UTILITY OF DYSPNEA DISCRIMINATION INDEX AND ULTRASONOGRAPHY IN DISCRIMINATING BETWEEN A CARDIAC AND PULMONARY CAUSE FOR DYSPNEA IN THE EMERGENCY DEPARTMENT

A dissertation submitted in partial fulfillment of the rules and regulations for MD (General Medicine) Branch 1 examination of the Tamil Nadu Dr.M.G.R Medical University, Chennai, to be held in 2015

DECLARATION

This is to declare that this dissertation titled "Utility of dyspnea discrimination index and ultrasonography in discriminating between a cardiac and pulmonary cause for dyspnea in the emergency department" is my original work done in partial fulfillment of rules and regulations for MD (General Medicine) Branch 1 examination of the Tamil Nadu Dr.M.G.R Medical University, Chennai to be held in 2015.

CANDIDATE

Gina Maryann Chandy

Post graduate Registrar

General Medicine

Christian Medical College

Vellore

CERTIFICATE

This is to certify that the dissertation entitled "Utility of dyspnea discrimination index and ultrasonography in discriminating between a cardiac and pulmonary cause for dyspnea in the emergency department" is a bonafide work done by

Dr.Gina Maryann Chandy

towards the partial fulfillment of rules and regulations for MD (General Medicine) Branch 1 degree examination of the Tamil Nadu Dr.M.G.R Medical University, to be conducted in 2015.

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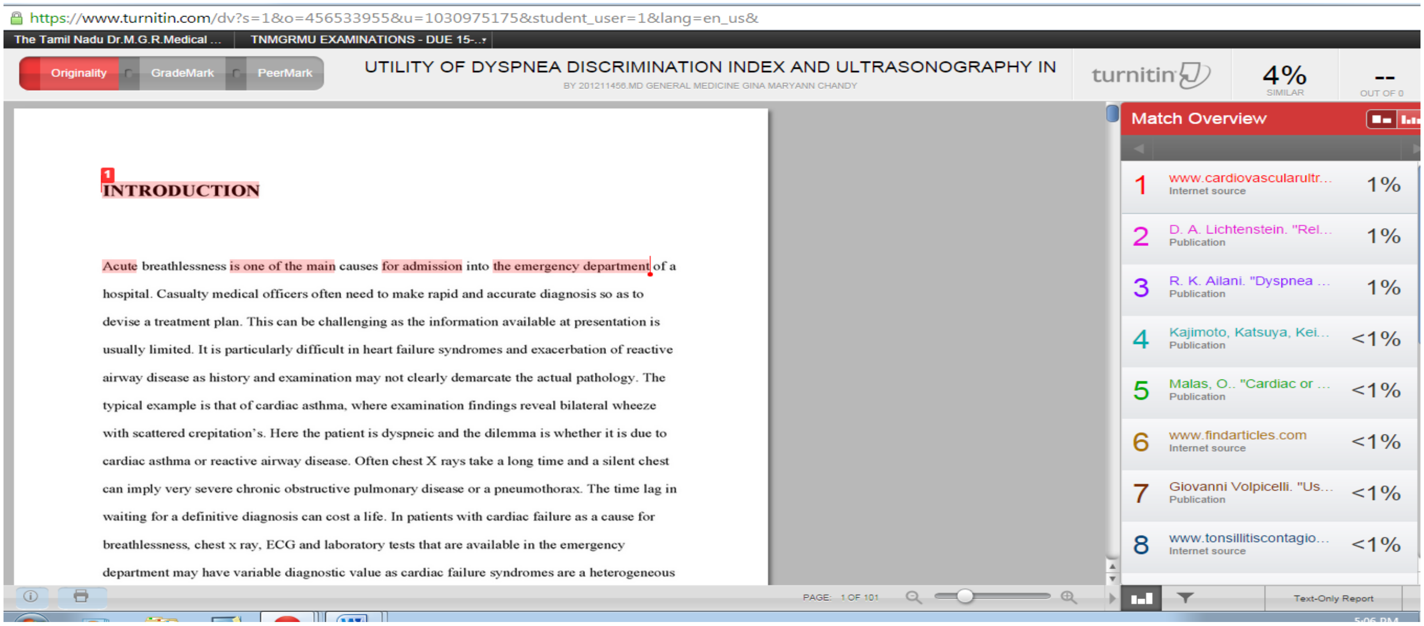
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INTRODUCTION
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devise a treatment plan. This can be challenging as the information available at presentation is
usually limited. It is particularly difficult in heart failure syndromes and exacerbation of reactive
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can imply very severe chronic obstructive pulmonary disease or a pneumothorax. The time lag in
waiting for a definitive diagnosis can cost a life. In patients with cardiac failure as a cause for
breathlessness, chest x ray, ECG and laboratory tests that are available in the emergency
department may have variable diagnostic value as cardiac failure syndromes are a heterogeneous
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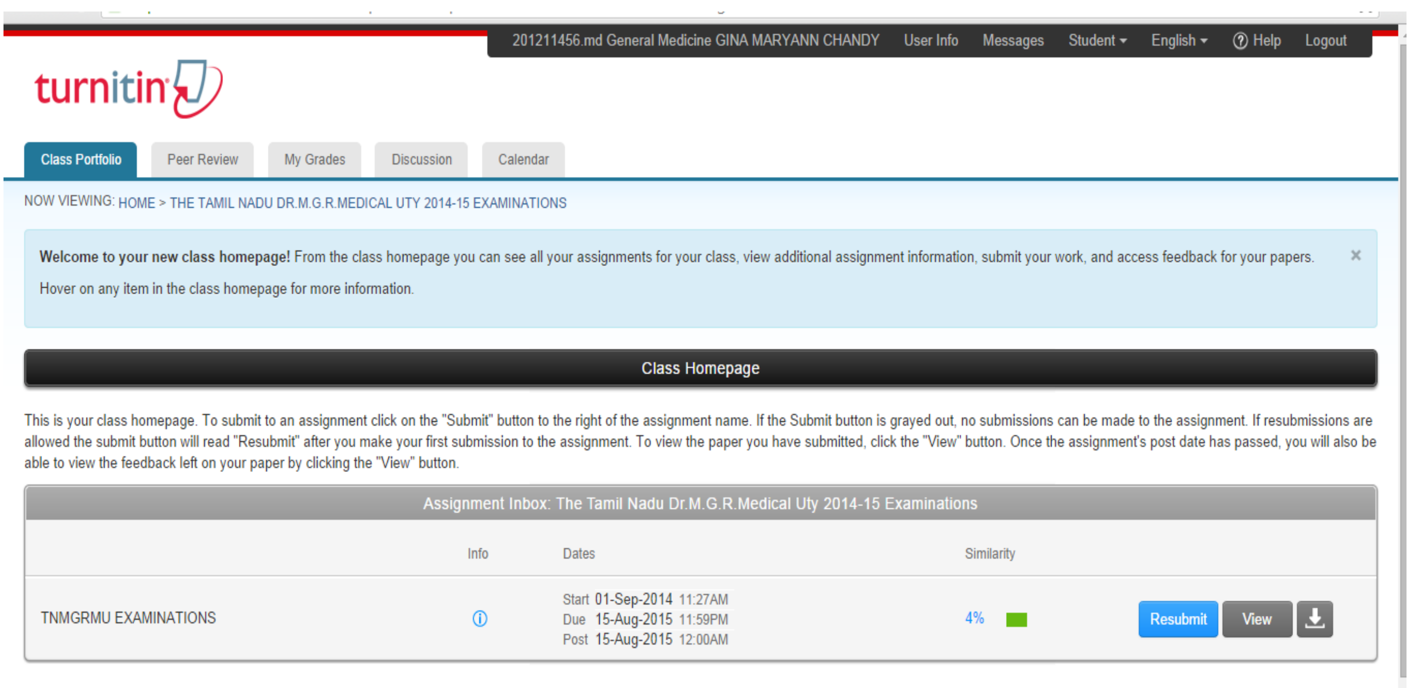
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Sub: **FLUID Research grant project:**
Utility of the dyspnoea discrimination index, NTproBNP and ultrasonography in discriminating between a cardiac and pulmonary cause for dyspnoea in the emergency department.
Dr. Gina Chandy, Medicine unit III, Dr. Sowmya Sathyendra, Dr KP Abhilash, Dr Manjeera Jagannati, Dr Nathaniel, Medicine, Dr Ashwin Oliver, Pulmonary Medicine, Dr JV Peter, Dr Kishore Pichamuthu, Critical Care, Dr Moses Kirubakaran, Emergency Medicine.

