≤ 2 mg/dl) in EHT patients and impaired (serum creatinine > 2 mg/dl) in only 9 RVHT patients. RVHT patients had higher systolic blood pressure, E/e' ratio, and greater prevalence of concentric hypertrophy but lower estimated glomerular-filtration-rate (eGFR) compared with EHT patients. Increased prevalence of LV diastolic dysfunction remained statistically significant in patients with RVHT after multivariable adjustment for age, sex, blood pressure, eGFR, diabetes, smoking, and statin use, with a relative risk (95% CI) for abnormal E/e' of 1.70 (95% confidence interval = 1.05–2.90; $P = 0.03$) compared with EHT. RVHT patients with severe renal dysfunction showed greater impairments in cardiac systolic and diastolic function compared with those in EHT patients or preserved renal function RVHT patients.

**CONCLUSIONS**
Among hypertensive patients undergoing echocardiography, cardiac structure and diastolic function are impaired in RVHT patients compared with EHT patients and remain different after adjustment for multiple significant covariables. When associated with significant renal dysfunction, RVHT aggravates LV hypertrophy and both systolic and diastolic dysfunction. Hence, identification of RVHT and renal dysfunction warrants development of targeted management strategies.

*Keywords:* blood pressure; diastolic function; hypertension; left ventricular hypertrophy; renovascular hypertension.

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Hypertension is one of the strongest predictors of cardiovascular disease and premature death.[1–3] In the United States, of approximately 75 million adults with hypertension,[4,5] approximately 5% have renovascular hypertension (RVHT)[6–10] due to occlusive disease of the main renal arteries.[11] RVHT usually results from renal artery stenosis (RAS) secondary to atherosclerotic renovascular disease, which is strongly associated with cardiovascular disease.[12] Heart failure is not uncommon in patients with RVHT, and RVHT identifies a very high-risk cohort with decreased survival.[13]In particular, left ventricular (LV) diastolic dysfunction is more frequently observed than systolic dysfunction in patients with RVHT.[13–15] Wright *et al.* reported that the majority of patients with RAS have LV hypertrophy (LVH) and diastolic dysfunction,[14] both of which progress with increasing LV mass index (LVMI) and cardiac dilatation in a subgroup of patients.[16] Notably, most of the studies involved RVHT and control patients with significant renal dysfunction and serum creatinine (SCr) >2 mg/dl.[13–16]

Hemodynamic overload leading to LVH may partly account for LV diastolic dysfunction in patients with essential hypertension (EHT).[4,5] In addition to hypertensive injury, patients with RVHT show elevated levels of various neurohumoral and growth regulatory factors. Activation and release of proinflammatory cytokines from stenotic kidneys, which might magnify cardiac remodeling and thereby diastolic dysfunction in patients with RVHT compared with patients with EHT facing similar elevation of blood pressure, have been identified in both experimental models[17] and human subjects with RVHT.[18] However, whether LV diastolic dysfunction is common in RVHT patients with and without marked renal functional abnormalities remains

Correspondence: Lilach O. Lerman (lerman.lilach@mayo.edu).

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**[1]Division of Nephrology and Hypertension, Mayo Clinic, Rochester, Minnesota; [2]Division of Cardiovascular Diseases, Mayo Clinic, Rochester, Minnesota; [3]Division of Vascular and Interventional Radiology, Mayo Clinic, Rochester, Minnesota.**

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unclear. Therefore, this study tested the hypothesis that LV diastolic function is more impaired in patients with RVHT than in patients with EHT.

## METHODS

### Patient selection and data collection

The study was approved by the Mayo Foundation Institutional Review Board. A retrospective study cohort was selected from hypertensive patients who were seen at Mayo Clinic, Rochester, Minnesota, between 1 January 2004 and 31 August 2012, and had undergone imaging to exclude RAS. Patients were included in the study only if they had signed informed consent to allow use of their data for research purposes and had available cardiac echocardiography data collected within a 3-year period. The inclusion criteria included being aged >50 and <75 years and, for RAS, standardized criteria analogous to enrollment in Cardiovascular Outcomes for Renal Atherosclerotic Lesions (CORAL) study to identify presence of atherosclerotic RAS (NCT00081731).[19] Details are provided in the Supplementary Material. Overall, 69 patients with evidence of RAS were included in the study in the RVHT group, and 75 unmatched hypertensive patients with no evidence of RAS were included in the study in the control (EHT) group. In EHT patients, either computed tomography or magnetic resonance angiography excluded RAS, whereas in all RVHT patients subsequent renal artery angiography confirmed RAS.

