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Contribution of caval index and ejection fraction estimated by e-point septal separation measured by emergency physicians in the clinical diagnosis of acute heart failure

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Abstract:

OBJECTIVES: Although the reliability of e-point septal separation (EPSS) and caval index (CI) is proven in the diagnosis of acute heart failure (AHF), how much they contribute to the initial clinical impression is unclear. This study aimed to determine the diagnostic contribution of EPSS and CI to the initial clinical impression of AHF.

METHODS: This is a prospective observational study conducted in an academic emergency department (ED). The patients admitted to the ED with acute undifferentiated dyspnea were included. Primary diagnosis was made after an initial clinical evaluation, and a secondary diagnosis was made after EPSS and CI measurements. Independent cardiologists made the final diagnosis. The primary outcome was the diagnostic contribution of EPSS and CI to the primary diagnosis.

RESULTS: A total of 182 patients were included in the study. The primary diagnosis was found with a sensitivity of 0.55 and specificity of 0.84 and the secondary diagnosis was determined with a sensitivity of 0.78 and specificity of 0.83 in predicting the final diagnosis. The agreement coefficient between the primary and final diagnosis was 0.44 and between the secondary diagnosis and the final diagnosis was 0.61. When the primary diagnosis was coherent with secondary diagnosis, sensitivity and specificity were found to be 0.74 and 0.90, respectively.

CONCLUSION: Although a detailed history and physical examination are the essential factors in shaping clinical perception, CI and EPSS combined significantly contribute to the initial clinical impression.

Keywords:

Echocardiography, emergency department, heart failure, ventricular ejection fractions (MesH Database)

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Introduction

Early detection and timely management of acute heart failure (AHF) have crucial importance in the emergency department (ED).[1,2] However, differentiating the noncardiac reasons for acute dyspnea can be challenging in patients who have cardiac failure with additional pulmonary

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Box-ED

What is already known on the study topic?

Caval index (CI) and ejection fraction estimated by e-point septal separation (EPSS) are frequently used diagnostic tools as a part of focused cardiac ultrasound examination in the ED.

What is the conflict on the issue? Has it importance for readers?

Although CI and EPSS are reliable methods in diagnosing acute heart failure, their contribution to the initial clinical impression is unclear.

How is this study structured?

This was a single-center, prospective, observational study conducted with 182 patients.

What does this study tell us?

In addition to initial clinical evaluation, the utility of EF estimated by EPSS and CI in patients with acute undifferentiated dyspnea may provide a better diagnostic approach in the ED.

comorbidities.[3] Elaborated workup, including laboratory and radiological studies, electrocardiography (ECG), and echocardiogram are commonly used to diagnose AHF in the ED.[4]

Focused cardiac ultrasound (FoCUS) is a fast and reliable point-of-care ultrasonography protocol,[5] which is recommended to use for time-sensitive assessment of symptomatic patients in the ED.[6] FoCUS can provide a quick estimation about general cardiac activity, cardiac contractibility, central venous pressure and volume status, pericardial effusion or tamponade, and cardiac standstill. In addition, ejection fraction (EF) can be determined by evaluating the left ventricle pump function; also, volume overload and right-sided cardiac pressure can be estimated by the caval index (CI).[7,8]

E-point septal separation (EPSS) is an easier and faster method to estimate left ventricle functions comparing to other conventional methods.[9,10] It can be measured performing transthoracic echocardiography using parasternal long axis.[11] The narrowest distance between the anterior leaflet of mitral valve and interventricular septum during the early diastole is measured using M-mode.[9-11] The shortest distance between the anterior leaflet of mitral valve and intraventricular septum during the early diastole is defined as EPSS. An EPSS distance >7 mm was accepted as a sign of severe LV dysfunction.[11,12]

This study aimed to determine the diagnostic contribution of FoCUS assessing EF estimated by EPSS and CI to the initial clinical diagnosis of AHF in the ED.