Ref: IRB Min. No. 8248 [OBSERVE] dated 19.03.2013

Dear Dr. Gina Chandy,

I enclose the following documents:-

1. Institutional Review Board approval 2. Agreement

Could you please sign the agreement and send it to Dr. Nihal Thomas, Addl. Vice Principal (Research), so that the grant money can be released.

With best wishes,

Dr. Nihal Thomas
Secretary (Ethics Committee)
Institutional Review Board

Dr Nihal Thomas
MBBS MD MNAMS DNB (Endo) FRACP(Endo) FRCP(Edin)
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Dear Dr. Gina Chandy,

The Institutional Review Board (Blue, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project entitled "Utility of the dyspnoea discrimination index, NTproBNP and ultrasonography in discriminating between a cardiac and pulmonary cause for dyspnoea in the emergency department." on March 19, 2013.

The Committees reviewed the following documents:

1. Format of IRB Application
2. Proforma
3. Informed Consent Form and Information Sheet (English and Tamil)
4. Cvs of Drs. Gina Chandy, Sowmya Sathyendra, KP Abhilash, Manjeera Jagannati, Nathaniel, Ashwin Oliver, JV Peter, Kishore Pichamuthu, Moses Kirubakaran.
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The following Institutional Review Board (Research & Ethics Committee) members were present at the meeting held on March 19, 2013 in the CREST/SACN Conference Room, Christian Medical College, Bagayam, Vellore 632002.

Name	**Qualification**	**Designation**	**Other Affiliations**
Dr. Susanne Abraham	MBBS, MD	Professor, Dermatology, Venereology & Leprosy, CMC.	Internal, Clinician
Dr. Benjamin Perakath	MBBS, MS, FRCS	Professor, Surgery (Colorectal), CMC.	Internal, Clinician
Dr. Ranjith K Moorthy	MBBS M Ch	Professor, Neurological Sciences, CMC	Internal, Clinician
Dr. P. Prasanna Samuel	B Sc, M.Sc, PhD	Professor Dept. of Biostatistics, CMC	Internal, Statistician
Dr. T.Balamugesh	MBBS, MD(Int Med), DM, FCCP (USA)	Professor, Dept. of Pulmonary Medicine, CMC.	Internal, Clinician
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We approve the project to be conducted as presented.

The Institutional Ethics Committee expects to be informed about the progress of the project, any **adverse events** occurring in the course of the project, any **amendments in the protocol and the patient information / informed consent**. On completion of the study you are expected to submit a copy of the **final report**. Respective forms can be downloaded from the following link: http://172.16.11.136/Research/IRB_Polices.html in the CMC Intranet and in the CMC website link address: http://www.cmch-vellore.edu/static/research/Index.html.

A sum of Rs.2, 200/- (Rupees Two Thousand Two Hundred only) will be granted for 6 months.

Yours sincerely

Dr. Nihal Thomas
Secretary (Ethics Committee)
Institutional Review Board

Dr Nihal Thomas
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Initially I would like to thank God almighty for His grace that has kept me safe thus far.

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I would like to thank Dr.Kishore Pichamuthu, who trained me prior to doing the ultrasounds.

I also would like to thank all the casualty medical officers who called me as soon as a breathless patient was admitted and cooperated willingly as I did my study.

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I would like to express my gratitude towards the Department of Medicine that has given us the opportunity to learn and do our own thesis. Especially for the interest they all as a unit take in the making our work perfect and productive. I would like to thank the faculty who has taken time to teach us epidemiology and statistics.

I would like to thank my husband Dr.Shawn Thomas, parents and brother who were a constant support through this period. I would also like to thank Dr.Ashwin and Dr.Deepti Bal for all the advice and help.

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INTRODUCTION

Acute breathlessness is one of the main causes for admission into the emergency department of a hospital. Casualty medical officers often need to make rapid and accurate diagnosis so as to devise a treatment plan. This can be challenging as the information available at presentation is usually limited. It is particularly difficult in heart failure syndromes and exacerbation of reactive airway disease as history and examination may not clearly demarcate the actual pathology. The typical example is that of cardiac asthma, where examination findings reveal bilateral wheeze with scattered crepitation’s. Here the patient is dyspneic and the dilemma is whether it is due to cardiac asthma or reactive airway disease. Often chest X rays take a long time and a silent chest can imply very severe chronic obstructive pulmonary disease or a pneumothorax. The time lag in waiting for a definitive diagnosis can cost a life. In patients with cardiac failure as a cause for breathlessness, chest x ray, ECG and laboratory tests that are available in the emergency department may have variable diagnostic value as cardiac failure syndromes are a heterogeneous set of clinical syndromes.

Typically diagnosis is made with history and clinical examination is such cases but studies have proven that this yields very poor sensitivity with good specificity. To improve this, there have been many bed side maneuvers and tests postulated and studied. Bedside tests that deliver rapid and reliable results are a cornerstone of diagnostics in the emergency set up.

A new combination of bedside tools

After detailed research about the useful tools in discriminating the cause for breathlessness, we decided to combine two techniques to assess cause. The basic principles being that the test should not be cumbersome and sensitivity and specificity should both be adequately good.

