JACC: CARDIOVASCULAR IMAGING
VOL. 4, NO. 9, 2011

ISSN 1936-878X/$36.00
PUBLISHED BY ELSEVIER INC.
DOI:10.1016/j.jcmg.2011.07.004

CVN Interview

ORIGINAL RESEARCH

Serial Doppler Echocardiography and Tissue Doppler Imaging in the Detection of Elevated Directly Measured Left Atrial Pressure in Ambulant Subjects With Chronic Heart Failure

Jay L. Ritzema, MD, PHD,*# A. Mark Richards, MD, DSC,* Ian G. Crozier, MD,† Christopher F. Frampton, PHD,* Iain C. Melton, MD,† Robert N. Doughty, MD,‡ James T. Stewart, MD,‡ Neal Eigler, MD,§‖ James Whiting, PHD,§‖ William T. Abraham, MD,¶ Richard W. Troughton, MD, PHD*

Christchurch and Auckland, New Zealand; Los Angeles, California; Minneapolis, Minnesota; Columbus, Ohio; and Queensland, Australia

OBJECTIVES This study sought to determine the accuracy of Doppler echocardiography and tissue Doppler imaging (TDI) measurements in detecting elevated left atrial pressure (LAP) in ambulant subjects with chronic heart failure using directly measured LAP as the reference.

BACKGROUND Echocardiographic indexes including the ratio of transmitral to annular early diastolic velocities (E/e′) may identify raised invasively measured left ventricular filling pressures when tested in cross-sectional studies in some populations. The accuracy of these indexes when measured sequentially remains untested. We determined the accuracy of Doppler echocardiography and TDI measurements in detecting elevated directly measured LAP in ambulant subjects with stable chronic heart failure.

METHODS Fifteen patients with New York Heart Association functional class II to III heart failure and a permanently implanted direct LAP monitoring device underwent serial echocardiography. Simultaneous resting mean LAP, Doppler mitral inflow, mitral annular TDI, and pulmonary venous inflow velocities were obtained on each occasion. Receiver-operator characteristic curve analysis was used to compare the accuracy of the Doppler variables to detect an elevated device LAP ≥15 and ≥20 mm Hg.

RESULTS The patients (13 men, mean age: 71 years, mean left ventricular ejection fraction: 32 ± 12%) underwent 60 simultaneous echocardiographic studies and LAP measurements with a median of 4 (1 to 7) studies per patient. Mean LAP was 16.9 (range 5 to 39 mm Hg) at echocardiography (n = 60). E/e′ had the greatest accuracy for detection of LAP ≥15 mm Hg with an area beneath the receiver-operator characteristic curve >0.9. In comparison, area under the curve for mitral E velocity and mitral E/A were 0.77 and 0.76, respectively ($p < 0.008$ vs. E/e′ medial and average).

CONCLUSIONS Single and serial measurements of mitral inflow and mitral annular TDI velocities (E/e′) can reliably detect raised directly measured LAP in ambulant subjects with compensated chronic heart failure. (Hemodynamically Guided Home Self-Therapy in Severe Heart Failure Patients [HOMEOSTASIS]; NCT00547729) (J Am Coll Cardiol Img 2011;4:927–34) © 2011 by the American College of Cardiology Foundation

From the *Department of Medicine, University of Otago, Christchurch, New Zealand; †Department of Cardiology, Christchurch Hospital, Christchurch, New Zealand; ‡Department of Cardiology, Auckland City Hospital, Auckland, New

JACC: CARDIOVASCULAR IMAGING, VOL. 4, NO. 9, 2011
SEPTEMBER 2011:927–34

Indexes such as the ratio of transmitral to annular early diastolic velocities (E/e′) have been successfully used to identify raised left ventricular (LV) filling pressure in hospitalized subjects (1–3). However, a recent study has questioned the utility of E/e′ in patients with acutely decompensated advanced heart failure, particularly in patients with cardiac resynchronization therapy and/or extensive LV remodeling (4). Moreover, testing of E/e′ and other echocardiographic indexes has generally been performed at a single time-point and has compared these indexes to a range of invasively measured indexes of LV filling pressure. To date, no studies have tested the accuracy of repeated measurements of echo estimates of LV filling pressure and none have compared directly measured left atrial pressure (LAP) (5), which is an important determinant of pulmonary capillary pressure and therefore of pulmonary edema and symptoms (6). We sought to determine the accuracy of echo indexes for the detection of elevated LAP at single and serial time-points in patients with advanced chronic heart failure and an implanted sensor that accurately measures direct LAP.