Methods

Study design and setting

This prospective observational study was conducted in an academic ED. The data were collected between December 2015 and December 2016.

Institutional review board approval was obtained from the Akdeniz University Board of Ethics on Non-invasive Clinical Human Studies Ethics Committee (Date:25.11.2015, Number: 343).

Selection of participants

All patients older than 18 years who were admitted to the ED with acute undifferentiated dyspnea were evaluated to participate in the study. The patients who were pregnant, had a chest trauma in the last 3 weeks, had an ST elevation acute coronary syndrome, an apparent reason for dyspnea such as acute exacerbation of obstructive lung diseases, pneumothorax, recurrent admission due to dyspnea in the last 4 weeks, the patients who transferred to ED with a confirmed diagnosis of AHF, known mitral stenosis, aortic regurgitation, and pulmonary hypertension at the admission excluded from the study. Enrollment was performed consecutively, 7 days a week, and 24 h a day. Institutional review board approval was obtained for the study, and the patients gave written informed consent before they were enrolled in the study.

Sample size estimation

The study sample size was calculated using G-Power for Mac OS X (V.3.1.9.2; Universitat Düsseldorf, Germany). In the literature, the admission rate of the patients who visit ED with undifferentiated dyspnea was 31%.[13] For detecting 10% of clinically significant difference, the estimated sample size of 157, assuming a confidence interval of 95%, type 1 error of 0.05, and power of 80%.

Methods and measurements

Ten emergency physicians who completed at least 2 years of EM residency training and attended 2 days of Emergency Medicine Association of Turkey Basic Ultrasound Course participated in 2 h of didactic and 2 h of practical training about the study and FoCUS, including EF measurement using mitral valve EPSS and volume status assessment with CI.

In the first phase of the study, patient demographics, history, physical examination, ECG, and chest X-ray findings were recorded on the first data collection form by the treating physicians who were EM attendings or senior residents. In the second phase, FoCUS was performed by an investigator blinded to the first phase of the study immediately after the first phase and before the initiation of treatment. The EF and CI were recorded on a second data collection form by the blinded investigator

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and the data presented to the treating physician. At the end of each phase (1: initial clinical evaluation and 2: measurement of EF and CI), treating physician marked one of the following clinical decisions on data collection forms as "not an AHF," "an AHF," or "not sure."

Diagnoses that were made based on the first phase of the study were defined as the "primary" diagnosis. The diagnoses that were made after the second phase of the study were defined as the "secondary" diagnosis. Sonographic data were used to make the secondary diagnosis. After performing EPSS and CI measurements in the second phase of the study, patients were managed at the discretion of the treating physician. In addition to EF measurements performed by an independent cardiologist, other diagnostic tests were utilized in differentiating final diagnosis, including BNP, d-dimer, or chest CT. All patients were consulted with a cardiology and EM attending physician. EF measured by an independent cardiologist on the day of the ED admission and final diagnosis was recorded 15 days after the ED admission from the electronic hospital records. The final diagnoses were made by the attending cardiologists who were responsible for the patients who admitted to the cardiac care unit or EPs for the patients who discharged from the ED by the day of ED admission and the other responsible specialists for those admitted to hospital wards.

A Mindray DC-8 ultrasound unit with a 1.3–4.6 MHz phrased array transducer (Shenzhen Mindray Bio-Medical Electronics, NJ, USA) was used to calculate EF using the EPSS index. Distance between the anterior tip of the mitral valve to the interventricular septum was measured in a supine position in M-mode during the mid-diastolic cycle from either parasternal long or short axis where the view was most apparent [Figure 1]. An EPSS of >7 mm was defined as "reduced LVEF."[12]