The two tests include the dyspnea discrimination index which consists of the product of peak expiratory flow rate and partial pressure of oxygen divided by 1000 and a multifactorial ultrasound screening tool. The index is easy to measure and there are minimal costs associated with acquiring a peak flow meter. The lung screening method chosen was the LCI: lung cardiac inferior vena cava screening as it is comprehensive, simple and requires only a simple hand held ultrasound machine. This tool is supposed to be a three minute assessment test hence helping in rapid diagnosis.

Neither the index nor the ultrasound screening test has been studied in the Indian set up. Critical care units have used ultrasound for many years now to assess fluid status, lung zones for patients with worsening breathlessness and cardiac contractility in shock. Its utility in the Indian emergency set up has not been advocated or studied.

Hence in this study we aim to study the utility of dyspnea discrimination index along with the ultrasound tool in distinguishing between a cardiac and pulmonary cause for dyspnea in patients who present to the emergency with acute onset breathlessness.

AIMS

To assess the utility of the Dyspnea discrimination index along with a multifactorial ultrasound screening tool to differentiate between a cardiac and pulmonary cause for breathlessness in patients who present with acute or acute on chronic breathlessness to the emergency department.

OBJECTIVES

A) To calculate the Dyspnea discrimination Index (DDI) and Percentage Dyspnea Discrimination Index (%DDI) for all patients presenting to the emergency department with dyspnea.

B) To assess the sensitivity, specificity, positive and negative predictive values of Dyspnea Discrimination Index and Percentage Dyspnea Discrimination Index in identifying pulmonary and cardiac causes for dyspnea.

C) To do a discriminate analysis on factors evaluated at admission like PaCO2, PaO2, Peak expiratory flow rate, Percentage peak expiratory flow rate which would help identify the factors with discriminative power between a cardiac and pulmonary etiology.

D) To assess the utility of a screening lung and cardiac plus IVC ultrasound in distinguishing a cardiac and pulmonary etiology for the dyspnea

Review of literature

Dyspnea is defined by the American Thoracic Society as “a subjective experience of breathing difficulty that comprises of qualitatively distinct sensations that are of varying intensity. The experience derives from interactions between multiple physiological, psychological, social and environmental factors and may induce secondary physiological and behavioral responses(1).” Dyspnea is a common chief complaint among patients presenting to the emergency department.

In a prospective observational study it was noted that the most common diagnoses among elderly people who presented with dyspnea to the emergency department were decompensated heart failure, pneumonia, chronic obstructive pulmonary disease, asthma and pulmonary embolism(2).

Breathing difficulty can predominantly be categorized into one of two groups; respiratory dyspnea or cardiovascular dyspnea. Respiratory system dyspnea consists of disorders of the central controller, the gas exchanger and ventilator pump, while the cardiovascular system dyspnea includes cardiac diseases. Other causes of breathlessness like trauma, neurological, muscular or toxin induced are usually obvious and do not pose a diagnostic dilemma.

CLINICAL SCENARIO:

Breathing difficulty that occurs over minutes to hours has a particular limited number of causes. The cause can be deciphered by paying attention to associated signs and symptoms which give clues toward the diagnosis. Examples of the same are retrosternal chest pain with radiation that suggests cardiac ischemia, fever, cough with sputum that suggests a respiratory tract infection and urticaria with rash and wheeze which suggests bronchospasm. There are situations where the associated symptoms and signs are minimal or they overlap. Even in the pre-hospital set up 8% of all emergency calls are for patients with breathlessness. As there is the possibility of misdiagnosis of asthma for a cardiac disease there has been documented mortality probably because of delay in management(3). Symptomatology is not adequately reliable in the acute setting as there is significant overlap. A study published in August 2014 in Egyptian journal of chest diseases and tuberculosis looks at the clinical spectrum and symptomatology of asthmatics who present to the emergency department. It shows that 95.2% had dyspnea on exertion and chest pain was experienced by 48.5% of the asthmatics. Hence this proves that symptoms are not reliable in differentiating cardiac and pulmonary cause of breathlessness(4).

Various causes for breathlessness because of cardiac and respiratory pathology with which patients present to the emergency department are(3):

Very common →

- Asthma,
- Chronic obstructive pulmonary disease
- Pulmonary edema because of left ventricular failure

Common →

- Pneumonia
- Pneumothorax
- Pulmonary embolism
- Pleural effusion

Rare →

- Metabolic acidosis
- Aspirin poisoning
- Renal failure

CLINICAL DILEMMA:

It is often seen that patients who present with breathlessness have clinical indicators that can be cardiac or pulmonary. An example is the presence of cardiac asthma in those with pulmonary edema(5). Physical examination, laboratory tests and chest X rays can often be nonspecific(6,7). In such situations it is difficult to assess the primary cause for breathlessness and hence planning management is tricky.

Treatment of cardiac and pulmonary causes for breathlessness is grossly different and hence accurate diagnosis is the key to prompt, appropriate management. Earlier, appropriate management has been shown to decrease overall morbidity and mortality(8). Administering management for both conditions can also prove to be detrimental. Issues like tachycardia caused by beta adrenergic drugs, when given in a cardiac condition, can worsen ischemia of the myocardium(9,10) can be avoided or minimized by making accurate diagnosis in the emergency department itself(11).

Multiple modalities have been studied in the attempt to distinguish cardiac and pulmonary dyspnea. Questionnaires, differentiation scores, blood tests and sonological tools are some of what is being looked at. Questionnaires like “shortness of breath questionnaire” and “chronic obstructive pulmonary disease population screener” have been studied, but its utility in the emergency set up is doubtful(12,13). Tools such as peak expiratory flow rate and capnometry have been studied as adjuncts to diagnosis of cause of breathlessness(14,15). But on their own they are not adequately accurate.

Blood tests like N-terminal pro brain natriuretic peptide, troponins, creatine phosphokinase and creatine kinase-MB have been evaluated in length(16,17). The issue of time that’s taken for the laboratory to give results for these tests did impede results but that was overcome with studies using rapid card tests that give instantaneous results.

Ultrasound has been used in different ways in the emergency department and has proved to be very useful in diagnosis. Only sonological imaging of the lung was used in some studies. The LUS; lung ultrasound study published in 2013 demonstrated that LUS imaging changed the diagnosis in the emergency department by 44% and also changed the therapeutic management by 58%(18). Newer studies look at combination imaging of lung, heart and inferior vena cava. This has been found to increase the sensitivity and specificity tremendously(19,20). Some studies have also used a combination of blood test and imaging(21).

A SIMPLE SOLUTION:

Peak expiratory flow rate is defined as “the maximum flow rate generated during a forceful exhalation, starting from full lung inhalation”((22). Most people above 5 years of age are capable of accurately performing the same. The most frequent use of peak expiratory flow rate measurements is in home monitoring of asthma, where it has been studied to be beneficial for short and long term monitoring. Peak expiratory flow rate varies based on height, age and gender and hence there are existent normograms creating for the same. Many types of peak flow meters are presently available. Some are simple hand held devices, while others have electronic measurement, recording and relaying facilities.