See page 935

ABBREVIATIONS AND ACRONYMS

E/e′ = ratio of transmitral to annular early diastolic velocities

LAP = left atrial pressure

LV = left ventricle

MR = mitral regurgitation

NYHA = New York Heart Association

PCWP = pulmonary capillary wedge pressure

TDI = tissue Doppler imaging

METHODS

Patients. Fifteen patients with New York Heart Association (NYHA) functional class II to III heart failure regardless of LV ejection fraction enrolled in the HOMEOSTASIS (Hemodynamically Guided Home Self-Therapy in Severe Heart Failure Patients) trial underwent serial echocardiography at 2 centers. The 15 subjects enrolled in this substudy were recruited from the 2 centers in New Zealand that were participating in the HOMEOSTASIS trial. This trial is a human feasibility study to evaluate the safety and functionality of a permanently implantable LAP monitoring system (HeartPOD, St. Jude Medical Inc., Minneapolis, Minnesota) (7). Inclusion criteria were NYHA functional class II to IV heart failure >6 months regardless of LV ejection fraction. Subjects had to have at least 1 exacerbation of heart failure requiring parenteral therapy during the preceding year.

Exclusion criteria included atrial fibrillation, stenotic valve lesions, hypertrophic cardiomyopathy, moderate or severe semilunar valvular regurgitation, valvular prosthesis, and the presence of a pericardial effusion. Patients with atrial fibrillation were initially excluded from the HOMEOSTASIS study due to the increased potential of thromboembolic complications with the direct LAP sensor. A New Zealand multicenter research ethics committee approved the study. All patients gave written informed consent.

Echocardiography. Serial echocardiography was undertaken after implantation of the LAP monitoring device and at 2, 4, 6, and 12 weeks and every 3 months thereafter during 1 year of follow-up. Usual heart failure medications were taken by all subjects on the day of echocardiography. Images were acquired with the patient in the left lateral decubitus position during quiet respiration. Acquisition of 2-dimensional images and Doppler indexes were undertaken according to American Society of Echocardiography guidelines (8–10). Sonographers were blinded to the current LAP measurement. The lowest filter settings were used to ensure that a complete Doppler spectrum was obtained in each instance. A sweep speed of 50 to 100 mm/s was used. Care was taken to minimize the angle between the Doppler signal and the plane of longitudinal excursion of the LV.

The data acquired was stored electronically and later analyzed offline using CardioVascular (ProSolv, Indianapolis, Indiana) and EchoPAC (GE Healthcare, Chalfont St. Giles, UK) software by a single investigator (J.R.) who was blinded to LAP. Mean values of each parameter were determined by measuring 3 consecutive cardiac cycles (excluding premature beats and the subsequent cardiac cycle).

Zealand; §Cardiology Division of the Department of Medicine, Cedars-Sinai Medical Center, Los Angeles, California; ‖CRMD Technology Incubation, St. Jude Medical, Minneapolis, Minnesota; ¶Division of Cardiovascular Medicine, Ohio State University, Columbus, Ohio; and the #Department of Cardiology, Princess Alexandra Hospital, Queensland, Australia.
The HOMEOSTASIS trial (HeartPOD LAP monitoring device) was sponsored by St. Jude Medical Inc. Dr. Ritzema was supported by a grant from the National Heart Foundation of New Zealand. Drs. Eigler and Whiting have a financial interest in the manufacturer of the study device. Drs. Abraham and Troughton have received honoraria or consulting fees from St. Jude Medical. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received December 19, 2010; revised manuscript received July 12, 2011, accepted July 13, 2011.

Table 1. Baseline Demographics and Laboratory Values at the Time of Initial Echocardiographic Study

		Range
Sex, men/women	13/2	
Age, yrs, median	70	60–83
BSA, m^2	2.0 ± 0.2	1.6–2.3
Etiology: ischemic/idiopathic/HTN	12/2/1	
NYHA functional class II/III	8 (53)/7 (47)	II–III
6-min walk test, m	363 ± 83	205–490
Creatinine, mg/dl	1.5 ± 0.4	0.9–2.4
CRT	7 (47)	
Heart rate, min^{-1}	65.4 ± 11	50–89
Systolic BP, mm Hg	110.7 ± 23	72–150
Diastolic BP, mm Hg	64.3 ± 13.2	44–90
LAP, mm Hg	17.3 ± 8	7–28.7

Values are n, mean ± SD, or n (%) and range; n = 15.
BP = blood pressure; BSA = body surface area; CRT = cardiac resynchronization therapy device; HTN = hypertension; LAP = left atrial pressure; NYHA = New York Heart Association.

