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Determination of diagnostic value of inferior vena cava diameter in distinguishing cardiac causes from non-cardiac causes in patients with acute dyspnea

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General Note

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ABSTRACT

Introduction: Cardiac insufficiency is a major cause of mortality and morbidity in the world. In a patient with acute dyspnea in emergency department, physicians use various diagnostic methods such as history taking and physical examination. In physical examination findings as orthopnea, increasing jugular venous pressure (JVP), Gallop Rhythm suggests acute heart failure (AHF). The use of CXR and BNP are paraclinical methods that can support the findings, but are time and cost consuming. Bedside ultrasound is a quick and accessible method for emergency staff to detect AHF from other cause of dyspnea. The aim of this study was to determine the diagnostic value of inferior vena cava diameter (or IVC) clinically in differentiating cardiac causes from non-cardiac causes in patients with acute dyspnea. *Material and Methods:* This prospective and observational study was carried out using convenience sampling among patients referred to the Emergency Department. Patients with acute dyspnea were included in the study. After assessing the previous history of the disease, diagnostic strategies and initial treatment started for patients. For all patients, chest-x-ray (CXR) was performed and then underwent IVC ultrasound examination. The caval index was also calculated after the measurement of IVC diameter in the inhalation and exhalation. *Results:* In these study 173 patients included, 51 patients have cardiac and 122 patients have non-cardiac diagnosis. After the CXR examination, it was found that 23 patients have interstitial pulmonary edema, where a significant relationship was found between CXR and final diagnosis (P <0.001). Caval index was calculated for all patients and its sensitivity and specificity in the diagnosis of non-cardiac disease was determined. Cut-point for caval Index was 38.97. The sensitivity and specificity of this criterion in the diagnosis of cardiac disease were calculated as 92.2% and 91%, respectively. *Conclusion:* Caval index (< 38.97) is capable of showing causes of cardiac disease in patients with dyspnea.

Keyword: Dyspnea, Caval Index, IVC diameter, cardiac Disease, AHF.

1. INTRODUCTION

Dyspnea is defined as an unpleasant experience of shortness of breath that reduces the quality of life and the patient's functional capacity according to the severity of the disease [Camm, 2009]. There are different causes for the dyspnea that include a wide range of pathologic and life-threatening factors. Respiratory failure leads to tachycardia, tachypnea, stridor, and the use of accessory muscles, such as sternocleidomastoid, sternoclavicular and intercostal. It may also decrease the ability to speak normally as a result of dyspnea, agitation and lethargy due to hypoxia, and/ or the level of consciousness may be decreased in patient [Guiotto, 2010 & Blehar, 2009].

Evaluation and management of patients referred to the emergency department (ED) with a severe dyspnea complaint is a challenging issue, because it is a non-specific symptom in patients with heart failure and pulmonary problems. Therefore, emergency physicians should be able to quickly determine the therapeutic response after initial treatment of dyspnea [Hutchinson, 2017]. Acute heart failure (AHF) is one of the most common causes of mortality and morbidity worldwide. An estimated 650,000 people in the United States are referred to ED annually for AHF, that monetary burden of disease is estimated to be about $ 27.9 million [Schappert, 2008 & Hebl, 2012]. To provide care to these patients, AHF differentiation is necessary from other causes of dyspnea. Recent studies have shown that clinical evaluation through Inferior venacava (IVC) can be suitable for rapid and non-invasive measurements to determine the respiratory volume of the patient and differentiate AHF from other common causes of dyspnea [Blehar, 2009]. Today, there are various tools to diagnose the causes of dyspnea. In the studies conducted by the European Cardiovascular Society, the limitations of the current methods include electrocardiogram, chest X-ray, peptide testing, Brain natriuretic peptide (BNP), and blood tests has been evaluated. In addition, it has been revealed that doctors use different diagnostic methods, such as biographies, orthopnea, increasing jugular venous pressure (JVP), Gallop Rhythm for the purpose of finding AHF in the patient referred to the ED [Miller, 2012].

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The methods currently used to distinguish between these two cases require a great deal of time and cost, and sometimes the transfer of the patient to other parts such as radiology is imperative, which also raises the concern of the emergency medicine specialist to diagnose the disease. The current differential methods are time and cost consuming. Sometimes the transfer of the patient to other parts such as radiology is obligatory, that this also raises the concerns of the emergency medicine specialist. It must be given based on the criticality of the patient's condition and the possibility of deterioration of the respiratory condition. At present, measurement of physiological changes in IVC has been carried out in many studies for various purposes [Pastorelli, 2017 & Keijzers, 2017]. Several studies have also been conducted directly on emergency patients with acute dyspnea, suggesting that low caval index is sensitive and specific in detecting AHF [Miller, 2012 & Gaskamp, 2016].