### Clinical parameters

All of the clinical and anthropometric variables were recorded at the time of the echocardiogram. Retrospective chart reviews of all the identified patients were done. Clinical variables, including medication use, past medical history, and mortality data, were abstracted from the electronic medical records. Follow-up was censored at (i) the last observed clinical visit at Mayo Clinic; (ii) the end of the study period; or (iii) death. Follow-up in RVHT patients included blood pressure outcomes of revascularization. To assess the association of RAS and cardiac dysfunction, we compared the prevalence of LVH and LV systolic and diastolic dysfunction among patients with RVHT and EHT.

### Echocardiographic parameters

The echocardiographic data used in this study were recorded by staff cardiologists with advanced training in echocardiography, and echocardiograms were performed by experienced sonographers according to American Society of Echocardiography guidelines. LV systolic function was assessed from LV ejection fraction (LVEF), LV stroke volume index (cardiac output/heart rate per body surface area), and LV cardiac index (cardiac output per body surface area). For the purpose of the study, cardiac structural changes were determined by evaluation of LVMI, presence or absence of LVH, left atrial volume index, and characterization of cardiac geometry. LVMI and relative wall thickness were used to classify cardiac geometry as normal, concentric remodeling, eccentric hypertrophy, and concentric hypertrophy. Diastolic function was assessed by M-mode and tissue Doppler echocardiography. M-mode parameters analyzed were peak early diastolic velocity (E), peak atrial velocity (A), E/A ratio, and isovolumic relaxation time. The tissue Doppler echocardiography parameters analyzed were peak early diastolic velocity (e') and E/e' ratio. Diastolic function was graded as normal, mild (grades I and Ia), moderate (grade II), or severe (grade III) diastolic dysfunction.[20–22]

### Statistical analysis

Statistical analyses were performed using JMP version 8.0 (SAS Institute, Cary, NC). Results were expressed as mean ± SD for normally distributed data, and median (range) for non-normally distributed data. Baseline differences among the groups were determined by *t* tests or $\chi^2$ tests, as appropriate. By multivariable analysis, echocardiographic parameters were adjusted for age, sex, coronary artery disease, coronary artery bypass grafting, and other baseline variables where the observed difference between the groups was statistically significant. $P < 0.05$ was considered statistically significant. Survival analysis used Kaplan–Meier (log-rank) followed by multivariable Cox regression analysis, and revascularization outcomes in RVHT used *t* tests. Person-years of follow-up were calculated from the date of the echocardiography to the date of death or censoring (last clinic visit or 31 August 2012, whichever came first).

Detailed methods are provided in the Supplementary Methods.

## RESULTS

Demographic information of the patients is provided in Table 1. RVHT patients were slightly older than EHT patients, and their baseline systolic and mean blood pressures were significantly higher. Body mass index, sex, and race distribution were similar between the 2 groups. Active smoking was more common among EHT patients, whereas diabetes mellitus requiring oral hypoglycemic agents and/or insulin was more prevalent among RVHT patients. The prevalence of coronary artery disease was high in both groups, and their likelihoods of undergoing surgical coronary artery revascularization were similar. RVHT patients used a higher number of antihypertensive drugs and were more commonly treated with statins. Renal function was slightly lower in RVHT patients, and plasma renin activity was higher, whereas protein excretion was similar to that of EHT patients. One RVHT patient was treated medically, whereas all others subsequently underwent renal artery revascularization.

### Cardiac structure and function

Cardiovascular assessments are reported in Table 2. There were significant differences in the prevalence of cardiac structural changes between the 2 groups. In the RVHT group, the E/e' ratio was higher, fewer patients had normal cardiac geometry compared with the EHT group, and