Doppler measurements. Standard Doppler mitral inflow measurements were acquired on each occasion. Tissue Doppler imaging (TDI) included the early (e′) and late diastolic (a′) velocities from medial and lateral mitral annular margins (9). The ratio of early transmitral mitral to early myocardial relaxation velocity (E/e′) was calculated for both the medial (E/e′medial) and lateral (E/e′lateral) mitral annular sites and the average (E/e′average) from both annular sites (11). TDI data were excluded from analyses in 1 subject found to have pericardial constriction with normal myocardial function. The intraobserver variability for echocardiographic measurements was determined by repeating the measurement of 10 variables in 9 subjects.

Left atrial pressure recordings. Mean LAP was obtained from high-fidelity LAP waveforms of 15-s duration that were acquired immediately prior to Doppler echocardiography of mitral inflow. TDI indexes were acquired thereafter. Previous analyses in this cohort have shown that device LAP correlates very strongly with pulmonary capillary wedge pressure (PCWP) at follow-up right heart catheterization (r = 0.98) at 3 and 12 months. Mean sensor drift was <1.3 mm Hg and the average difference between device LAP and PCWP = 1.3 ± 3.8 mm Hg at 1 year (7).

Statistics. Statistical analyses were performed using SPSS software (version13, SPSS Inc., Chicago, Illinois). The dependency among the repeated measurements within individuals was appropriately accounted for using repeated measures analyses. Mixed model analysis of variance was used to test the association between LAP and echo indexes within individuals across all echocardiographic studies. Receiver-operator characteristic curve analysis was used to compare the sensitivity and specificity of the Doppler variables to detect LAP ≥15 and ≥20 mm Hg. All data are presented as mean ± SD, unless otherwise stated. Statistical significance was defined as $p < 0.05$ (2-tailed).

RESULTS

Baseline characteristics. Fifteen subjects with NYHA functional class II to III heart failure were recruited (Table 1). Twelve had ischemic heart disease. Seven subjects had a cardiac resynchronization device for the duration of the study. Most subjects had significant LV dilation and systolic dysfunction (Table 2), although 2 subjects had an LV ejection fraction ≥40%. A spectrum of overall diastolic filling patterns ranging was seen (Table 2).

Serial LAP measurement and echocardiographic studies. Sixty simultaneous echocardiographic studies and LAP measurements were obtained with a

Table 2. Baseline Echocardiographic Measurements

	Mean ± SD	Adequately Obtained (%)
LVEDV, ml	243.9 ± 111	100
LVEDVI, ml/m^2	123.5 ± 56	100
LVESVI, ml/m^2	89.9 ± 55	100
LVEF, %	31.6 ± 12	100
LVSV, ml	66.3 ± 18	100
E velocity, cm/s	75.8 ± 24	93.3
A velocity, cm/s	68.2 ± 24	93.3
A duration, ms	172.1 ± 32.8	66.7
E/A	1.3 ± 0.9	86.7
DT, ms	214.5 ± 67	86.7
S, cm/s	36.6 ± 17	73.3
D, cm/s	51.5 ± 27	80
PVAR velocity, cm/s	24.7 ± 9	46.7
PVAR duration, ms	202.3 ± 36	33
e′medial, cm/s	3.8 ± 1.2	93.3
e′lateral, cm/s	5.2 ± 2	93.3
a′medial, cm/s	5.3 ± 2.3	100
a′lateral, cm/s	5.3 ± 2.6	100
E/e′medial	21 ± 10.4	93.3
E/e′lateral	16.6 ± 9.3	93.3
LAmax, ml	105.6 ± 26	66.7
LAmaxI, ml/m^2	54.9 ± 13	66.7

n = 15. All Doppler measurements are single plane (apical 4-chamber) unless noted. Volumetric data are biplane measurements. Data included from 2 subjects with left ventricular ejection fraction ≥40%.
E/e′average = ratio of the early mitral inflow velocity and mean of the medial and lateral annular tissue Doppler velocities; I = indexed to body surface area; LAmax = maximal left atrial volume; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; LVESV = left ventricular end-systolic volume; LVSV = left ventricular stroke volume; PVAR = pulmonary venous atrial reversal.