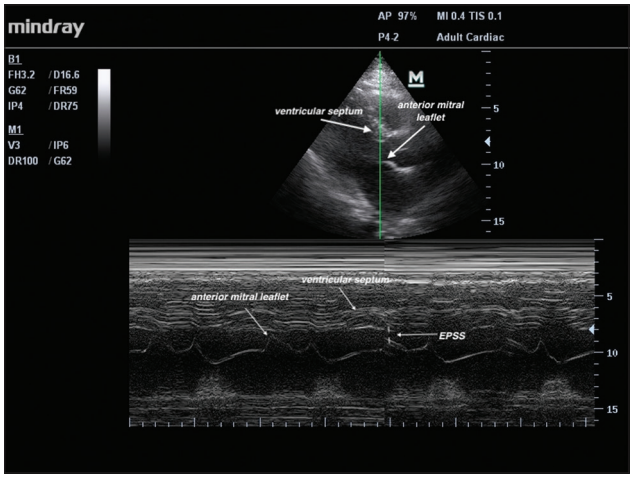

Figure 1: E-point septal separation measurement

CI was calculated with measuring the diameter of inferior vena cava (IVC) at its maximum diameter in expiration (e) and its minimal diameter in inspiration (i) by M-mode in the subxiphoid area proximal to the confluence of the hepatic vein or 2 cm distal to the right atrium entrance using the formula as (IVCe – IVCi)/IVCe × 100%. All ultrasonography views are recorded to evaluate interrater reliability by an independent, experienced cardiac ultrasonographer.

Outcomes

The primary outcome of this study was the diagnostic contribution proportion of EF measured by EPSS and CI, measured by emergency physicians to the initial clinical impression of AHF in the ED.

Data analysis

For descriptive data, categorical variables were described with proportions; continuous data were described with mean and SD or median and interquartile range. Sensitivity, specificity, negative, and positive likelihood ratios (LR– and LR+, respectively) were calculated. Paired test, Student's *t*, and Mann–Whitney *U*-test were used to compare continuous variables; Chi-square and Fisher's exact test were used to compare the categorical variables. Cohen's kappa test was used to evaluate the interrater agreement of ultrasound operators. MedCalc statistical software (version 10.1.6.0; MedCalc Software, Ostend, Belgium) was used for all statistical analyses, and $P < 0.05$ was considered statistically significant. Decimals in the results were rounded to provide better read.

Results

A total of 213 patients were evaluated for the study. After excluding 31 patients, 182 patients were included in the study [Figure 2]. The demographic features of

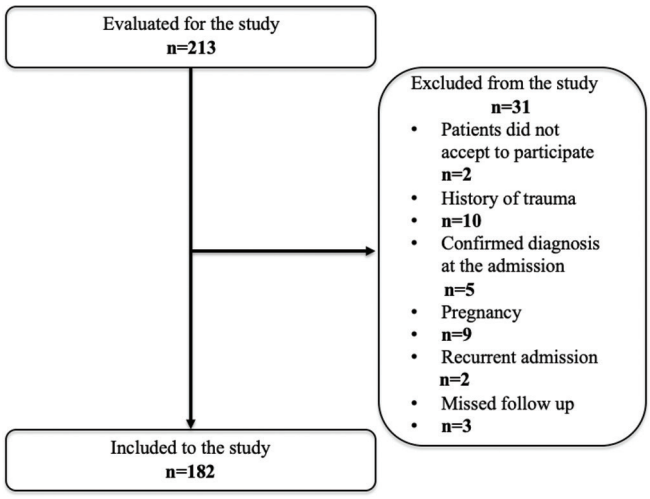

Figure 2: Patient flowchart

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Table 1: Demographic features of the patients