**Table 1.** Clinical characteristics of patients with essential (EHT) or renovascular (RVHT) hypertension

| Characteristic | EHT (n = 75) | RVHT (n = 69) | *P* value |
|---|---|---|---|
| Age, y | 65 (50–75) | 69 (52–75) | 0.003 |
| Sex, male/female | 41/34 | 32/37 | 0.32 |
| Body mass index, kg/m$^2$ | 29 ± 6 | 30 ± 6 | 0.19 |
| Race, white/other/unknown | 72/1/2 | 63/1/5 | 0.30 |
| Duration of follow-up, y | 8.8 (2–9.1) | 8.8 (1.1–9.1) | 0.35 |
| Systolic blood pressure, mm Hg | 129 ± 23 | 147 ± 23 | <0.0001 |
| Diastolic blood pressure, mm Hg | 72 ± 14 | 76 ± 13 | 0.08 |
| Mean arterial pressure, mm Hg | 91 ± 16 | 100 ± 14 | 0.0007 |
| Heart rate, bpm | 66 ± 12 | 68 ± 13 | 0.50 |
| Total cholesterol, mg/dl | 169 (27–313) | 162 (88–382) | 0.79 |
| Hemoglobin, g/dl | 14 ± 2 | 13 ± 1 | 0.13 |
| Comorbidities | | | |
| Diabetes mellitus | 15 (20%) | 27 (39%) | 0.01 |
| Coronary artery disease | 36 (48%) | 38 (55%) | 0.40 |
| Family history of coronary artery disease | 42 (57%) | 40 (59%) | 0.88 |
| Smoking status | | | 0.003 |
| Current smoker | 18 (24%) | 3 (4%) | |
| Former smoker | 35 (47%) | 45 (66%) | |
| Nonsmoker | 21 (28%) | 20 (29%) | |
| Recent myocardial infarction/stroke | 6 (8%) | 5 (7%) | 0.86 |
| Coronary artery bypass grafting | 11 (15%) | 18 (26%) | 0.09 |
| Atrial fibrillation | 15 (20%) | 12 (17%) | 0.69 |
| Sleep apnea | 17 (23%) | 19 (27%) | 0.50 |
| Cardiovascular medications | | | |
| Antihypertensive | 3 (0–6) | 3 (0–7) | 0.03 |
| Diuretics | 48 (64%) | 50 (72%) | 0.28 |
| Calcium channel blockers | 21 (28%) | 29 (42%) | 0.08 |
| Beta-blockers | 57 (76%) | 53 (77%) | 0.91 |
| Angiotensin-converting enzyme inhibitors | 26 (35%) | 30 (43%) | 0.28 |
| Angiotensin receptor blockers | 14 (19%) | 20 (30%) | 0.14 |
| Alpha-blockers | 8 (11%) | 6 (9%) | 0.69 |
| Statins | 37 (50%) | 47 (68%) | 0.03 |
| Hormone replacement therapy | 5 (7%) | 3 (4%) | 0.54 |
| Renal function | | | |
| Serum creatinine, mg/dl | 1 (0.5–1.9) | 1.2 (0.6–5.1) | <0.0001 |
| eGFR-MDRD, ml/min/1.73/m$^2$ | 72 (34–143) | 49 (11–101) | <0.0001 |
| Proteinuria, mg/24h | 128 (23–1584) | 152 (27–1583) | 0.48 |
| Systemic plasma renin activity, ng/ml/h[a] | 0.6 (0.6–9.9) | 1 (0.6–22) | 0.03 |

Data are presented as median (range), number (%), or mean ± SD, as appropriate.
Abbreviation: eGFR-MDRD, estimated glomerular filtration rate–modification of diet in renal disease.
[a]Available for 18 (24%) and 27 (39%), of EHT and RVHT patients, respectively.

concentric hypertrophy and concentric remodeling were more prevalent (Figure 1). Moderate to severe impairment of LV diastolic function was prevalent among RVHT patients. Echocardiographic parameters were subsequently adjusted for sex, coronary artery disease, and demographic covariables that were significantly different between the groups (age, baseline blood pressure, diabetes mellitus, smoking status, number of antihypertensive medications, use of statins, and

**Table 2.** Echocardiographic assessments* of patients with essential (EHT) or renovascular (RVHT) hypertension

| Assessment | EHT (n = 75) | RVHT (n = 69) | Unadjusted *P* value | Adjusted∞ *P* value |
|---|---|---|---|---|
| Left ventricular end diastolic diameter, mm | 50 (37–72) | 49 (36–65) | 0.73 | <0.0001 |
| Left ventricular mass index, g/m$^2$ | 100 (55–215) | 114 (57–237) | 0.03 | <0.0001 |
| Left atrial volume/BSA, ml/m$^2$ | 35 (16–163) | 36 (15–97) | 0.28 | 0.004 |
| Medial annulus e', m/sec | 0.06 (0.03–0.11) | 0.05 (0.02–0.11) | 0.02 | 0.05 |
| E/e' ratio | 13 ± 5 | 16 ± 7 | 0.003 | <0.0001 |
| Left ventricular geometry | | | 0.0008 | 0.001 |
| Normal | 30 (40%) | 8 (11%) | | |
| Concentric remodeling | 15 (20%) | 20 (29%) | | |
| Eccentric LVH | 15 (20%) | 14 (20%) | | |
| Concentric LVH | 15 (20%) | 27 (39%) | | |
| Ejection fraction, % | 64 (20–77) | 65 (13–79) | 0.54 | <0.0001 |
| Cardiac index, L/min/m$^2$ | 3.1 (2.2–8.1) | 3 (1.6–4.5) | 0.26 | 0.04 |
| Diastolic function | | | 0.01 | 0.001 |
| Normal | 19 (25%) | 7 (10%) | | |
| Mild (grade I and Ia) | 17 (23%) | 21 (30%) | | |
| Moderate (grade II) | 13 (17%) | 21 (30%) | | |
| Severe (grade III) | 5 (7%) | 11 (16%) | | |

Echocardiography performed 5 (0.03–33) and 2 (0.03–35) [median (range)] months before renal imaging in all EHT and RVHT patients, respectively. Data are presented as median (range), number (%), or mean ± SD, as appropriate.