JACC: CARDIOVASCULAR IMAGING, VOL. 4, NO. 9, 2011
SEPTEMBER 2011:927–34

median of 4 (1 to 7) studies per patient over a median follow-up period of 23 (range 0 to 52) weeks. One patient had a single echo study. Variation from follow-up occurred due to patient death (5 studies), intercurrent illness (9 studies), recurrent arrhythmias (7 studies), and technical reasons including LAP sensor malfunction (39 studies). There was wide variation in LAP at the time of echocardiography (range 5 to 39 mm Hg). An LAP >15 or 20 mm Hg was seen in 51.7% and 35% of studies, respectively. All subjects exhibited variation in LAP across visits and the coefficients of variation in individuals' LAP at the time of echocardiography ranged from 16.7% to 61.3% across all echo studies. The highest LAPs (>25 mm Hg) were associated with diastolic mitral regurgitation (MR). The coefficients of variation for the intraobserver variability of echocardiographic measurements were 4.0%, 5.5%, and 6.7% for E, DT, and e′, respectively. Tissue Doppler and transmitral indexes were reliably obtained in the majority (≥80%) of studies. Complete mitral inflow measurements were occasionally not possible due to fusion of E and A waves. High-quality Doppler spectra of pulmonary venous flow were acquired in 71.7% of studies. In 26 (43.3%) echocardiographic studies, subjects had moderate or greater MR and in 12 (20%) there was severe MR.

Correlation of echo indexes with LAP across serial studies. There were significant correlations between serial LAP measurements and E/e′medial ($r = 0.46$, $p < 0.005$) (Fig. 1) within individuals across serial echocardiographic studies. Correlations between serial LAP and E/e′average or E/e′lateral (Fig. 1), mitral inflow, or pulmonary vein parameters did not achieve statistical significance when corrected for multiple measurements within individuals.

The relationship between LAP and E/e′medial was unchanged when analyzed as change from baseline or percent change from baseline ($r = 0.46$; $p < 0.005$, for both comparisons).

Detection of elevated LAP. Doppler variables accurately detected LAP ≥20 and ≥15 mm Hg (Table 3). Areas under respective receiver-operator characteristic curves for the detection of LAP ≥15 were 0.95 (E/e′average), 0.94 (E/e′medial), and 0.90 (E/e′lateral). An E/e′average of ≥14, E/e′medial of ≥15, and E/e′lateral ≥12 had sensitivity of 84%, 84%, and 73% and specificity of 96%, 91%, and 87%, respectively, for the detection of LAP ≥15 mm Hg. The E/e′ ratio was consistently the