Regarding to the above-mentioned aspects and the limited studies done in this field, we aimed to investigate the rapid diagnosis of AHF in patients with acute dyspnea using the IVC diagnostic method.

2. MATERIAL AND METHODS

This prospective and observational study was carried out using convenience sampling among patients referred to the ED of Imam Reza Hospital. After explain the study to the patients, written informed constant form has completed. This study approved by Ethical committee of Mashhad University of Medical Sciences by ethical code 6923625. Considering the sensitivity and specificity of the caval index below 33%, which is equal to 80%, the sample size was determined as 171 [Miller, 2012].

Inclusion criteria included Patients aged 50 and over and patients with acute dyspnea.

Exclusion criteria were: Patients with mechanical ventilation, trauma, patients with portal hypertension, patients with a history of abdominal surgery 14 days ago, pregnant patients, Diabetes ketoacidosis (DKA), and bowel obstruction.

After initial evaluations, a total of 175 patients were enrolled and history of any disease was recorded based on the history of the patients. Finally, a definitive diagnosis and grouping of patients in terms of cardiac disease and non-cardiac disease was performed.
Bedside ultrasound (US) of inferior vena cava (IVC) measurements was performed for all patients undergoing a Chest-X-Ray (CXR). All clinical tests and radiology were collected in the emergency room during the hospitalization. To measure the IVC during passive breathing of patient, the patient was in a supine position with 30- degree head elevation. Prior to giving intravenous fluids or diuretics US evaluation with 3.2 MHZ probe Honda sonography were done.

Measurement of Anterior–posterior diameter of IVC in exhalation (maximum diameter) and inhalation (minimum diameter) distal to hepatic vein in US subxiphoid approach determined the caval index.

All measurements were performed in 3 respiratory phases to calculate respiratory variation. After measuring IVC diameters in the inhalation and exhalation phases, the caval index rate was calculated for all patients according to the following formula:
(IVC diameters during exhalation - IVC diameters in the inhalation / IVC diameters during exhalation) × 100

Data analysis

Data were analyzed by SPSS software version 22 and chi-square test for data analysis. The significance level was considered to be less than 0.05.

3. RESULTS

In this study, a total of 175 patients with acute dyspnea were studied. Two patients were excluded due to their high weight and our inability for measuring IVC diameter in US. Of the 173 enrolled patients, 92 (53.2%) were female and 81 (46.8%) were male, and the mean age was 67.10 years. The history of disease was evaluated among patients, the results of which are listed in Table 1.

Table 1 Frequency of history of disease in patients

Percent	Number	Complication
%13.3	23	History of heart failure
%9.2	16	History of asthma or COPD
%26.6	46	History of hypertension
%10.4	18	History of diabetes
%5.8	10	History of coronary heart disease
%12.7	22	A history of renal failure
%22	31	No history of previous illness

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After the examinations and complementary tests, a final diagnosis was made for the patients. According to Table 2, COPD with 26.6% showed the highest prevalence in our study.

Table 2 Frequency of final diagnosis of patients

Percent	Number	Diagnosis final
%13.3	23	Heart disease
%9.2	16	Asthma
%26.6	46	COPD
%10.4	18	Pneumonia
%5.8	10	Pulmonary embolism
%12.7	22	Other causes (sepsis, pulmonary, psychosomatic, pneumothorax, etc.)

Overall, based on the diagnosis of dyspnea, 51 cases (29.5%) showed heart disease, followed by had non-cardiac causes (122; 70.5%). In addition, the mean systolic blood pressure in patients was determined to be 136 mm Hg. As a result of clinical examinations of the patients, 45 subjects had one or more of elevated JVP symptoms, fine rales, Edema of the lower limb, gallop or S3. Heart disease diagnosis was given to 43 patients. By these findings final diagnosis confirmed by 3 physicians include Internal Medicine, cardiac and Emergency Medicine specialists. Using chi-square test, there was a significant relationship between final examination and diagnosis (p <0.001; Table 3).

Table 3 Relationship between patient examination and final diagnosis

Examination	Diagnosis		Total
	Cardiac (Number / percent)	Non-cardiac (Number / percent)	
elevated JVP, fine rales, lower extremity edema, Gallup or S3	43 (% 95/6)	2 (4%/4)	45
Wheezes	0	17 (% 100)	17
Coarse rales	0	29 (100%)	29
Lung Sound reduction	0	25 (100%)	25
Normal lung sound	6 (% 11/1)	48 (88/9)	54
Other	2	1	3
Total	51	122	173

CXR was also evaluated in two groups of patients with a diagnosis of cardiac and non-cardiac disease. The CXR results demonstrated that 23 patients had interstitial edema or cephalization, all of whom ultimately diagnosed as cardiac disease. Chi-square showed a significant relationship between CXR and final diagnosis (p <0.001; Table 4).