Abbreviations: BSA, body surface area; e', medial mitral annulus peak diastolic velocity; E, peak mitral inflow velocity; LVH, left ventricular hypertrophy.

[a]Adjusted for age, sex, baseline blood pressure, baseline hemoglobin levels, baseline renal function (serum creatinine and estimated glomerular filtration rate), use of statins, coronary artery disease, diabetes, smoking status, and number of antihypertensive medications.

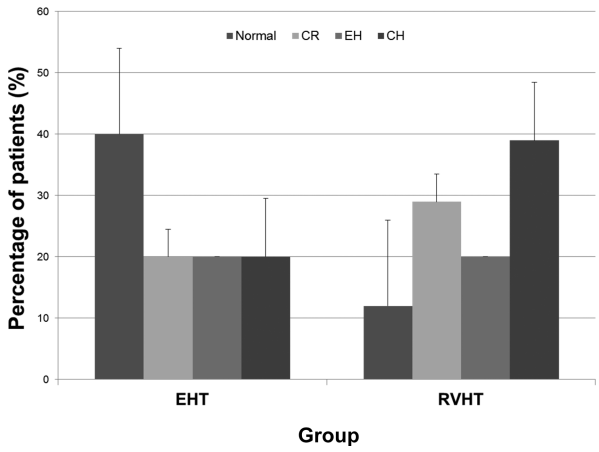


**Figure 1.** Distribution of cardiac geometry patterns in essential hypertension (EHT) and renovascular hypertension (RVHT) patients, presented as percentage of patients (%) with SE. $P = 0.0008$. Abbreviations: CH, concentric hypertrophy; CR, concentric remodeling; EH, eccentric hypertrophy.

baseline renal function). The differences in cardiac structure and function between the 2 groups remained statistically significant after adjustment for these covariables. In addition, LV end diastolic diameter decreased, left atrial volume increased, and LV cardiac index became significantly lower in RVHT after multivariable analysis.

### Correlation of baseline renal function with cardiac remodeling

In EHT patients, eGFR did not correlate with either systolic (LVEF) or diastolic functional parameters (medial annulus-e', E/e' ratio) (Figure 2a). In contrast, among RVHT patients, eGFR strongly correlated with systolic (directly with LVEF) and diastolic parameters (directly with medial annulus e', and inversely with E/e' ratio) (Figure 2b).

In receiver operating characteristics curves of SCr for E/e' ratio (Figure 3a), medial annulus e' (Figure 3b), and LVEF (Figure 3c), area under curves were 65%, 69%, and 75%, respectively. SCr provided improved sensitivity and specificity for predicting abnormal E/e' ratio, medial annulus e', and LVEF at a cutoff of 1.2 mg/dl, 1.2 mg/dl, and 1.8 mg/dl, respectively. Patients with RVHT were more likely to have abnormal E/e' ratio compared with EHT patients, (relative risk (RR) = 1.70; 95% confidence interval (CI) = 1.05–2.90; $P = 0.03$) but not abnormal LVEF (RR = 0.96; 95% CI = 0.85–1.1; $P = 0.48$).

### Outcomes and predictors of mortality

In RVHT patients, 6–12 months after revascularization, a fall in systolic, diastolic, and mean arterial blood pressures was noted (Table 3), but no change in renal function was noted. Indeed, 7% of RVHT patients developed end-stage renal disease and started chronic maintenance dialysis, compared with