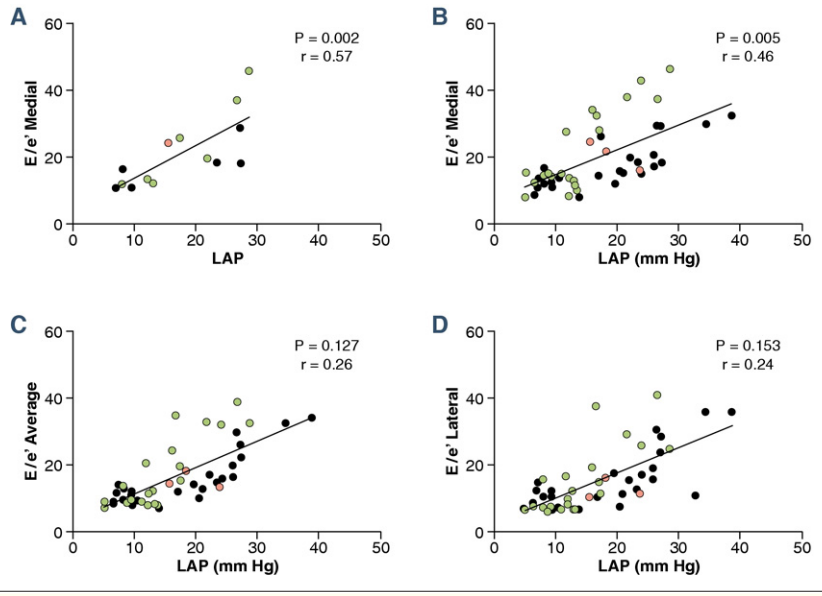

Figure 1. Intrapatient Correlation of E/e′ With Simultaneous LAP

Results are shown for baseline left atrial pressure (LAP) versus baseline E/e′ medial **(A)**, and serial data for LAP versus E/e′ medial **(B)**, E/e′ average **(C)**, and E/e′ lateral **(D)**. In **B** to **D**, r is the pooled intrapatient correlation coefficient from mixed model analysis. The **fitted line** reflects the pooled intrapatient association also derived from the mixed model analysis. **Green** indicates data from subjects with a cardiac resynchronization device, **red** indicates data from subjects with a left ventricular ejection fraction ≥40%. n = 14 (15 subjects enrolled, tissue Doppler imaging data were excluded from analyses in one subject found to have pericardial constriction). E/e′ average = ratio of the early mitral inflow velocity and mean of the medial and lateral annular tissue Doppler velocities.

Table 3. Sensitivity, Specificity, and Accuracy of Serial Doppler Measurements for the Estimation of LAP

Variable	p Value	AUC	Cutpoint (≥)	Sensitivity	Specificity	PPV	NPV	Accuracy
Detecting LAP ≥15								
E/e′average	0.0001	0.95	14	84	96	95	85	90
E/e′medial	0.0001	0.94	15	84	91	91	84	88
E/e′lateral	0.0001	0.90	12	73	87	86	74	80
E velocity	0.001	0.77	60	71	71	72	70	71
E/A	0.001	0.76	0.85	70	83	83	69	76
PVARdur-Adur	0.017	0.83	14	80	82	57	93	82
Detecting LAP ≥20								
E/e′average	0.0001	0.87	15	82	81	70	89	81
E/e′medial	0.0001	0.85	15	88	74	65	92	79
E/e′lateral	0.0001	0.85	15	72	81	68	68	78
E velocity	0.019	0.69	61	71	62	54	78	65
E/A	NS	0.6	0.74	68	53	45	75	58
PVARdur-Adur	NS	0.82	19	75	84	50	89	83
Detecting LAP ≤12								
E/e′average	0.001	0.80	14	94	68	62	95	77
E/e′medial	0.001	0.78	15	88	68	60	91	75
E/e′lateral	0.001	0.8	11	70	75	60	83	73
E/A	0.005	0.74	85	94	64	55	96	74
E velocity	0.015	0.71	60	71	63	46	83	65
PVARdur-Adur	NS	0.72	12	83	64	71	78	74

Adur = A-wave duration; AUC = area under the curve; NPV = negative predictive value; NS = not significant; PPV = positive predictive value; PVARdur = duration of pulmonary venous atrial reversal; other abbreviations as in Tables 1 and 2.

best Doppler parameter for predicting LAP ≥20 and ≥15 mm Hg across all echocardiographic studies regardless of which annular site was used. Serial E/e′average and medial measurements were better able than E and E/A to detect an LAP ≥15 mm Hg (Fig. 2). Consideration of other echo indexes in addition to E/e′ did not improve the accuracy for the detection of an elevated LAP. The ability to identify low LAP was limited in this study by relatively few LAP <8 mm Hg (n = 6); however, 33% of LAP were <12 mm Hg. The E/e′ ratio still provided modest accuracy in detecting LAP <12 mm Hg (Table 3).

When only a single time-point for each individual (the first echo study) was included in the analysis, E/e′medial demonstrated greater accuracy for detecting LAP ≥20 (area under the curve: 0.88, sensitivity: 100%, specificity: 75%)

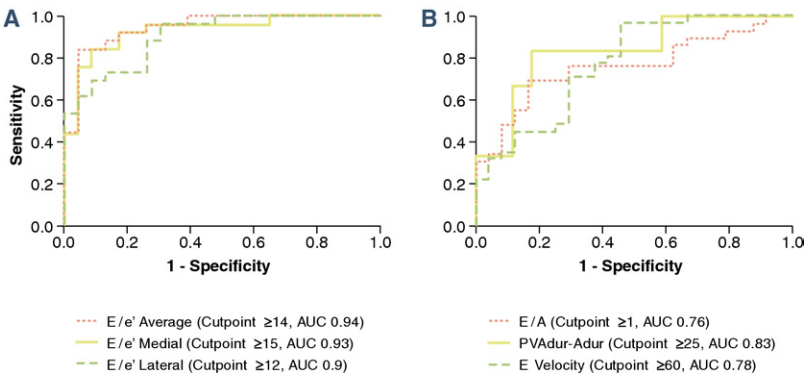

Figure 2. ROC Curves for the Prediction of LAP ≥15 mm Hg Using Echo Doppler Indexes

Results are shown for prediction of LAP ≥15 mm Hg using E/e′ at the different annular sites **(A)** and by mitral inflow and pulmonary venous velocities **(B)**. n = 15 but tissue Doppler imaging data were excluded from analyses in one subject found to have pericardial constriction. AUC = area under the curve; ROC = receiver-operator curve; other abbreviations as in Figure 1.

