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Research Article

# Elevated Tissue Doppler E/E' on Index Admission Can Help Identify Patients at Increased Risk for 30 Day Readmission

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**Abstract**

**Background:** Readmissions for congestive heart failure (CHF) are a major healthcare problem that contributes significantly to the overall healthcare expenditure. About 24% of patients are readmitted to the hospital within 30 days of discharge. We investigated whether a non-invasive estimate of left atrial filling pressure, an elevated ratio of early trans mitral flow velocity to early diastolic mitral annular velocity (E/E'), during the index admission for CHF could independently predict 30 day readmission.

**Methods:** This was a single center retrospective cohort study of consecutive CHF patients hospitalized from January 2011 to September 2013. Demographic and clinical variables were obtained and E/E' measured during the index hospitalization. Patients were then followed for readmission at 30 day. Statistical comparisons were made between readmitted and non-readmitted cohorts.

**Results:** A total of 212 consecutive patients with a diagnosis of CHF were included in the study. The mean age was 76.6±12.9 vs. 72±12.4 (p=0.64) while mean left ventricular ejection fractions was 0.33±0.14 vs. 0.37±0.15 (p=0.8943) in the readmitted and non-readmitted cohorts respectively. 22.30% of the study patients were readmitted within 30 days of the index hospitalization. The mean E/E' in the readmitted group was 17.7 compared to 12.81 in the non-readmitted group (p=0.0002).

**Conclusion:** Elevated Tissue Doppler E/E' on index admission for CHF is predictive of 30 day readmissions. E/E' represents a simple, non-invasive tool for identifying CHF patients at highest risk for 30 day readmission.

## Introduction

### Background

Congestive heart failure (CHF) is a leading cause of hospital admissions and readmissions. Approximately 5.1 million people in the United States suffer from heart failure [1]. It is responsible for 55,000 yearly deaths with half of all patients diagnosed with heart failure dying within 5 years of diagnosis [1]. The associated costs run intobillions of dollars with each hospitalization costing $17,654 to $25,325 dollars depending on whether heart failure was a primary or secondary diagnosis [2,3]. The bulk of healthcare expenditure related to CHF is related to readmissions [4].

Post hospitalization follow-ups and home visits by nursing personal have helped reduce readmission rates [5-8]. A number of studies have demonstrated the inability of physicians to evaluate volume status by physical examination alone [9-11]. This may partly be related to the fact that left ventricular filling pressures begin to rise long before the development of symptoms. Swan-Ganz catheters are able to provide hemodynamic data to guide medical therapy. However, due to associated morbidity and the availability of non-invasive means its role is increasingly being questioned. The ESCAPE trial showed no benefit of routine Swan-Ganz catheterization in the systolic heart failure population [12,13]. Therefore, even though a number of discharge performance metrics exist, heart failure still accounts for 24.7% of all readmissions [14].

Clinical assessment of volume status in patients with chronic CHF can often be difficult to determine since the clinical variables for the determination of volume may not be present in two third of the patients with CHF. Patients may seem euvolemic and asymptomatic but continue to have elevated filling pressures [15]. The standard of care has been to discharge CHF patients once symptoms have abated and parenteral medications transitioned to oral forms. In the absence of continued titration of medications to optimal tolerable dosages, patients fail to achieve therapeutic benefit and sustain frequent exacerbations and readmissions.

E/E' is the ratio of early transmitral flow velocity to early diastolic mitral annular velocity. It is a non-invasive echo cardiographic

parameter that has been shown to correlate well with LVEDP and by extension pulmonary venous occlusion pressures is easy to obtain, is standard in many labs, and correlates with pulmonary capillary wedge pressure and has prognostic implications in acute myocardial infarction and CHF [16-19]. Elevations in the ratio have been associated with increased mortality. Studies have consistently shown that filling pressures and hence E/E' start to elevate long before symptoms or overt heart failure develops [4,18,20]. We hypothesize that E/E' may help identify patients that are at highest risk for readmission within 30 days of discharge.

## Methods

This was a retrospective study conducted at Kettering Medical Center (KMC) in Ohio between Jan 1st 2011 to Sept 30th 2013. Patients who met the inclusion criteria were stratified into two groups. One group comprised of CHF patients readmitted within 30 days from the index hospitalization and the second group consisted of those who were not.