Age, mean±SD	69.4±12
Sex (male/female), *n*	91/91
Symptoms, *n* (%)	
Dyspnea	182 (100)
Orthopnea	149 (82)
PND	117 (64)
Comorbidities, *n* (%)	
Hypertension	99 (54)
Coronary artery disease	59 (32)
Diabetes mellitus	81 (44.5)
Congestive heart failure	91 (50)
Dysrhythmia	104 (57)
Valvular heart disease	16 (9)
COPD	68 (37)
Vital signs, mean±SD	
SBP, mmHg	144±30
DBP, mmHg	81±17
Heart rate, bpm	99±22.5
SaO_2, %	91±7
Respiratory rate, rpm	30±7
Diagnosis, *n* (%)	
AHF	85 (47)
Non-AHF	97 (53)
Pneumonia	29 (16)
COPD*	25 (14)
Malignancy	18 (10)
Psychogenic disorder	8 (4)
Kidney failure	7 (3)
Pulmonary embolism	4 (2)
Others	6 (3)
Transition of care, *n* (%)	
Hospitalization	81 (44.5)
AHF	45 (24)
Non-AHF	36 (19)
Discharged	101 (55.5)
AHF	40 (21)
Non-AHF	61 (33.5)

*Newly onset COPD or nonsevere COPD exacerbation. SD=Standard deviation, PND=Paroxysmal nocturnal dyspnea, COPD=Chronic obstructive pulmonary disease, SBP=Systolic blood pressure, DBP=Diastolic blood pressure, bpm=Beats per minute, SaO_2=Oxygen saturation, rpm=Respiration per minute, AHF=Acute heart failure

the patients are shown in Table 1. Interrater agreement between EPs and cardiologists in classifying the EF status was found to be a kappa coefficient of 0.84.

Primary diagnosis based on initial clinical evaluation was found to be with a sensitivity of 0.55 and specificity of 0.84 (LR+ 3.74; LR− 0.49) in predicting final diagnosis. The secondary diagnosis was made after the EF, and CI measurements were found to be with a sensitivity of 0.78 and specificity of 0.83 in predicting the final diagnosis (LR+ 4.70; LR− 0.27). The agreement coefficient between the primary diagnosis and final diagnosis was 0.44 and between the secondary diagnosis and the final diagnosis was 0.61. In the cases when the primary diagnosis was coherent with secondary diagnosis, sensitivity and specificity were found to be 0.74 and 0.90, respectively (LR+ 7.53; LR− 0.29).

The sensitivity and specificity of the EPSS measured by EPs in predicting AHF were found to be 0.81 and 0.78, respectively (LR+ 3.69; LR− 0.24). CI could not be calculated in 33 out of 182 patients (clear images could not be elicited because of the obesity, anatomic difficulties, or patient intolerance), and the data of 149 patients were analyzed. Sensitivity, specificity, LR+, and LR− of CI and LVEF measured by EPs are shown in Table 2.

Discussion

The utility of FoCUS in the ED was first recommended in 2010 and has become a widely used diagnostic method for EPs in the management of acute cardiac disorders.[6] Assessments of EF and CI are two essential components of the FoCUS in evaluating acute undifferentiated dyspnea, especially in differentiating AHF.[6,14] Although diagnostic accuracy of EF and CI for AHF was validated in the previous studies,[9-12,15,16] contribution proportion of EF estimated by EPSS and CI to the initial clinical impression of AHF was reported with larger data in this study.

Our results confirmed that the utilization of EF estimated by EPSS and CI in addition to primary diagnosis, based on the initial clinical evaluation (history, physical examination, ECG, and chest X-ray), could provide a better diagnostic value. The agreement coefficient between the primary diagnosis and definitive diagnosis was 0.44 and between the secondary diagnosis and the definitive diagnosis was 0.61. This result suggested that the secondary diagnosis of EPs is more accurate than the primary diagnosis. Therefore, as the predictive values also suggested, the coefficient agreement also showed that the secondary diagnosis is more applicable than the primary diagnosis in the ED. Anderson *et al*. reported a sensitivity of 0.48 and a specificity of 0.98 using EF and CI in the diagnosis of AHF.[17] Gallard *et al*. utilized cardiopulmonary ultrasonography in undifferentiated dyspnea using EF, tissue, mitral Doppler E/A ratio, left ventricle filling pressure, and thoracic ultrasonography. It is reported that a diagnostic accuracy of 0.90, a sensitivity of 0.80, and a specificity of 0.93 of the cardiopulmonary ultrasonography in the diagnosis of AHF.[16] Our results also showed similar predictive values to the previous studies with a sensitivity of 0.78 and a specificity of 0.83 in predicting the final diagnosis. In light of these data, it is suggested that the EF estimated by EPSS and CI combined provides a significant contribution to the definitive diagnosis of AHF in addition to initial clinical diagnosis of the patients with undifferentiated dyspnea.