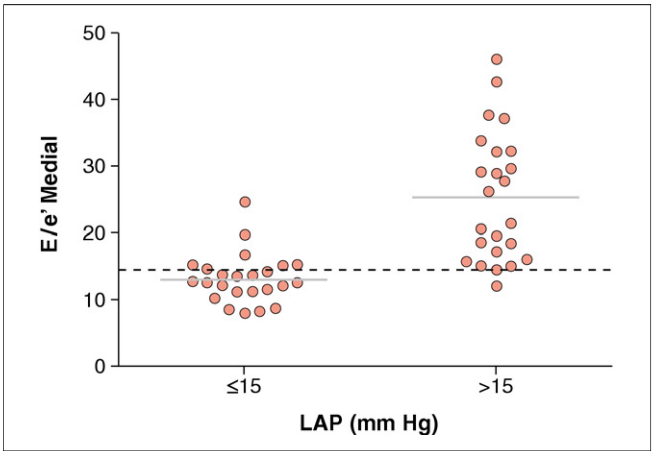

Figure 3. Mean LAP Versus Categorical E/e′ Medial Ratio (≤15 and >15) for All Studies (n = 48)

n= 14 (15 subjects enrolled, tissue Doppler imaging data were excluded from analyses in 1 subject found to have pericardial constriction). Abbreviations as in Figure 1.

and ≥15 mm Hg (area under the curve: 1, sensitivity: 100%, specificity: 100%).

As shown in Figure 3, although an optimal single cutpoint for E/e′medial of ≥15 accurately identified an LAP ≥15, an E/e′medial <12 essentially "ruled out" an elevated LAP with a sensitivity of 96% and a negative predictive value of 90%, whereas an E/e′ >18 "ruled in" an elevated LAP (specificity: 96%, positive predictive value: 95%). Intermediate values of E/e′ (8 to 14) have reduced discriminatory power.

DISCUSSION

Although the accuracy of Doppler indexes including E/e′ in identifying invasively measured elevated LV filling pressures has been demonstrated in multiple catheter laboratory-based cross-sectional studies, their accuracy during sequential testing in ambulant subjects had not been established. The availability of an implantable sensor that accurately measures direct LAP provided a unique opportunity to validate the accuracy of Doppler estimates of filling pressure in ambulant subjects. This is the first time that directly measured LAP has been used as the "gold-standard" reference in investigations of this kind. We found single and serial measurements of E/e′medial correlated significantly with simultaneous LAP. When serial testing was undertaken in these subjects, an E/e′ ≥15 accurately detected an LAP elevated into the decompensated range, with an E/e′ >18 essentially "ruling in" an elevated LAP and an E/e′ <12 essentially excluding an elevated LAP. These results indicate that physicians can be confident that E/e′