## Data Collection

Charts were reviewed and data collected in a consecutive manner for the above specified study duration. Echocardiographic and clinical variables were then compared for each of the two groups. Data collection was performed by four investigators (MBQ, GMN, PK, and NW).

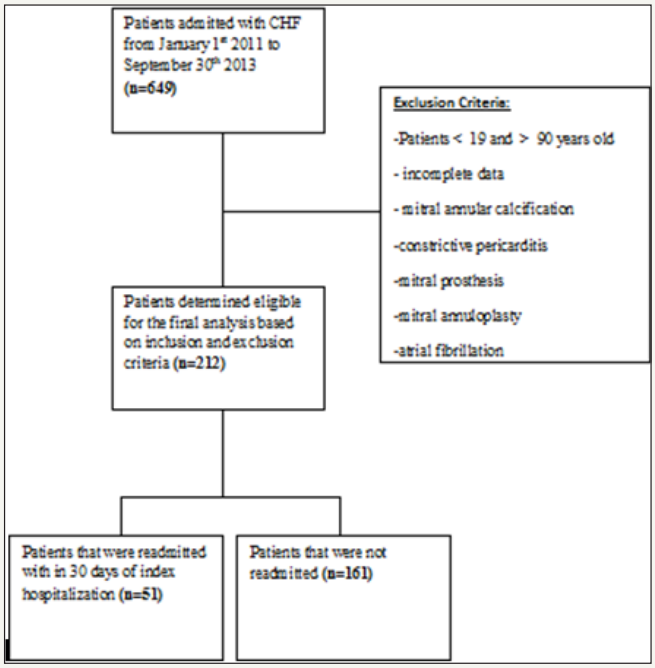


**Figure 1:** BSE image showing
1a: Transverse section of composite clad
1b: Zoomed image of clad region

Echocardiographic reports on index admission were reviewed for all patients admitted and discharged with an ICD-9 diagnosis of CHF. E/E' calculated from the lateral mitral annulus was documented. This was due to our institutional practice and was primarily for technical reasons. Information on ejection fraction (EF), left ventricular hypertrophy of varying severity (severe, moderate, mild, and borderline) and left atrial size as documented by interpreting cardiologist was recorded. Basic demographic, laboratory data within 24hrs of admission, comorbidities, medications with routes of administration, length of hospitalization(calculated from date of admission and date of discharge), all-cause mortality for the duration of the study was collected from the medical records of the two groups. NYHA class was determined from the admission history and physical if not documented by the admitting provider (Table 1). The medical records system is fully electronic with area surrounding hospitals using the same electronic medical system (EPIC ® ) The study was approved by KMC's institutional review board (IRB) and conducted under their supervision.

The study was approved by KMC's institutional review board (IRB) and conducted under their supervision. A strict inclusion and exclusion criterion was used in order to ensure uniformity and limit confounding factors (Figure 1).

### Inclusion criteria

a. All patients admitted between the ages of 19-90 years with a discharge diagnosis of congestive heart failure and newly diagnosed congestive heart failure or CHF exacerbation. Patients were identified using ICD 9-code , 428.0, 428.1, 428.22, 428.23, 428.30,428.31, 428.32,428.9

b. Patients with a repeat admission within 30 days of discharge from the hospital

c. Echocardiography done within 48 hrs of admission

### Exclusion criteria

a. Patients below the age of 19 and above the age of 90 were excluded

b. Patients with incomplete echocardiographic data set and those in whom E/E' could not be adequately assessed such as mitral annular calcification, constrictive pericarditis, mitral prosthesis, mitral annuloplasty, atrial fibrillation during echocardiographic assessment were excluded.

The two groups were compared for the primary end point of

a. Length of Hospital stay

b. Duration of IV diuretic use on index admission

c. E/E'

Continuous variables were expressed as mean±standard deviation (SD) and categorical variables as counts and percent. The two groups were compared by using Student's t-test for continuous variables and the chi square test or Fisher's Exact Test for categorical variables. Differences between continuous variables were assessed using MANOVA. All inferential analyses used two-sided p values with significance if less than or equal to 0.05. Potential predictors for readmissions were selected with a stepwise, backward and forward procedures with logistic regression analysis which were entered into the model at $p< 0.10$ and retained at $p<0.05$.A

probability value of less than 0.05 was considered significant and all calculations and statistical tests were performed using JMP statistical software version 10.0.0 (SAS institute, Cary, NC)

## Results

649 patients admitted with CHF from January 1st 2011 to September 30th 2013 were screened out of which 212 patients were deemed eligible for the final analysis based on inclusion and exclusion criteria. There were 51 patients that comprised the readmitted group and 161 formed the non-readmitted group. No subject was lost to follow-up.