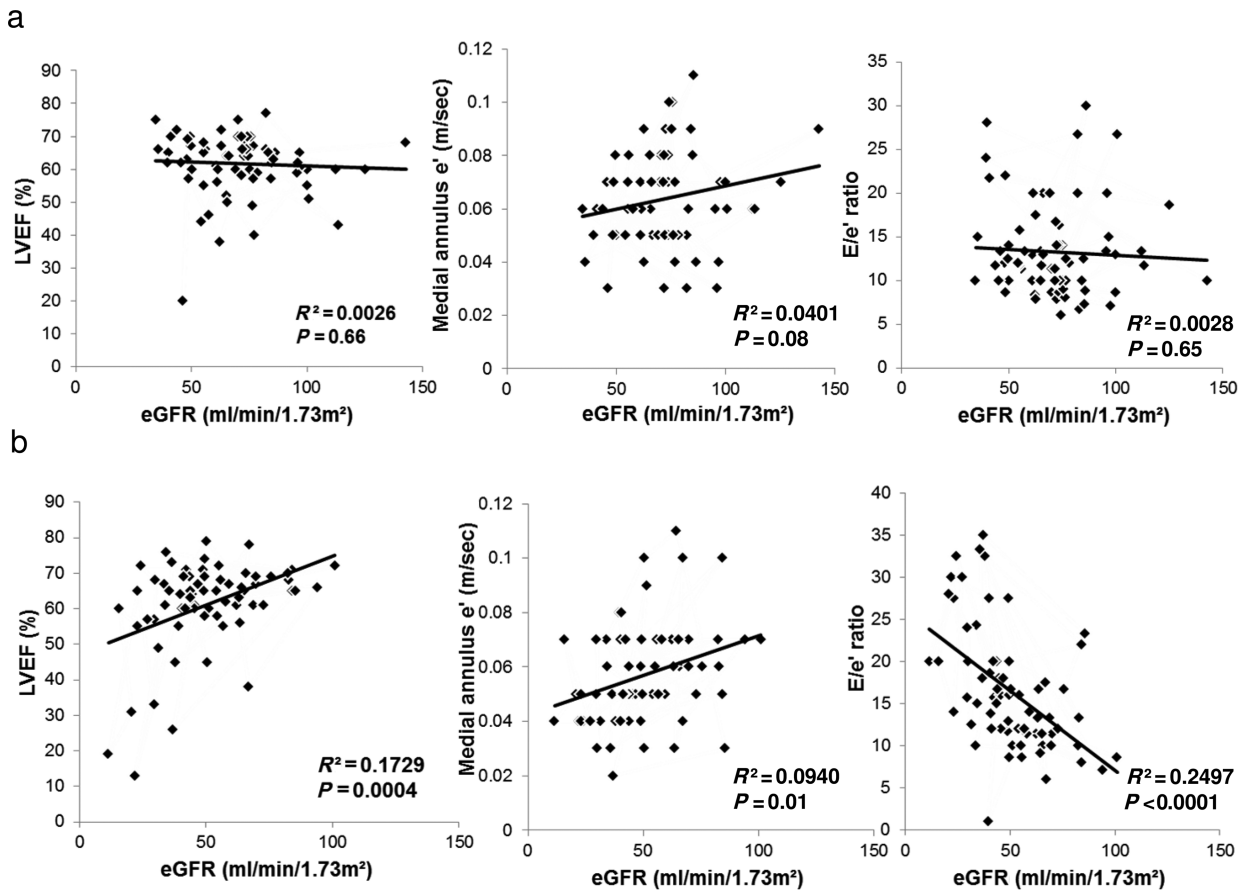


**Figure 2.** Scatter plot of bivariable fit of left ventricular ejection fraction (LVEF), medial annulus e', or E/e' ratio by renal function (estimated glomerular filtration rate (eGFR)). (**a**) In essential hypertension (EHT). (**b**) In renovascular hypertension (RVHT).

1% of EHT patients ($P = 0.08$), although survival was similar in both groups ($P = 0.24$) (Figure 4). None of the baseline risk factors predicted mortality in univariable analysis (Table 3).

### Subgroup analysis: RVHT with and without significant renal dysfunction

To examine the independent impact of renal dysfunction, the RVHT group was subdivided in a pilot fashion into 2 groups based on SCr level of ≤2 mg/dl (RVHT-I, n = 60) or >2 mg/dl (RVHT-II, n = 9). Systolic and mean blood pressures were higher in RVHT-I, whereas median age and prevalence of diabetes mellitus were higher in RVHT-II patients. Abnormal cardiac geometry, elevated LVMI, LV end-diastolic echo dimensions (LVEDD), and E/e' ratio, and decreased LVEF in the RVHT-II group compared with the EHT and RVHT-I groups remained statistically significant after adjusting for age, sex, baseline blood pressure, eGFR, proteinuria, smoking status, diabetes mellitus, coronary artery disease, number of antihypertensive medications, and statin use. Of the patients in the RVHT-II group, 33% died during the course of follow-up, compared with 18% in the RVHT-I group and 13% in the EHT group ($P = 0.28$).

Please see details in the Supplementary Results.

## DISCUSSION

The major finding of this study is that cardiac structure and function (particularly diastolic function) are worse in RVHT patients compared with EHT patients referred for echocardiography, even after adjustment for differences in the degree of hypertension and renal function. Furthermore, despite no further elevation of blood pressures, patients with RVHT accompanied by significant renal dysfunction (SCr >2 mg/dl) show marked cardiac structural (concentric and eccentric hypertrophy) and functional (both LV systolic and diastolic) abnormalities. This study therefore underscores RVHT as a significant risk factor for cardiovascular disease. Single blood pressure measurements were obtained at the time of renal imaging, and although these readings may not necessarily reflect the patients' blood pressure patterns over the preceding years, these findings may support the notion that elements beyond hypertension alone increase cardiovascular risk in RVHT.