Table 4 Relationship of CXR with final diagnosis

CXR	Diagnosis		Total
	Cardiac (Number / percent)	Non-cardiac (Number / percent)	
Interstitial edema or cephalization	23 (100%)	0	23
Normal	26 (25%/7)	75 (74%/3)	101
Consolidation	0	26 (100%)	26
Pleural effusion	0	21 (100%)	21
Other	2	1	3
Total	51	122	173

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In US examination of IVC, mean exhalation IVC diameter (IVCe) and inhalation IVC diameter (IVCi) were measured in cardiac and non-cardiac patients (table 5). It was found that the IVC diameter of the inhalation and exhalation was higher in cardiac patients as compared to non-cardiac patients. Furthermore, the IVC diameter in the inhalation was less than exhalation. In addition, in both the cardiac and non-cardiac patients, the mean value of the caval index was also measured. The subxiphoid view and the IVC cross-sectional view are shown in Figure 1.

Table 5 The mean IVC diameters in the inhalation and exhalation based on the final diagnosis

	Diagnosis	
Mean	Cardiac	Non-cardiac
IVCe (cm)	2.15±0.227	1.58±0.222
IVCi (cm)	1.63±0.177	0.74±0.13
Caval index	23.66±10.34	52.41±10.273

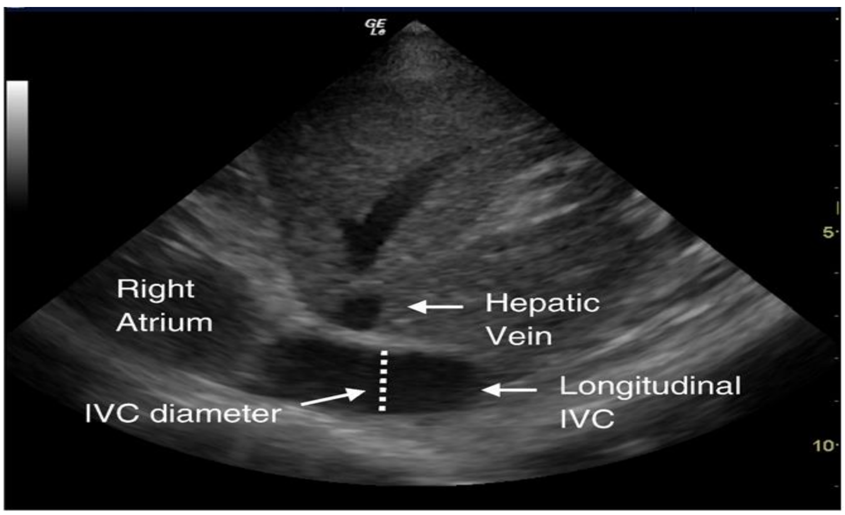

Figure 1 subxiphoid view and the IVC cross-sectional view

The caval Index was calculated for all patients according to the following formula and its sensitivity and specificity were determined in the diagnosis of cardiac and non-cardiac disease (Fig. 2). Cut-point was also found to be 38.97 for the caval index, which the sensitivity and specificity of this criterion in the diagnosis of heart disease were calculated as 92.2% and 91.0%, respectively (Table 6).

(IVC diameters during exhalation - IVC diameters in the inhalation / IVC diameters during exhalation) × 100

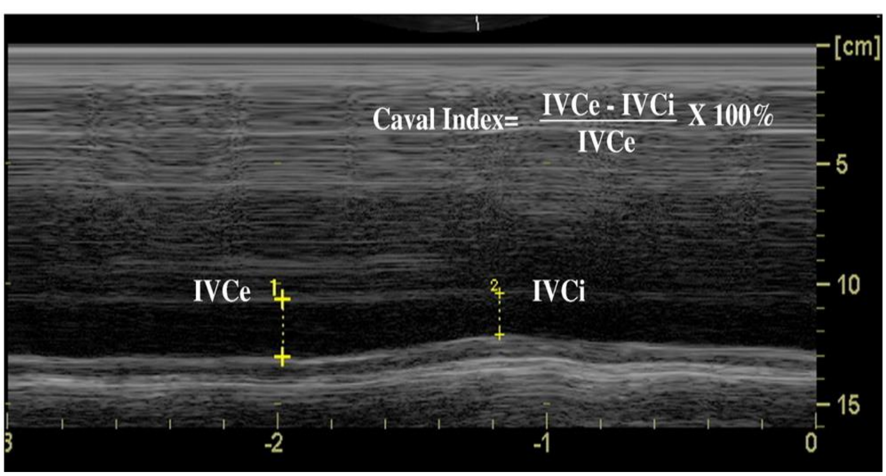

Figure 2 Caval Index

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Table 6 Sensitivity and specificity for the caval index