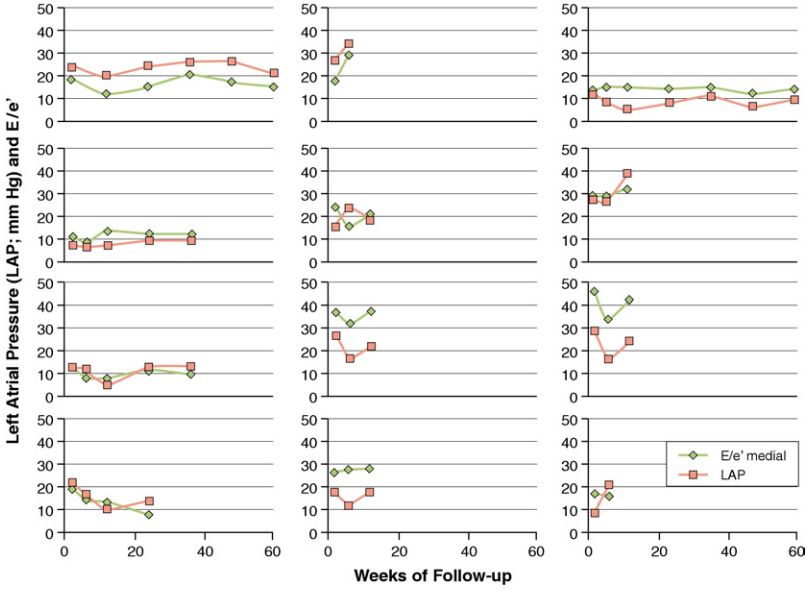

Figure 4. Concordant Temporal Changes in Left Atrial Pressure (mm Hg) and E/e′ Medial Ratio in 12 Subjects With 2 or More Echocardiogram Studies

n = 12, one subject was excluded as he had pericardial constriction, 1 subject had only a single study and 2 subjects did not have more than one E/e′ measurement.

can be used to accurately identify elevated (>15 mm Hg) filling pressures during outpatient follow-up of ambulant patients with advanced chronic heart failure.

Serial LAP and echocardiographic measurements. There are conflicting data regarding the utility of echo indexes of LV filling pressure to track short-term (hours) changes in PCWP (4,12,13) in subjects in the intensive care unit. This is the first study to determine the relationship between serial simultaneously measured LAP and Doppler indexes of diastolic function in ambulant subjects with advanced heart failure. When we tested the association between repeated concurrent echocardiographic and LAP measurements in our cohort, there was a significant association between LAP and E/e′medial, indicating that these indexes track each other over time (Fig. 4). This finding was consistent within individuals and across the group, despite these subjects having LV volumes and cardiac resynchronization therapy comparable to those enrolled in a recent study of subjects with acutely decompensated heart failure, in which Doppler estimates of PCWP were less accurate (4).

There was a slightly more modest correlation between LAP and E/e′ in our study when compared with previous studies when E/e′ was compared with a single invasive measurement of LV filling pressure, which is likely to reflect several factors including smaller sample size, less heterogeneity in patients, and appropriate statistical adjustment for multiple measurements from individuals in the current study. The association between E/e′ and LAP was less robust at higher LAP (>20 mm Hg). A linear increase in E velocity did not occur when LAPs were very high (>30 mm Hg); this could reflect an increased LV early diastolic pressure reflecting severe relaxation abnormalities and lower transmitral gradients in early diastole in severe heart failure. In chronic heart failure, there is a monophasic decline in the e′ velocity with increasing relaxation abnormality and diastolic dysfunction, but once this velocity approximated ≤2 cm/s, these velocities did not change despite further variation in LAP. Some of the scatter at higher pressures may reflect MR as all significantly elevated LAPs (>25 mm Hg) were associated with at least moderate functional MR and the accuracy of E/e′ measurements in this setting is uncertain, particularly when LV systolic function is preserved (14). However, in this heterogeneous population with advanced predominantly systolic heart failure and at least mild-moderate secondary MR, E/e′ reliably detected an elevated LAP.

The TDI indexes were highly reproducible in this study and were obtained in most subjects. Measurement variability was consistent with other reports.

There were no significant associations among repeated single Doppler mitral inflow, pulmonary venous flow measurements, and LAP, which may reflect greater difficulty in acquisition of these indexes and the impact of other diastolic processes such as left atrial function and myocardial relaxation (15,16).

Study limitations. This study included mainly older adults with severe heart failure; therefore, applicability to a wider heart failure population including younger patients or less severe heart failure is less certain. Subjects with atrial fibrillation were not enrolled, but findings from previous studies suggest these data are likely to be applicable. Although the number of subjects included in the study was small, and incomplete follow-up could potentially have introduced bias, the total number of echocardiographic studies analyzed was comparable to existing reports (1,12). However, these findings require validation in a larger cohort of patients. To reduce the dependency of repeated measures occurring within individuals, mixed-model analysis of variance was used for any correlations. The variable multiple observations per subject may have biased the receiver-operator characteristic curve analyses and decision statistics because the data do not constitute independent observations.

CONCLUSIONS

Measurement of E/e′ reliably detected normal or raised directly measured LAP in ambulant subjects with advanced chronic heart failure. These findings provide validation of the accuracy of serial Doppler estimates of LV filling pressure and support the serial use of this noninvasive index to assess filling pressures.