Our results extend previous reports of more prevalent LV diastolic dysfunction in patients with RVHT.[13–15] However, most previous studies included a smaller number of patients and control subjects with renal dysfunction[14,16] and/or patients with RVHT undergoing renal artery revascularization.[13,23] Our study included a larger

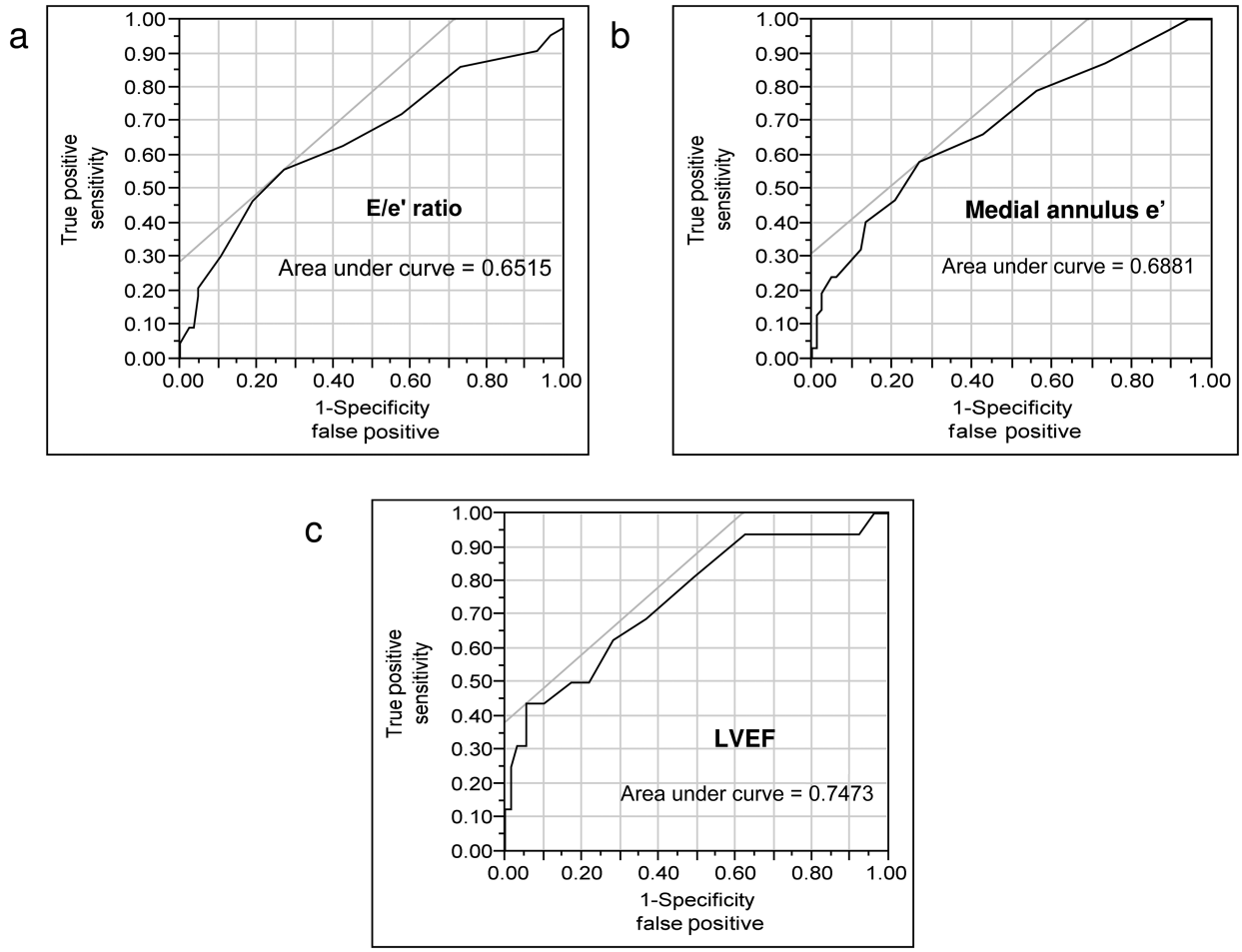


**Figure 3.** Receiver operating characteristics (ROC) curves of serum creatinine (SCr). (**a**) For E/e' ratio. (**b**) For medial annulus e'. (**c**) For left ventricular ejection fraction (LVEF). For ROC curves of SCr and E/e' ratio, values <8 were considered normal, E/e' >15 was considered abnormal, and E/A >1.5 was used in borderline cases. For ROC analysis of SCr and medial annulus e' or LVEF, values <0.06 m/s or <50%, respectively, were considered abnormal. Threshold cutoff of SCr of 1.2 mg/dl, 1.2 mg/dl, and 1.8 mg/dl predicted abnormal E/e' ratio, abnormal medial annulus e', and abnormal LVEF, respectively. Further details are available in the Supplementary Materials.

number of patients, most of who had SCr levels <2 mg/dl. Nevertheless, we found significant concentric cardiac hypertrophy or remodeling in patients with RVHT compared with EHT, possibly related to their higher systolic and mean blood pressures, whereas cardiac systolic function was relatively preserved. Although their number was small, we observed that compared with the EHT and RVHT-I groups, patients with substantial renal dysfunction in the RVHT-II group had significantly higher LVMI, LVEDD, and E/e' ratio, suggesting involvement of factors other than pressure overload in cardiac remodeling. Receiver operating characteristics analysis revealed that renal insufficiency modestly increased the sensitivity of predicting abnormalities associated with LV diastolic and systolic dysfunction.