95% CI attribute	Sensitivity 95% CI	caval index
100%	14%	11%>
100%	22%	15%>
% 91	92%	38%/9>
55%	98%	51%>

The ROC curve for the caval index is plotted as shown in Fig. 3, and the area under the curve was determined as 96.2%, followed by the lower limit (93%) and the upper limit (99%).

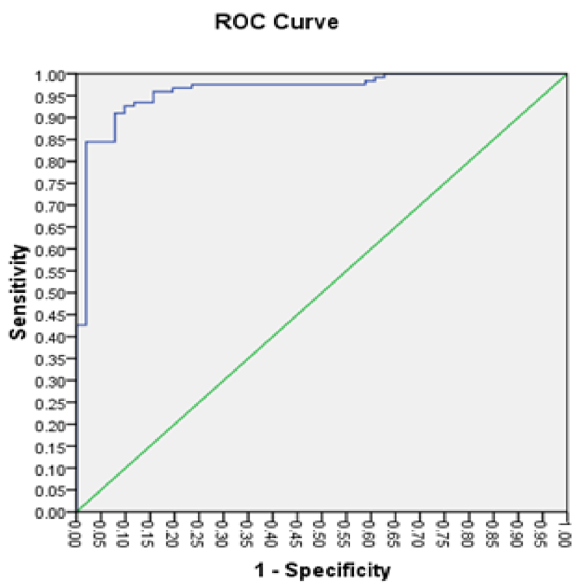

Figure 3 Sensitivity and specificity for caval index

Based on the Table 7, the relationship between caval index and the causes of the disease was assessed which 91% of patients without cardiac disease had a caval index below 38.98%, while 92.2% of patients with heart disease showed a caval index greater than 38.97 (figure 3).

Table 7 Association of caval index with diagnosis of disease

Caval	Therapeutic intervention				Total
	Cardiac		Non-cardiac		
	Number	Percent	Number	Percent	
Lower 38.97	4	7/8	111	91/0	**115**
Upper 38.97	47	92/2	11	9/0	**58**
Total	51	100	122	100	**173**

4. DISCUSSION

One of the important challenges for evaluation and management of patients referred to the ED for dyspnea, due to the non-specific symptoms, is the differentiation of dyspnea in patients with heart failure and other diseases. This requires the identification of the cause of dyspnea for the correct treatment of patients due to the lack of accurate diagnosis or misdiagnosis. Among the various diagnosis of dyspnea, Acute heart failure (AHF) is one of the most common and important causes of dyspnea that requires quick identification and timely treatment [Brennan, 2007 & Mueller-Lenke, 2006]. Regarding to the lack of sufficient evidence, this study was aimed to differentiate cardiac and non-cardiac causes among patients with acute dyspnea.

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Based on the diagnosis, the patients were divided into two groups of patients who were cardiac and non-cardiac causes of dyspnea. Among all patients, 29.5% showed cardiac disease. In a study by Miller et al at the Henry Ford Hospital in the United States, out of 89 examined patients, there were 35 patients with heart failure and 54 with non-cardiac failure [Miller, 2012], which was similar to our study because the number of heart disease was found to be lower than non-cardiac disease. In addition, our findings revealed that initial examination of patients was helpful in early diagnosis and initiation of treatment of patients. Forty-five subjects had one or more of elevated JVP symptoms, fine rales, Edema of the lower limb, gallop or S3.

In a similar study, Miller et al. showed a sensitivity and specificity of 13% and 99% for third heart sound (S3) in diagnosis of cardiac disease. Sensitivity and specificity of the Jugular vein distension were 39% and 92% in the diagnosis of heart disease. Additionally, the sensitivity and specificity of the leg edema in the diagnosis of heart disease were 50% and 78% [Miller, 2012].