The utility of this tool has been extrapolated to help in delineating the cause of breathlessness in the emergency scenario. Peak flow metry has been studied on its on in the emergency set up and

it was concluded that values where significantly higher in patients with cardiac causes of dyspnea (224+/- 82 L/min versus 108+/- 49 L/min)(12). But there was no single cut off value delineating the two causes.

It was hypothesized and proven that peak expiratory flow rate in combination with partial pressure of oxygen, used as a ratio may increase the sensitivity of discrimination between cardiac and pulmonary cause of breathlessness, when used in the emergency set up. This ratio was named the Dyspnea discrimination index and was used in the emergency department. The parameters in unison add to the discriminative power of the score and have been postulated to be a good clinical adjunct to diagnosis.

DDI score = (PEFR x PaO2) / 1000

DDI% = (%PEFR x PaO2) / 1000

It has been calculated for patients presenting with breathlessness in the emergency set up in America and values have been compared(23).

VARIABLES	CARDIAC DYSPNOEA n=24	PULMONARY DYSPNOEA (n=39)	P value
PaO2	**68+/-12.2**	**58.7+/-13.2**	**0.007**
	(43.6-92.4)	**(32.3-85.1)**	
PEFR(L/min)	**267+/-97**	**144+/-66**	**<0.001**
	(73-461)	**(12-276)**	
%PEFR	**15+/-19**	**35+/-17**	**<0.001**
	(20-96)	**(1-69)**	
DDI	**18.4+/-7.9**	**8.4+/-4**	**<0.001**
	(2.6-34.2)	**(0.4-16.4)**	
%DDI	**4+/-1.4**	**2.1+/-1**	**<0.001**
	(1.2-6.8)	**(0.1-4.1)**	

Hence from this the outcomes evaluated are the specificity, sensitivity, positive & negative predictive value.

Comparison Variable	Optimal Cut off Point	Sensitivity, %	Specificity, %	Positive Predictive Value, %	Negative Predictive Value, %
PEFR	200	72	71	80	63
%PEF	42	59	78	81	54
DDI	13	82	74	84	71
%DDI	3.0	77	70	81	66

DDI score cut off taken in the above mentioned study, after plotting a receiver operating characteristic curve, was 1.6(23). There have been no similar assessments done on Indian populations. Hence there is scope to assess this tool in India, as an adjunct to clinical diagnosis. The western studies have shown that clinical diagnosis in the emergency had an accuracy of 69%. DDI score on its own had an accuracy of 79% (21). Hence it can be looked at as an adjunct to clinical diagnosis, so as to increase diagnostic accuracy.

ULTRASOUND IN DIFFERENTIATING CAUSE FOR BREATHLESSNESS:

A combination of history, examination and tests like chest X ray have only intermediate accuracy for bedside diagnosis of cause of breathlessness. Hence there is a need to look for tools, scores to help with diagnosis (22). The ultrasound is one such studied entity.

Ultrasound was invented in 1957 by Ian Donald. It was only used later in 1958 for obstetric evaluation (24). The use of ultrasound in the emergency department was first initiated in 1994(25), but since has rapidly caught the attention of physicians and is being used in most spectrums of diagnostics.

Air was thought to impede ultrasonography and hence lung was considered an organ not amenable to evaluation using the same. Imaging that is easy to avail is the chest x ray, which is not always adequate for diagnosis. There is also a time lag before the X ray can be taken. Hence there is a clear need for good bedside imaging. Ultrasound has been studied in detail and the presence of air shadows has been used to differentiate various pathologies.

LUNG ULTRASOUND:

There are seven principles of lung ultrasound:

1) Lung ultrasound is done best with simple equipment
2) In the thorax, fluid and gas are opposite in location or can be mingled by processes that are pathological. This generates artifacts that can be used to benefit diagnosis.
3) The lung is very voluminous. Hence standardized areas are defined for examination.
4) Pleural line is from where all signs arise.
5) Static signs most often are artifactual.
6) The signs that arise from the pleural line are dynamic.
7) Majority of lung associated life threatening disorders abut the pleural line, hence stressing the usefulness of lung ultrasound if used in these situations.

A range of frequencies (4-12MHz) can be used to study the lung. Higher frequencies are preferred to look at lung peripheries plus to look at lung comets. Lower frequencies are to image deeper lung tissue to look at features like consolidation and pleural effusion. Six regions which are marked out by the anterior and posterior axillary lines should be examined in sequence; upper and lower zones of the anterior, posterior and lateral aspect of the chest wall. The ultrasound probe is placed in the intercostal space with the probe marker facing the patients head end. Ribs cause artifactual shadows that are anechoic. Between the two ribs there is a hyper echoic lines just below the probe. This is the interface between the aerated lung and the soft tissues of the chest wall, which represents the pleural line. Lung ultrasound image is full of artifacts as air stops the progress of the beam. Two types are commonly visualized;

A LINES:

Regularly spaced, hyper echoic, horizontal lines representing pleural line reverberation artifacts. These are artifacts of repetition which are motionless. These are seen in normal lung fields most commonly. But in patients with chronic obstructive pulmonary disease and bronchial asthma exacerbation A lines would be the only finding, unless there is a concomitant pneumonia.

A lines are also the only lung findings in pulmonary embolism.

B LINES:

Narrow based lines which arise from the pleural line and traverse up to the edge of the ultrasound screen. This artifact occurs because of a large amount of variation of the acoustic impedance of the object with its surroundings. They arise at the border between aerated and compressed lung and are often described to be multiple, comet tail or ray like, vertical lines that extend from the pleura to the lower edge of the screen without fading. B lines are noted to move synchronously with the lung during inspiration and expiration and hence tend to erase A lines. When several B lines are present together in clusters, it is termed as lung rockets.

Other things observed in lung imaging is the dynamic lung movement called lung sliding. This is more prominently seen in the base of the lungs. Absence of lung sliding can imply the presence of pneumothorax. In pneumothorax, other findings that would be absent are B lines. Absent lung sliding is a very sensitive finding and may be noted in very small pneumothorax which are not picked up on chest X ray(26).

Pleural effusions are also picked up at the bases as a homogenous hypoechoic finding between the diaphragm and the lung base. The effusion may be locculated or have fibrin strands running through. Massive obesity may obscure optimal visualization of effusions. Complex locculated effusions can appear different with hyper echoic, locculated fluid that is not at the base of the lung. It may even be isoechoic with the liver, especially if it is an empyema or malignant effusion(27). The presence of air and fluid in the pleural cavity is a very complicated sonological picture.

Consolidations are also seen with the same ultrasound probe. Water as it is a good ultrasound transmitter, and a consolidation is water rich. Occasionally collapsed lung can also be mistaken for consolidation sonologically it appears like improperly defined lung tissue which is hypoechoic in nature. At those points normal lung tissue is not seen. Artifacts from the pleural line are seen. Within the consolidation there are hyper echoic, puntiform structures that can be seen, which are corresponding with air in the bronchi. This is also known as ultrasound air bronchogram. The bubbles are noted in respiration to move.