The readmitted group was older 76.6±12.9 vs 72±12.4 (CI:-0.37 to -8.56, p<0.01) than the non-readmitted group. There were no gender differences related to readmissions (60.78% vs 60.87% for males, 39.22% vs 39.13% for females, p=1) and race. The majority of patients were Caucasians (92.16% vs 95.03%) with few African Americans(7.84% vs 4.35%). This is representative of our patient population (Table 1).

**Table 1:** Baseline demographic and clinical characteristic.

| Variable | | Readmitted (N=51) | Non- Readmitted (N=161) | p Value (t Test) |
|---|---|---|---|---|
| Age | | 76.6 ±12.9 | 72 ±12.4 | (CI:-0.37 to -8.56) p<0.01 |
| Gender | Male<br>Female | 31(60.78%)<br>20(39.22%) | 98(60.87%)<br>63(39.13%) | p=1.00 |
| Race | Caucasian<br>African American<br>Others | 47(92.16%)<br>4(7.84%)<br>0 (0%) | 153(95.03%)<br>7(4.35%)<br>1 (0.62%) | p=0.467 |
| BMI | | 28.1±6.74 | 30.5±8.15 | (CI:0.10 to 4.63) p<0.97 |
| Coronary artery disease | Yes<br>No | 41(80.39%)<br>10(19.61%) | 105(65.22%)<br>56(34.78%) | p=0.055 |
| Diabetes | Yes<br>No | 25(49.02%)<br>26(50.98%) | 77(47.83%)<br>84(52.17%) | p=1.00 |
| Hypertension | Yes<br>No | 43(84.31%)<br>8(15.69%) | 147(91.30%)<br>14(8.70%) | p=0.186 |
| Ischemic cardiomyopathy | Yes<br>No | 34(66.67%)<br>17(33.33%) | 54(33.54%)<br>107(66.46%) | p<0.0001 |
| Non-ischemic cardiomyopathy | Yes<br>No | 5(9.80%)<br>46(90.20%) | 22(13.75%)<br>138(86.25%) | p=0.631 |
| BiV AICD | Yes<br>No | 4(7.84%)<br>47(92.16%) | 10(6.21%)<br>151(93.79%) | p=0.747 |
| Single chamber defibrillator | Yes<br>No | 13(25.49%)<br>38(74.51) | 23(14.29%)<br>138(85.71%) | p=0.085 |
| Ejection fraction (Mean±SD) (N) | | 0.33±0.14 (51) | 0.37±0.15(160) | (CI:-0.00 to 0.08) p<0.95 |
| Left atrial size | | 4.07±0.66 | 3.71±1.79 | (CI: -0.23 to 0.19)p<0.423 |
| NYHA- Class | | 3.07±0.27 | 3.04±0.26 | (CI:-0.11 to 0.05) p<0.255 |
| Sodium | | 136.17±5.16 | 136.98±4.80 | (CI:-0.82 to 2.43) p<0.83 |
| Blood urea nitrogen | | 33.47±19.4 | 28.13±19.87 | (CI:-11.5 to 0.915) p<0.04 |
| Creatinine | | 1.75±1.12 | 1.59±1.09 | (CI:-0.51 to 0.19) p<0.19 |
| Hemoglobin (Mean±SD)(N) | | 11.22±1.68 (50) | 11.89±2.11 (160) | (CI:0.08 to 1.24) p<0.98 |
| Cardiology consult | Yes<br>No | 35(68.63%)<br>16(31.37%) | 105(65.22%)<br>56(34.78%) | p=0.735 |
| Length of stay (Days) | | 4.41±3.09 | 5.44±3.54 | (CI:0.00 to 2.05) p<0.97 |
| Duration of IV diuretics (Mean±SD)(N) | | 3.04±2.05 (43) | 3.89±2.56(137) | (CI:0.09 to 1.61) p<0.98 |
| e/e'(Mean ±SD)(N) | | 17.7±6.29(51) | 12.81±5.43 (159) | (CI:-6.87 to-2.96) p<0.0001 |

No differences in BMI (28.1±6.74 vs 30.5±8.15 (CI: 0.10 to 4.63, p<0.97) and EF (0.33±0.14 vs 0.37±0.15 (CI: -0.00 to 0.08, p<0.95) were seen between the two groups. The EF of one study participant could not be recorded due to non-documentation in the echocardiography report.