Among the RVHT patients, cardiac impairments ranging from abnormal cardiac geometry, elevated E/e' ratio, and impaired LV diastolic function persisted after adjusting for multiple covariables, including age, sex, baseline blood pressure, diabetes mellitus, smoking status, use of statins, and baseline renal function. In particular, RVHT conferred elevated relative risk for abnormal E/e'. The mechanisms by which RVHT impairs cardiac function could be multifactorial. First and foremost, changes in cardiac structure and function are attributable to the elevated arterial pressure, which was higher in patients with RVHT than with EHT. Yet, in addition to hemodynamic overload, patients with RVHT show elevated levels of neurohumoral and growth regulatory factors.[18] Plasma renin activity was also higher in RVHT patients compared with EHT patients, implicating amplified activation of the systemic renin-angiotensin-aldosterone system modulating target organ injury. However, PRA was measured under uncontrolled and variable conditions and was unavailable for some of the patients. Moreover, we have previously identified magnified systemic inflammation[24] and release of proinflammatory markers from stenotic kidneys[18] of patients with RVHT compared with matched patients with EHT. Inflammation can promote myocardial fibrosis and consequently dysfunction[25] and has been linked to abnormal LV geometry and function in uremic, hypertensive, and elderly subjects.[26] Although none of the study participants were on dialysis at the time of entry into the

**Table 3.** Age- and sex-adjusted univariable analysis of baseline risk factors for mortality in 144 hypertensive patients during 1,123.8 person-years (essential hypertension = 595.3 and renovascular hypertension = 528.5)

| Risk factor | Cases | HR (95%CI) | *P* value |
|---|---|---|---|
| Baseline blood pressure | — | 0.9 (0.9–1.0) | 0.90 |
| Coronary artery disease | 74 | 1.1 (0.8–1.5) | 0.88 |
| Diabetes mellitus | 42 | 0.8 (0.5–1.9) | 0.65 |
| Active smoking | 21 | 1.3 (0.8–2.0) | 0.70 |
| Baseline renal function (eGFR) | — | 0.9 (0.98–1.00) | 0.23 |
| Left ventricular ejection fraction | — | 0.99 (0.97–1.0) | 0.57 |
| Recent cardiovascular/ cerebrovascular event | 11 | 1.1 (0.6–2.0) | 0.88 |
| Statins | 84 | 0.9 (0.6–1.3) | 0.84 |
| Presence of hemodynamically significant RAS | 69 | 1.2 (0.9–1.7) | 0.62 |
| RAS + severe renal dysfunction[a] | 9 | 1.2 (0.6–2.4) | 0.83 |

Abbreviations: CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio; RAS, renal artery stenosis.

[a]Includes renovascular hypertension patients with serum creatinine >2 mg/dl.

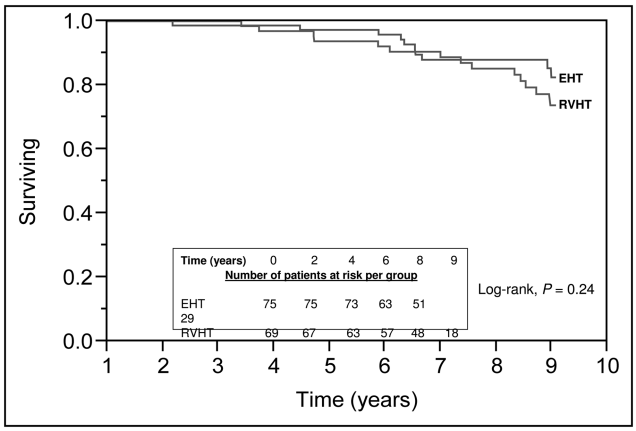


**Figure 4.** Survival plot of patients in essential hypertension (EHT) and renovascular hypertension (RVHT) groups. Numbers of events were 10 and 14 in the EHT and RVHT groups, respectively.

study, factors related to uremia may also aggravate vascular remodeling.[27,28] Furthermore, in experimental renovascular disease, renal function modulates remote myocardial microvascular integrity, independent of hypertension.[17] These observations underscore functionally important cardiorenal cross-talk, possibly mediated by renal injury signals, which may induce cardiac remodeling and impair its function beyond the hemodynamic effects of hypertension.