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Table 2: Diagnostic characteristics of the findings in detecting acute heart failure

	Cut-off point	Sensitivity (95% CI)	Specificity (95% CI)	NLR (95%CI)	PLR (95%CI)
Primary diagnosis	+/–	55 (48-70)	84 (75-90)	3.74 (2.29-5.87)	0.49 (0.36-0.63)
Cough	+/–	40 (27-49)	44 (33-52)	1.35 (1.1-1.9)	7.1 (4.7-9.0)
Orthopnea	+/–	94 (86-98)	28 (20-38)	0.2 (0.1-0.5)	1.32 (1.15-1.5)
PND	+/–	72 (61-82)	43 (33-52)	0.65 (0.43-0.9)	1.28 (1.02-1.55)
CXR	+/–	67 (58-75)	90 (82-94)	0.36 (0.23-0.48)	7.2 (5.1-8.4)
LBBB	+/–	18 (11-29)	88 (82-94)	0.91 (0.8-1.03)	1.76 (0.85-3.61)
RBBB	+/–	4 (1.4-12)	91 (84-96)	1.05 (0.96-1.12)	0.4 (0.18-1.81)
Dysrhythmia	+/–	41 (33-55)	77 (68-85)	0.76 (0.59-0.91)	1.81 (1.23-2.91)
Rales	+/–	95 (88-99)	27 (20-38)	0.17 (0.07-0.48)	1.31 (1.16-1.51)
Wheezing	+/–	14 (6-22)	64 (55-74)	1.32 (1.14-1.57)	0.4 (0.19-0.68)
Pretibial edema	+/–	74 (64-84)	51 (42-62)	0.5 (0.32-0.73)	1.5 (1.23-1.98)
Secondary diagnosis	+/–	78 (68-87)	83 (77-92)	0.27 (0.16-0.38)	4.7 (3.37-8.84)
EPSS	7 mm	81 (71-89)	78 (66-84)	0.24 (0.16-0.4)	3.69 (2.33-4.77)
CI	32.5%	81 (70-87)	32 (24-46)	0.42 (0.31-0.52)	1.19 (0.84-1.31)
VCe	19.6 mm	74 (62-81)	35 (22-49)	0.73 (0.61-0.84)	1.13 (0.79-1.34)
VCi	13.6 mm	74 (61-83)	59 (44-76)	0.71 (0.59-0.83)	1.16 (0.86-1.39)

PND=Paroxysmal nocturnal dyspnea, CXR=Chest X-ray, LBBB=Left bundle branch block, RBBB=Right bundle branch block, EPSS=E-point septal separation, CI=Caval index, VCe=Vena cava inferior expirium diameter, VCi=Vena cava inferior inspirium diameter, NLR=Negative likelihood ratio, PLR=Positive likelihood ratio

In this study, the diagnostic performance of EF using the EPSS method measured by EPs was similar to the previously reported results.[10,12,15] Furthermore, similar to previous studies, a strong correlation was determined between the cardiologists and EPs in the classification of EF after a short-term FoCUS training. In previous studies, the correlation between cardiologists and EPs in classifying the EF was reported as a kappa coefficient of 0.75[12] and 0.7,[15] whereas 0.84 in this study. From this strong correlation, it can be deduced that EPs can accurately estimate EF using the EPSS method after a short course of structured training. Utility of this method by EPs would facilitate success in the acute management of undifferentiated dyspnea in the ED.