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The two groups were similar in terms of NYHA Class (3.07±0.27 vs 3.04±0.26, CI: -0.11 to 0.05, p <0.255), sodium (136.17±5.16 vs 136.98±4.80, CI: -0.82 to 2.43, p<0.83) and creatinine (1.75±1.12 vs 1.59±1.09 CI: -0.51 to 0.19, p<0.19). The blood urea nitrogen levels were higher in the readmitted than in the non-readmitted group (33.47±19.4 vs 28.13±19.87, CI:-11.5 to 0.915, p<0.04). Diabetes and hypertension occurred with the same prevalence 49.02% vs 47.83%, p =1.00 and 84.31% vs 91.30%, p=0.186. There was a higher trend of coronary artery disease in the readmitted group than the non-readmitted group (80.39% vs 65.22%, p =0.055). This was however not statistically significant. Ischemic cardiomyopathy occurred more frequently in the readmitted group 66.67% vs 33.54%, p<0.0001 attaining statistical significance (Table 1).

There were no differences in regards to non-ischemic cardiomyopathy (9.80% vs 13.75%, p=0.631), CRT-D (7.84% vs 6.21%, p=0.747) and AICD (25.49% vs 14.29%, p=0.085). Cardiology consultation did not seem to make a difference (68.63% vs 65.22%, p=0.735). The readmitted and non-readmitted groups had comparable length of hospital stay (4.41±3.09 vs 5.44±3.54, CI: 0.00 to 2.05 p<0.97) and duration of intravenous diuretics (3.04±2.05 vs 3.89±2.56, CI: 0.09 to 1.61 p<0.98). The readmitted group had a significantly higher E/E' (17.7±6.29 vs 12.81±5.43, CI: -6.87 to -2.96 p<0.0001) (Table 1).

**Table 2:** Multivariate logistic regression for readmitted vs non-readmitted groups.

| Variable | Odds Ratio (OR) | Confidence Intervals (CI) | p Value |
|---|---|---|---|
| Age | 0.22 | (95% CI: -0.04 to 0.03) | 0.64(NS) |
| Coronary artery disease | 1.19 | (95% CI: -1.06 to 0.27) | 0.27(NS) |
| Hypertension | 5.56 | (95% CI: -1.36 to -0.12) | 0.018 |
| Atrial Fibrillation | 4.11 | (95% CI: 0.02 to 0.93) | 0.042 |
| Diabetes | 0.23 | (95% CI: -0.56 to 0.33) | 0.629(NS) |
| Ischemic CMP | 8.38 | (95% CI: 0.33 to 1.62) | 0.003 |
| Non-ischemic CMP | 0.04 | (95% CI: -0.79 to 0.90) | 0.84(NS) |
| Length of Stay | 4.29 | (95% CI: -0.48 to-0.03) | 0.038 |
| BUN | 0 | (95% CI: -0.03 to 0.03) | 0.97(NS) |
| Creatinine | 0.88 | (95% CI: -0.30 to 0.93) | 0.348(NS) |
| e/e' | 13.85 | (95% CI: 0.06 to 0.20) | 0.0002 |
| Ejection Fraction | 0.02 | (95% CI: -3.53 to 3.10) | 0.8943(NS) |
| Duration of IV Diuretics | 0.45 | (95% CI: -0.38 to 0.19) | 0.50(NS) |

In the logistic regression model E/E', ischemic cardiomyopathy, length of stay, hypertension and atrial fibrillation were the most powerful predictors for readmission ( OR:13.85, 95%CI:0.06 to 0.20, p=0.0002, OR:8.38, 95% CI:0.33 to 1.62, p=0.003, OR:4.29,95% CI:-0.48 to -0.03. p=0.038, OR:5.56, 95%CI:-1.36 to -0.12, p=0.018, OR:4.11, 95% CI:0.02 to 0.93, p=0.042) (Table 2).