In this study, CXR, IVC and caval index were measured in cardiac and non-cardiac patients for diagnosis. CXR and BNP are valuable diagnostic measures used to confirm diagnosis or rejection of the disease. In our study, CXR was taken from all patients, which was performed as portable in unstable patients. Twenty-two patients in this study had interstitial edema or cephalization in the CXR, which eventually detected heart disease for all of them. In a study by Miller and colleagues, sensitivity and specificity were reported as 41% and 96% for CXR [Miller, 2012]. In another study, Mueller et al. used chest X-ray in order to diagnose the cause of dyspnea in patients with heart disease, and 69% of patients revealed accurate findings of radiography [Mueller-Lenke, 2006].

In addition, Knudsen et al. also showed that alveolar edema, cephalization, and interstitial edema had more than 90% specificity for the diagnosis of heart disease, but patients showed a sensitivity of 50% [Knudsen, 2004]. Measuring physiological changes of IVC is used in many studies to find out the vascular volume in patient with dyspnea. Miller et al., indicated that mean IVCe in patients with heart disease was 2.13 and non-cardiac disease patients was determined as 1.63 and mean IVCi in patients with or without heart disease was 1.70 and 0.72, respectively, where similar findings was found as compared with our results, the diameter of IVC in the inhalation was less than exhalation, as well as the IVC of the inhalation and exhalation was more common in patients with heart failure [Miller, 2012].

Anderson et al also compared the effects of cardiac, inferior vena cava, and lung ultrasonography on the diagnosis of heart failure in patients with severe dyspneic and reported that the sensitivity of IVCCI was below 20%, 52%, while specificity was determined as 86 % [Anderson, 2013]. It has been shown that intrathoracic pressure decreases during inhalation in patients with dyspnea, which can increase the amount of venous return and IVC collapse.

Based on the research, the diameter of IVC during the inhalation phase is less than the expiratory phase. It has also been reported that in patients with hypovolemia, the amount of respiratory traction can lead to a higher caval index and in patients with hyperlipidemia, IVC enlargement leads to a reduction in elasticity and ultimately a change in venous return during inhalation [Guiotto, 2010 & Anderson, 2013].

After measuring IVC diameters, the caval index was evaluated in patients with inhalation and exhalation. In studies, caval Index measurements have been used to assess the response to fluid therapy for shock patients in the critical care unit [Valk,2014]. It has also been revealed in dialysis patients that the low index is associated with hyperemia and can be used as a guide for the duration of ultrafiltration [Muniz Pazeli, 2014]. In our study, caval index < 38.9% was found as a cut-point, with a sensitivity and specificity of 92% and 91% in the diagnosis of heart disease. Although caval index < 15% had a specificity of 100%, but showed a lower sensitivity (22%) for diagnose.

Also, caval Index below 51% revealed sensitivity of 98% and specificity of 55%. Miller and colleagues reported that caval index below 15% has sensitivity and specificity of 96% and 37%. They identified caval index below 33% had sensitivity and specificity of 80% and 81% attribute as a cut-point [Miller, 2012]. In our study, Caval Index >38.9% can able to detect 47 patients from 51 patients with heart disease. Among patients without heart disease, 111 out of 123 patients had caval index below 38.9% and only 11 patients exhibited higher index of 38.8%. According to studies, in patients with hypovolemia, respirophasic elasticity is altered, resulting in increased caval index. Among hypervolemic patients, dilated IVC was observed, which changes slightly during the inhalation.

In addition, the right cardiac tamponade similarly reduces the IVC elasticity and reduces the caval index [Kupper, 2016]. Studies on patients with heart failure reported IVC measurements in the prediction of high cardiac filling pressure, where caval index < 40%, 50% associated with pressure of right atrial cavity. One of the studies in the ED found that caval index < 15% in the patient with dyspnea had a specificity of 92% and is specific for hypervolemia and AHF sensitive (84%) [Miller, 2012].

Overall, our study found that caval index of 38.97 is capable of revealing a high probability of heart disease in patients with dyspnea. That patient's treatment can begin with high speed and precision. This not only benefits the patient; it also detects the

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dyspnea in the patient quickly and therefore helps in managing the patient in ED. However, this study is a new horizon for treating patients with acute dyspnea; nevertheless, more studies are needed based on the caval index and other diagnostic tests in the ED. Our study has some limitations; one of them is operator dependency of sonography. Another is non cooperative patients in acute phase of dyspnea.

5. CONCLUSION

Measuring the diameter of IVC and caval index can help to distinguish cardiac and non-cardiac causes of acute dyspnea and it help physicians to treat patients rapidly in ED. Caval index (< 38.97) shows cardiac cause of dyspnea and it seems to be a quick and cost-effective method for treating cardiac disease in a patient with dyspnea.

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Conflict of interest

The authors declare that there is no conflicts' of interest regarding the publication of this manuscript.

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