Mechanism of formation of the artifacts:

The comet tail artifact is seen when there is a large difference in the acoustic impedance noted between the surroundings and an object. A phenomenon of resonance is created by the beam. Distance is interpreted from the time lag between reverberations. This results in a center that behaves as a continuous source that generates many very closely placed pseudo interfaces. There is a resultant endless to and fro movement as the beam is trapped in a closed system. At the surface of the lung, air is the most prominent element. There is a tremendous difference in its acoustic impedance and that of bone, parenchyma and water. Hence as there is usually no expected bone on lung surface and lung parenchyma mainly consists of air and water, the imaging features are also implicative of the same.

CARDIAC ULTRASOUND:

The knowledge of the cardiac function is essential in assessing a breathless patient in the emergency department. Ejection fraction gives a good measure of the same. Ejection fraction can be measured by two methods namely M mode LV dimensional method and Simpson's meth

Ejection fraction represents the percentage of the end diastolic blood volume in the left ventricle that is ejected out of the left ventricle during systole (24). Normal ejection fraction is above fifty percent. Advantage of using this as a tool to assess LV function is its simplicity and familiarity.

Stroke volume to a certain extent depends on preload and after load. The ideal measure of myocardial contractility should not be affected by the same.

M-mode LV dimensional method:

The image obtained is the parasternal long axis view and the probe is placed in the second left intercostal space. M mode cursor is used to make the required measurements from which ejection fraction is calculated.

Simpsons Method:

In this method the views required are the A4c or A2c views and the endocardial borders are to be visualized well. Calculations are done from the same.

INFERIOR VENA CAVA VARIABILITY:

IVC variability is measured with a subcostal transthoracic approach. The transducer position is below the xiphisternum, slightly right to the midline with the direction of the transducer facing the sternal notch. IVC is visualized and recognized by the entry of the hepatic vein into the same and its entry into the right atrium. Measurements are made using M mode recordings. Respiratory variation in IVC diameter is only seen in people who do not have high right Atrial pressures. Hence can help assess cardiac function indirectly(28), more of the right heart. If IVC variability is good then it is unlikely that the breathlessness is because of a cardiac dysfunction. Hence when studied in conjunction with other ultrasound imaging has shown very high sensitivity and specificity in determining the cause of breathlessness in the emergency set up(29).

Multifactorial analysis using ultrasound

It was hence postulated that a combination of parameters evaluated by means of an ultrasound machine may be a good bedside tool to identify the cause of dyspnea. Left ventricular function assessment, valvular lesions plus a measure of fluid status is mandatory to assess cause and plan management thereafter. To assess left ventricular function the simplest way is use M mode. This is not time consuming, is accurate and can be calculated using the uncomplicated hand held imaging device. To assess severity of fluid overload, measurement of right atrial pressure would be ideal. Right atrial pressure can be estimated by measuring the diameter of the Inferior Vena Cava using the ultrasound probe. Other parameters assessed are Inferior Vena Cava variability with respiration and compressibility.

Gargani studied and concluded that adding lung ultrasound to echocardiography (integrated cardio-pulmonary USG) helps differentiate the main causes for acute onset breathlessness(1). Kajimoto et al studied lung ultrasound in combination with measurement of ejection fraction and Inferior vena cava variability as a tool to assess cause of breathlessness(2). This study revealed that this multifactorial analysis yielded very high sensitivity and specificity. Other multifactorial protocols were also proposed and have been proven to have good but varying degrees of accuracy and ease of performing the same. Some such protocols are the BLUE protocol, RADiUS protocol and the ETUDES scan((3)(4).

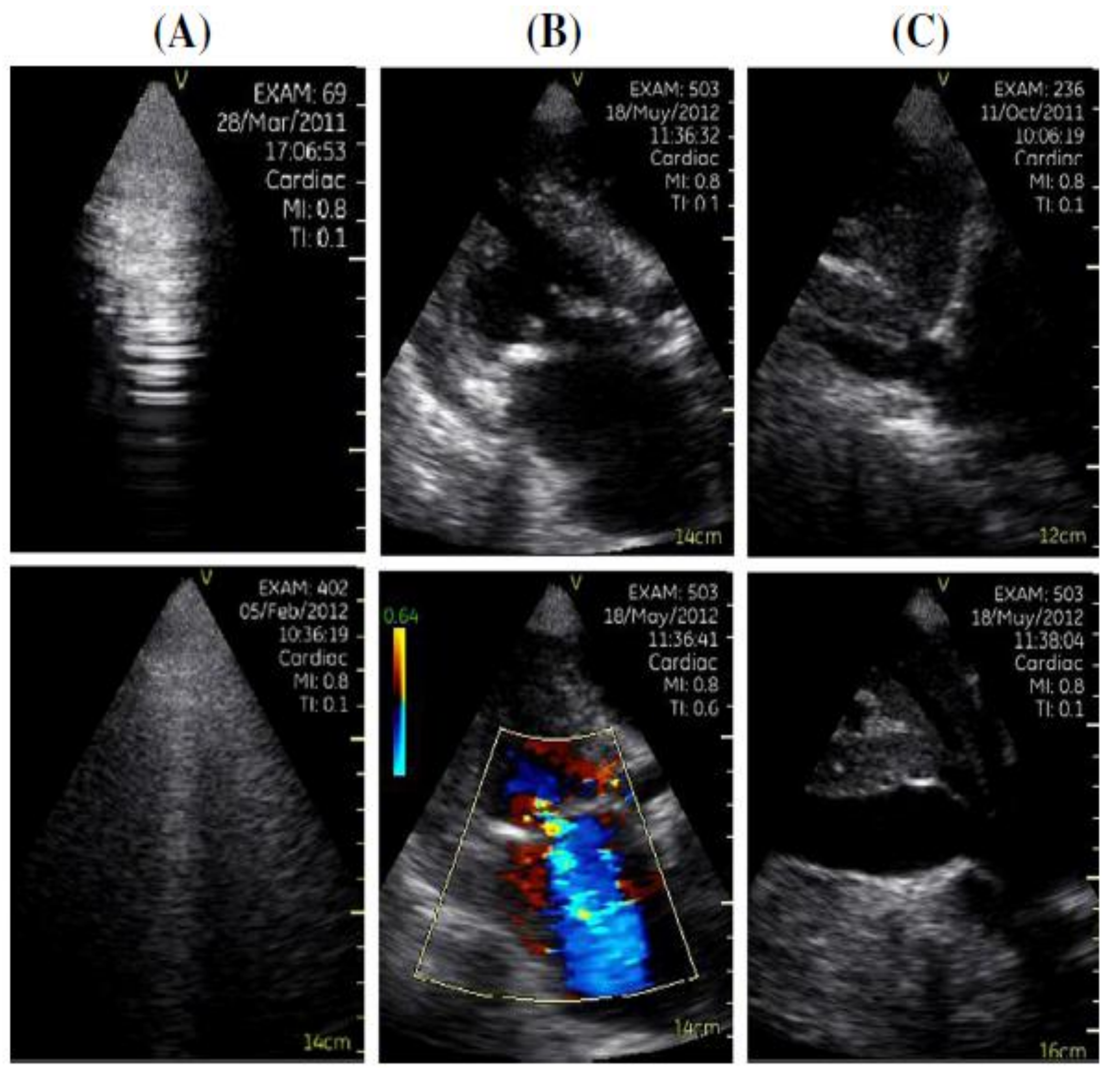
LCI SCREENING TOOL:

This is a diagnostic tool that has been studied in Tokyo and published in December 2012. It was designed to formulate a quick way to diagnose cardiac or respiratory dyspnea as treatment would vary based on etiology.