The prevalence of coronary artery disease was similar in patients with RVHT and EHT, as was the need for surgical coronary artery revascularization, possibly because of the relatively small number of patients included. The relationship between RVHT, cardiac geometry, diastolic function, and survival has been previously evaluated after renal artery revascularization. A decrease in LVMI after renal artery revascularization does not necessarily improve diastolic function,[23] although it might confer a benefit in patients with cardiac symptoms[29] and is independent of the change in blood pressure.[30] RVHT is prevalent in patients with combined congestive heart failure and chronic kidney disease, but its severity does not correlate with LVEF, LVMI, or the extent of myocardial fibrosis.[31] In addition to age, recent cardiovascular or cerebrovascular events, baseline eGFR, and presence of RAS with severe renal dysfunction were independent predictors of mortality. Cherr *et al.* demonstrated increased dialysis-free survival among patients showing improvement in eGFR after renal artery revascularization.[32] Clearly, the relationship between kidney and cardiac dysfunction is complex and warrants further studies.

Patterns of LVH and cardiac geometry have been studied in hypertensive patients with[33] and without chronic kidney disease,[34] in black patients with chronic kidney disease,[35,36] and in patients with diabetes and chronic kidney disease.[37] Concentric[37,38] and eccentric[35,36] hypertrophy patterns characterize cardiac geometry in patients with moderate to severe renal insufficiency. Cardiac geometry patterns of concentric and eccentric hypertrophy reflect architectural reorganization of cardiac myocytes in response to pressure and volume overload states, respectively.[39,40] Differences in prevalence of concentric hypertrophy between EHT and RVHT could be proportional to the degree of pressure overload. Although limited by small sample size, in our study eccentric hypertrophy was a more prevalent form of cardiac geometrical pattern than concentric hypertrophy in RVHT-II patients, which may suggest volume overload in these patients compared with EHT and RVHT-I. Furthermore, eccentric hypertrophy is reportedly more commonly associated with systolic dysfunction and concentric hypertrophy with diastolic dysfunction,[41,42] which may account for the higher prevalence of eccentric hypertrophy in RVHT-II with decreased LVEF.

Being a retrospective study, our study is prone to several limitations, including selection bias inherent to a cohort identified from an institutional procedural database. Our cohort was largely white, limiting implications in a more diverse population. Including only those patients who had an echocardiogram also induced selection bias, which may account for the high prevalence of coronary artery disease among our patients. Our study also relied on standard but stringent radiological parameters to identify patients with hemodynamically significant RAS. Furthermore, the subsequent fall in arterial blood pressure (despite unaltered renal function) after revascularization supports the renovascular etiology of hypertension in the RVHT group. All the patients in the EHT group underwent either computed tomography or magnetic resonance angiography to rule out RAS, and in all RVHT patients initial imaging (renal computed tomography/magnetic resonance angiography or Doppler ultrasound) was subsequently confirmed by renal artery angiography. None of the EHT patients had SCr >2 mg/dl, and a small sample size in the RVHT-II group limits its elucidation of the association between cardiac dysfunction and severe renal dysfunction in RVHT, which requires further studies. Duration of hypertension was unknown, and the study groups were dissimilar in baseline blood pressure, renal

function, and several comorbidities. Nevertheless, we observed significant differences in cardiac structure and function even after multivariable adjustment for all statistically significant covariables. The term "diastolic heart failure" has been replaced by "heart failure with preserved ejection fraction" because LV diastolic dysfunction is also seen in patients with reduced ejection fraction, as in our study. Therefore, for identification of our study cohort, we relied on echocardiographic evidence of LV diastolic dysfunction rather than a diagnosis code from the medical records. Nevertheless, we cannot exclude the possible contribution of differential ambient blood pressure levels during echocardiography to the differences in cardiac function between the groups.

Our study highlights the difference in pattern of LV geometry among essential hypertensive and renovascular hypertensive patients with relatively preserved renal function who were referred for echocardiography. Compared with patients with EHT, concentric cardiac hypertrophy/remodeling and diastolic dysfunction are more prevalent in patients with RVHT, suggesting that its deleterious effects on cardiac function start at an early stage. A decline in systolic function is exacerbated when marked renal dysfunction ensues and is responsible for the overall direct correlation between eGFR and LVEF. In addition to pressure overload, these associations might be speculatively attributable to increased circulating proinflammatory or uremia-related factors, which might magnify cardiac remodeling and aggravate dysfunction. These findings may be of value in identifying individuals with RVHT at risk for alterations in cardiac geometry and function and may support serial echocardiographic evaluations of these patients and monitoring the efficacy of treatment in reducing the incidence of cardiac dysfunction. Elucidating the independent impact of RVHT and renal failure on cardiac function may thus help direct preventive and management strategies in this group of patients.

## SUPPLEMENTARY MATERIAL

Supplementary materials are available at *American Journal of Hypertension* (http://ajh.oxfordjournals.org).

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## DISCLOSURE

The authors declared no conflict of interest.

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