## Discussion

Our findings suggest elevated E/E', ischemic cardiomyopathy, length of stay, hypertension and atrial fibrillation are strongly associated with 30-day readmission in CHF patients. There were no differences in all-cause mortality and duration of IV diuretics between the two groups. High blood urea nitrogen levels and age correlated with 30-day readmissions but did not hold on in the multivariate analysis model. Previous studies have examined the relationship of E/E' and readmission. But no study has shown the correlation of E/E' with 30 day readmissions. Kumiko and colleagues examined this relationship and found that E/E' greater than 23 and reduced ejection fraction was the strongest independent predictor of death and readmission [21]. They however, did not specify the time frame to readmission and examined readmissions over 351±252 days. This was also shown by Hisham and colleagues.

They showed brain natriuretic peptide (BNP) measurements and E/E' assessments 24 hrs prior to discharge could predict re-hospitalizations [22]. The mean time from hospital discharge and follow-up was 527±47 days. Both of these studies measured septal and lateral mitral annular velocities to calculate e/e' and averaged them. We used the lateral annulus for determining e/e' as previously described and was primarily for technical reasons and per institutional practice. The American society of echocardiography (ASE) guidelines recommend averaging E/E' derived from the septal and lateral mitral annular velocities as it would be a better estimate of filling pressure under globally reduced systolic function and wall motion abnormalities [23]. Our study looks into the correlation of E/E' with readmission and its generalizability in the context of multiple co morbidities in predicting readmission and not its accuracy in estimating filling pressures.

Our study could not assess the relationship of troponin and BNP on 30 day readmission. This was primarily due to incomplete information and a change of our laboratory to pro-bnpand high sensitivity troponin mid-way through 2013. Low ejection fraction did not correlate with 30day readmissions. This is consistent with prior studies looking into echocardiographic variables that have not shown correlation of low ejection fraction with readmission [21,22]. Elevated blood urea nitrogen correlated with 30-day readmission on univariate basis but once adjusted no correlation was seen. This could possibly be due to small sample size and for the very fact that CHF readmission is dependent on a number of factors. In the CHF-OPTIME trial elevated blood urea nitrogen levels correlated with 60-day readmission. Our study looked into



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30-day readmission and hence may account for the differences seen. Similarly, serum sodium concentrations did not correlate with readmission and can be accounted for by the same reasons outlined above and for the fact that the CHF-OPTIME trial had a sicker patient population with highest readmission rates associated with serum sodium concentrations below a mean of 134meq/dl.

The presence of hypertension and atrial fibrillation were found to be independent predictors of readmission. Our study did not explore the impact of uncontrolled hypertension and atrial fibrillation on readmission and only looked at the presence or absence of these risk factors. It makes sense that older patients with CHF have multiple co morbidities and the presence of these risk factors may lead to frequent exacerbations and readmissions.

In the era of bundled pay and pay for performance, 30-day readmission gains special importance. Our study is the first to identify E/E' as an inexpensive predictor that can help identify patients at highest risk for 30 day readmission. The community setting and echocardiographic assessment within 48hrs of admission reflect real time practice and adds to the generalizability of our findings. Ideally an estimation of E/E' should be performed on admission and 24 hrs prior to discharge. Persistently elevated values will indicate poor prognosis and high risk of readmission. This will need to be validated in a prospectively designed study.

In the real world this may not seem practical. A second modified echocardiogram will require additional resources. This may be alleviated by adding tissue Doppler capabilities to hand held echocardiographic devices. The rounding cardiologist could perform a quick bedside estimation and decide in combination of other clinical and laboratory parameters subsequent intensity of care. Third party payers will have to recognize the poor prognosis of this high risk CHF group and a modification to current payment models should be considered as admissions may not be preventable.

## Limitations

The major limitation of this study is its retrospective nature. Furthermore, it is a single center experience and as such our results cannot be generalized. We made a lot of effort in ensuring data accuracy by establishing robust quality controls, which consisted of a parallel review of the data collected by members of the study team (MBQ, GMN, PK, and NW). Two groups (MBQ, GMN and PK, NW) were made and the data collected by one group was reviewed by the other to ensure accuracy.

## Conclusion

Elevated Tissue Doppler E/E' on index admission for CHF is associated with 30 day readmissions. E/E' represents a simple, non-invasive tool for identifying CHF patients at highest risk for 30 day readmission.

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