In their study imaging was done in the Emergency department and it was compared for diagnostic accuracy with the gold standard, which was diagnosis at discharge(30).

The lung ultrasound was done dividing the chest wall into eight areas (two anterior and two lateral areas per side). The anterior zone of the wall of the chest was marked from the sternum to the anterior axillary line. This was further divided into the upper and lower halves (clavicle to the third intercostal space, from the third space up to the diaphragm). The lateral zone was marked from the anterior axillary line till the posterior axillary line. This was also divided into upper and lower halves. Lung ultrasound examination was always completed in one minute followed by the cardiac ultrasound.

Global left ventricular function was estimated along with an approximation of the severity of mitral or tricuspid regurgitation. The usual cardiac views were used for estimation, most commonly the apical four chamber view. Preserved left ventricular ejection fraction was defined as more than forty percent.



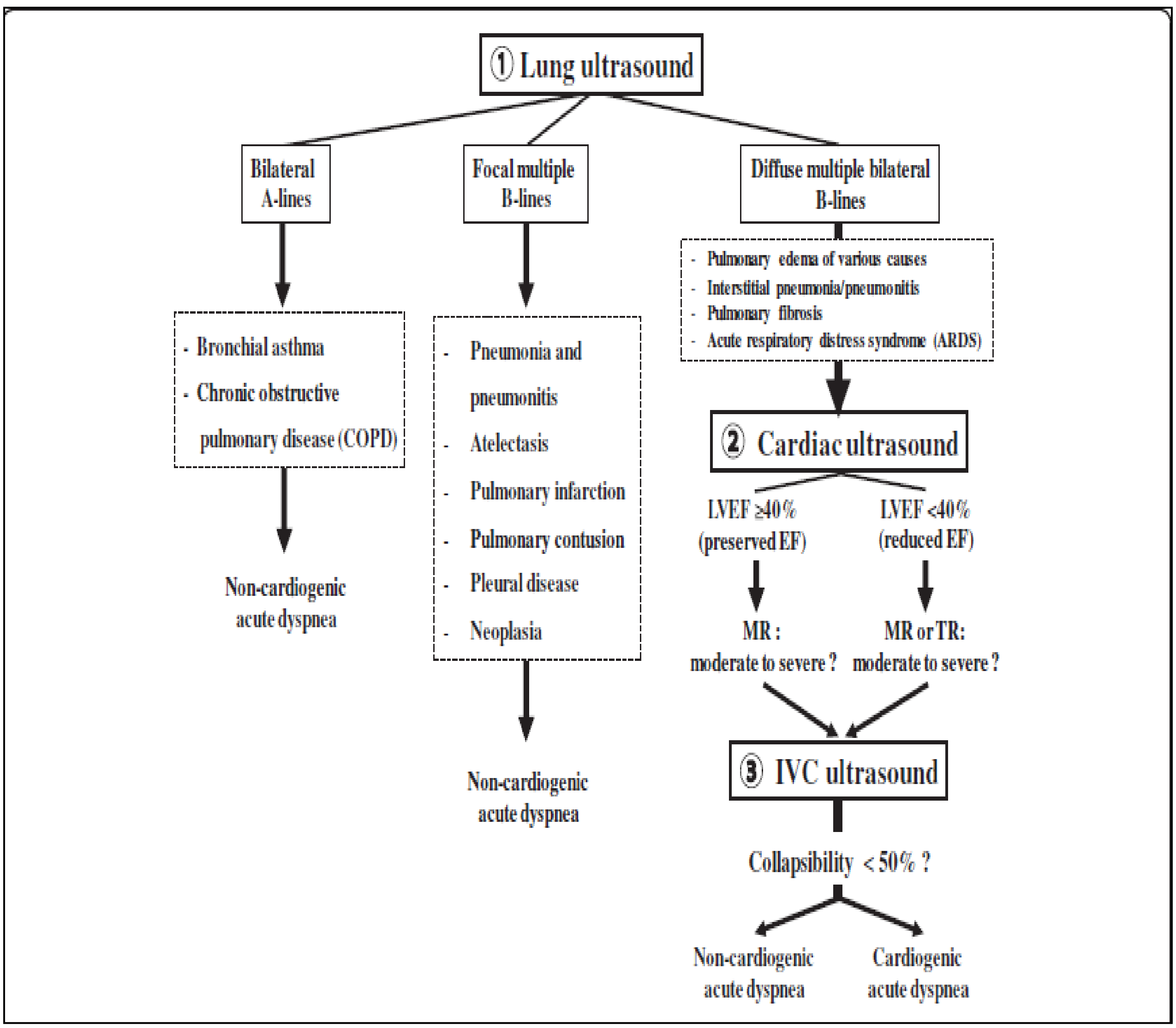
A upper: A lines	B upper: cardiac apical long axis view	C upper: IVC > 50% collapsibility
A lower: B lines	B lower: moderate mitral regurgitation	C lower: IVC < 50% collapsibility

This diagnostic tool demonstrated that the quick evaluation using ultrasound to look at the lung, heart and IVC has a higher accuracy in differentiating acute breathlessness because of cardiac failure from that of a lung cause, when compared to lung ultrasound alone or in combination with plasma BNP levels. The tool was found to be 94.3% sensitive, but only 91.9% specific in those settings. They also studied the tool in collaboration with NT pro BNP which was found to increase the specificity.

Hence as accuracy and sensitivity of the tool in combination is much more than individually, this study proves that it could be a very useful instrument in the emergency department. As the tool does not look at valvular heart lesions and diastolic dysfunction, procedure is fast and the machine required is a simple hand held machine (17).

TOOL	SENSITIVITY	SPECIFICITY	PPV	NPV	ACCURACY
USG LUNG	96.2	54	90.9	75	78.8
IVC variability	83	81.1	76.9	86.3	82.2
LUNG + BNP	88.6	67.6	80.6	79.8	80
LCI TOOL	94.3	91.9	91,9	94.3	93.3

The above table elucidates the sensitivity, specificity, positive and negative predictive value for each tool on its own and in combination with each other. The algorithm used to decipher the cause of breathlessness using the results attained is given below. This algorithm was what was used in our study:



This LCI screening tool is not the only combination tool used in the diagnosis of the cause of breathlessness. Most of these tools are created for the critical care set up but can be extrapolated and used in the emergency department with the same efficiency.