Acknowledgments

The authors would like to acknowledge technical support from Nicola Gardiner, Agatha Kwon, Helen Walsh, Gillian Whalley, and Mariska ter Bals.

Reprint requests and correspondence: Dr. Jay Ritzema, Department of Cardiology, Princess Alexandra Hospital, Ipswich Road, Woolloongabba, Queensland 4012, Australia. *E-mail: jayritzema@gmail.com.*

JACC: CARDIOVASCULAR IMAGING, VOL. 4, NO. 9, 2011
SEPTEMBER 2011:927–34

REFERENCES

1. Kasner M, Westermann D, Steendijk P, et al. Utility of Doppler echocardiography and tissue Doppler imaging in the estimation of diastolic function in heart failure with normal ejection fraction: a comparative Doppler-conductance catheterization study. Circulation 2007;116:637–47.
2. Nagueh SF, Middleton KJ, Kopelen HA, Zoghbi WA, Quinones MA. Doppler tissue imaging: a noninvasive technique for evaluation of left ventricular relaxation and estimation of filling pressures. J Am Coll Cardiol 1997;30:1527–33.
3. Ommen SR, Nishimura RA, Appleton CP, et al. Clinical utility of Doppler echocardiography and tissue Doppler imaging in the estimation of left ventricular filling pressures: a comparative simultaneous Doppler-catheterization study. Circulation 2000;102:1788–94.
4. Mullens W, Borowski AG, Curtin RJ, Thomas JD, Tang WH. Tissue Doppler imaging in the estimation of intracardiac filling pressure in decompensated patients with advanced systolic heart failure. Circulation 2009;119:62–70.
5. Lancaster GI, Srinivasan J, Jain H. Letter by Lancaster et al. regarding article, "Tissue Doppler imaging in the estimation of intracardiac filling pressure in decompensated patients with advanced systolic heart failure." Circulation 2009;120:e48.
6. Guyton AC, Lindsey AW. Effect of elevated left atrial pressure and decreased plasma protein concentration on the development of pulmonary edema. Circ Res 1959;7:649–57.
7. Troughton RW, Ritzema J, Eigler NL, et al., for the HOMEOSTASIS Investigators. Direct left atrial pressure monitoring in severe heart failure: long-term sensor performance. J Cardiovasc Transl Res 2011;4:3–13.
8. Lang RM, Bierig M, Devereux RB, et al. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group. J Am Soc Echocardiogr 2005;18:1440–63.
9. Quinones MA, Otto CM, Stoddard M, Waggoner A, Zoghbi WA. Recommendations for quantification of Doppler echocardiography: a report from the Doppler Quantification Task Force of the Nomenclature and Standards Committee of the American Society of Echocardiography. J Am Soc Echocardiogr 2002;15:167–84.
10. Zoghbi WA, Enriquez-Sarano M, Foster E, et al., for the American Society of Echocardiography. Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography. J Am Soc Echocardiogr 2003;16:777–802.
11. Garcia MJ, Thomas JD, Klein AL. New Doppler echocardiographic applications for the study of diastolic function. J Am Coll Cardiol 1998;32:865–75.
12. Dokainish H, Zoghbi WA, Lakkis NM, et al. Optimal noninvasive assessment of left ventricular filling pressures: a comparison of tissue Doppler echocardiography and B-type natriuretic peptide in patients with pulmonary artery catheters. Circulation 2004;109:2432–9.
13. Nagueh SF, Kopelen HA, Zoghbi WA. Feasibility and accuracy of Doppler echocardiographic estimation of pulmonary artery occlusive pressure in the intensive care unit. Am J Cardiol 1995;75:1256–62.
14. Olson JJ, Costa SP, Young CE, Palac RT. Early mitral filling/diastolic mitral annular velocity ratio is not a reliable predictor of left ventricular filling pressure in the setting of severe mitral regurgitation. J Am Soc Echocardiogr 2006;19:83–7.
15. Nishimura RA, Tajik AJ. Evaluation of diastolic filling of left ventricle in health and disease: Doppler echocardiography is the clinician's Rosetta Stone. J Am Coll Cardiol 1997;30:8–18.
16. Thomas JD, Weyman AE. Echocardiographic Doppler evaluation of left ventricular diastolic function: physics and physiology. Circulation 1991;84:977–90.

Key Words: heart failure ■ left atrial pressure ■ left ventricle ■ tissue Doppler imaging.