We also evaluated the diameters of IVC and CI in predicting AHF in this study. In contrast to previously reported results, our study showed no significant role of IVC diameters and CI in diagnosing AHF with a relatively larger and homogenous population. Several studies evaluated the utility of IVC diameters and CI in determining the AHF in undifferentiated dyspnea. Miller *et al*. reported a sensitivity of 0.80, a specificity of 0.81, PLR of 4.3, and NLR of 0.25 for detecting AHF in 35 out of 89 patients for a CI of <33%.[7] Anderson *et al*. reported a sensitivity of 0.52 and a specificity of 0.86 for detecting AHF in 44 out of 101 patients for a CI of <20%.[17] Yamanoğlu *et al*. reported a sensitivity of 0.84 and a specificity of 0.92 for detecting AHF for an inspiratory IVC diameter of 9 mm in 74 patients.[18] Blehar *et al*. also reported a sensitivity of 0.93 and a specificity of 0.84 for detecting AHF in 14 out of 46 patients for a CI of <15%.[19] In addition to the smaller populations of previous studies, exclusion of the clinical conditions such as tricuspid insufficiency or increased right atrium pressure which can be attributed to the isolated right heart failure, severe lung diseases, or acute renal failure which can lead to the isolated volume overload might affect the generalizability of the previous results. Excluding those clinical situations, the performance of CI and the diameters of IVC could be increased. However, the excluded clinical conditions by the previous studies were not considered as exclusion criteria in this study. This could be the main reason for the difference in the performance of CI and the diameters of IVC comparing to the previous studies.

Limitations

This study has a number of limitations. First, the treating physician did not evaluate the cardiac biomarkers, including natriuretic peptides, because these tests were not provided during the study. The utilization of cardiac markers during the second phase of the study would increase the reliability of the secondary diagnosis. Second, we were not able to visualize the IVC in 33 patients, and the data were collected from 149 (18%) patients. Although previous studies reported that IVC might not be visualized up to 15% of the population,[20] it may have affected our results. Third, while EF is generally helpful in systolic heart failure, it may misguide the EP if the patients have an AHF with preserved EF. Therefore, using the EPSS alone as a marker of heart failure might lead to miss the diagnosis of diastolic heart failure in some patients. Fourth, there were a larger proportion of patients with a history of CHF in AHF diagnosed group. Patients with a history of CHF presenting with acute dyspnea are likely to be diagnosed AHF even without the echocardiography assessment. Fifth, the cardiologist measured the EF after the initiation of the treatment. This might affect the

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correlation coefficient between the EPs and cardiologists. Sixth, final diagnosis was made by different treating physicians for the patients who admitted to the hospital. Different diagnostic strategies between the physicians might have an effect on the study results.

Conclusion

Although a detailed history and physical examination are the essential factors in shaping clinical perception, the utility of EF estimated by EPSS and CI combined significantly contributes to initial clinical diagnosis. Furthermore, the study showed that the CI measurement alone did not provide a significant benefit in the diagnosis of AHF, yet the assessment of EF using the EPSS method was a more reliable diagnostic tool comparing to CI *per se*.

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Author contribution statement
M.D and A.Y.E contributed to conception; M.D and A.Y.E contributed to design; A.Y.E contributed to supervision; M.D and A.Y.E, and E.G contributed to data collection and processing; M.D and A.Y.E., and I.U.O. contributed to analysis and interpretation; E.G., and I.U.O. contributed to literature review; E.G. and I.U.O. contributed to writing; and M.D, A.Y.E., I.U.O., and E.G. contributed to critical review.

Consent to participate
All patients consented to participate to the study. Signed consent forms available from the authors.

Conflicts of interest
None declared.

Ethical Approval
Institutional review board approval was obtained from the Akdeniz University Board of Ethics on Non-invasive Clinical Human Studies Ethics Committee (Date:25.11.2015, Number: 343).

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