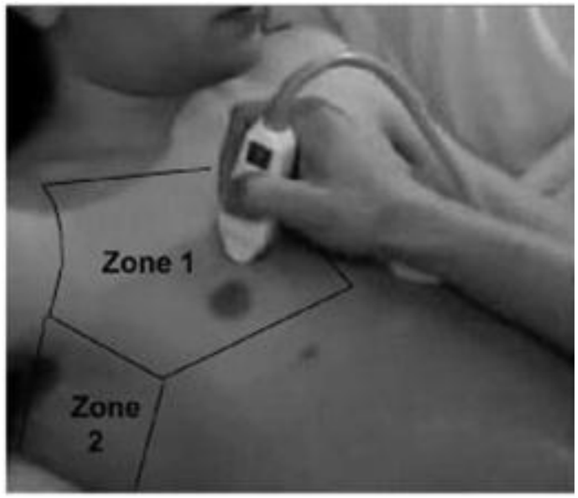
We have chosen to use the LCI screening tool because of its high sensitivity and simplicity, yielding results within a period of three minutes.

Other such protocols are like the BLUE protocol(31):

This was an observational study published in Chest 2008, where they used ultrasound on consecutive patients admitted in intensive care units with acute respiratory failure. The lung ultrasound results were compared to final diagnosis, and patients with rare or uncertain diagnosis were excluded. The study included 260 breathless patients who had a definitive diagnosis. The aspects assessed were; artifacts (A lines, B lines), lung sliding and alveolar consolidation or pleural effusion. Along with venous analysis, ultrasound results were assembled to form particular diagnostic profiles.

They found that lung profiles give correct diagnosis in 90.5%. Hence the tool can be used to assess breathlessness in critical care set up. This has not been evaluated in the emergency department as a diagnostic tool.

The following picture shows the aspects of the chest that are examined in blue protocol:



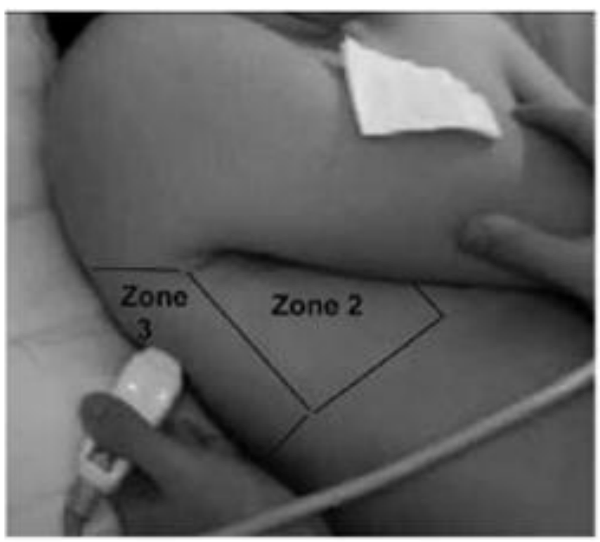
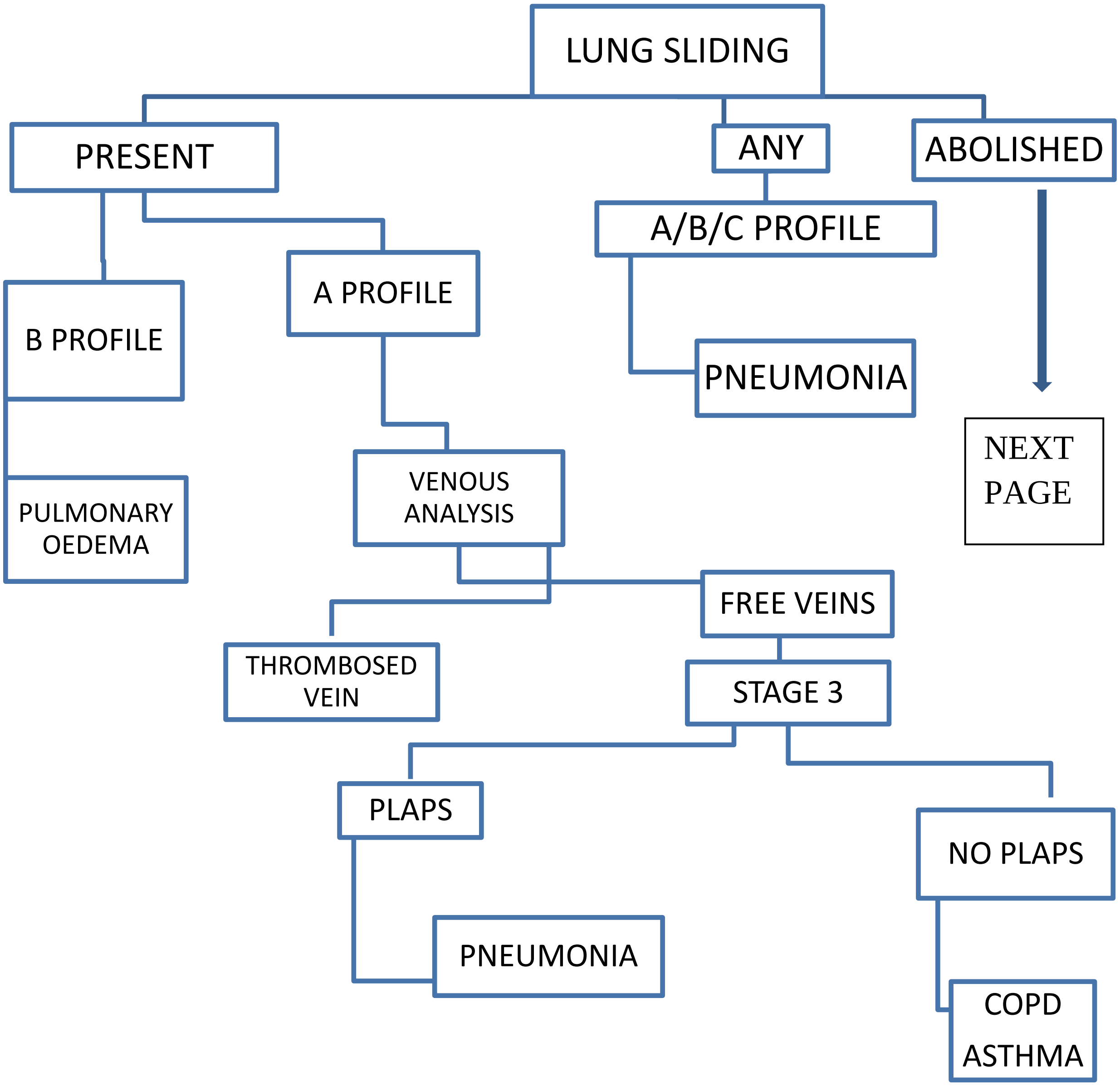
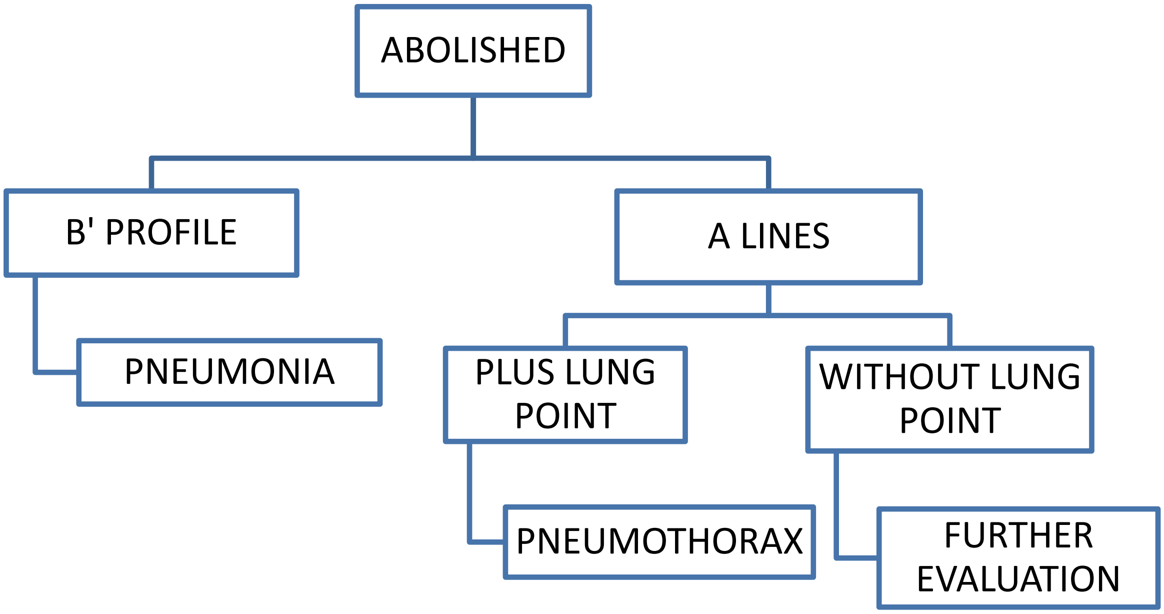


Figure showing zone 1, 2 & 3 in lung screening of Blue Protocol



BLUE Protocol



This is the algorithm formulated by the group that designed to BLUE protocol. Using this algorithm, the ultrasound findings are analyzed and a diagnosis made.

Brief explanation of the algorithm ensues. The B profile which consists of the anterior interstitial syndrome with lung sliding indicates pulmonary edema. The B' profile which has abolished lung sliding indicates pneumonia. The A/B profile with asymmetric anterior interstitial syndrome and the profile C which consists of anterior consolidation represent pneumonia, just like the A profile plus PLAPS. A profile along with venous thrombosis represents pulmonary embolism. Any normal profile was representative of COPD or Asthma.

These results correspond to particular physio-pathological patterns elucidated by ultrasound artifacts. This principle has been in clinical use since the year 1994.

Certain recent articles have added advice to use the ultrasound to assess diaphragmatic movement also. This would aid in diagnosing those aspects of breathlessness that are because of diaphragmatic palsy(32). This requires further thought and study.

RADiUS tool:

The RADiUS tool, which is the rapid assessment of dyspnea with ultrasonography was studied and published in 2011. It involves four different components of testing. The first is a focused cardiac examination; the second is the evaluation of the inferior vena cava. This is followed by the evaluation and assessment of the pleural line. There is room for the physician to include a focused assessment of the lower extremities to look for deep vein thrombosis. As this is time consuming and not required in all situations it is not part of the basic protocol.

Other similar protocols include the LUS; lung ultrasound protocol, which looks at whether the lung is wet, particularly being interested in if there are B lines. The ultrasound in breathlessness concept has also been looked at separately in diagnosis of breathlessness in pregnant women(33). There has been no observational study done in this context, but the publication present reports two cases where early sonology actually changed the diagnosis to pulmonary edema for a pregnant mother thought to be having an asthma exacerbation. As the difference in management is stark, the accuracy in diagnosis is most important. More studies are needed in the labour room set up.

Studies in elderly individuals with breathlessness have proven that ultrasound is a good tool in such condition(34). The RUSH (rapid ultrasound in shock) protocol has also been published and elaborated in detail. They have looked at the assessment stepwise and at the end analyzed the data together. Step one was to assess the cardiac function, step two was to look at the patients volume status, step three was to examine the large vessels for pathologies related to them and the final step was to put it all together(35).

ETUDES protocol:

Emergency thoracic ultrasound in differentiating the etiology of shortness of breath was studied and published in 2009. It concluded that bedside ultrasound of the thorax for B lines are a useful test to diagnose congestive cardiac failure. Accuracy in diagnosis is high when results are totally positive or totally negative. The protocol studying two zones has been noted to be as good as the eight zone protocol. Thoracic ultrasound is good when used on its own and when used along with NT-ProBNP evaluation of a breathless patient who presents to the emergency department(21)

GLOBAL SCENARIO:

Breathlessness is a common problem and is rampant in all populations. An Australian survey demonstrated that from a sample of 5331 people examined, 11.1% reported breathlessness and 3.4% of them has a MRC (Medical Research Council) scale of 2 to 4(36). In a population based study in Sweden there were 20.5% women and 12% men who were breathless, hence an overall 16.4% breathlessness prevalence rate(37). Hence it is a rampart problem. How many of these people actually reach the emergency department depends on the pre-hospital care in that locality.

Prevalence in primary care set up has been estimated. A study in the United States published the three year incidence rates of breathlessness to a primary care centre to be 3.7%(38). Which means a large part of the breathlessness population directly bypass the primary centre or do not even reach there.

Studies based in the emergency set up have demonstrated upto 25% of patients presenting there to have the primary complaint of breathlessness(39). A study published in Lancet also reveals that breathlessness was the complaint of 21% of patients that present to the emergency(40).

Hence the need for correct diagnosis and optimal management in the emergency set up itself. There is a very diverse spectrum of diseases that can lead to breathlessness and any can present to the emergency department.

Differentials which have been clearly elaborated in an article published in 2014(Impress2014) which were compiled from a good literature review(41):

- Asthma
- COPD
- Croup
- Heart failure
- Cardiomyopathy
- Cardiac arrhythmias
- Interstitial lung disease
- Pericarditis
- Lung cancer
- Pleural effusion
- Pulmonary fibrosis
- Pulmonary hypertension
- Tuberculosis
- Acute respiratory distress syndrome

Hence the need for a good clinical diagnosis.

INDIAN SCENARIO:

Very little data is present on the causes and incidence of breathlessness in the emergency department in India. Studies are required to elucidate the profile of patients presenting to the emergency department with breathlessness, with regard to severity, causes, prognosis and treatment given. Evaluation of scores like Dyspnea Discrimination Index and percentage DDI has not been done in the Indian setting. Ultrasound evaluation for breathlessness has also not been done in the Indian emergency scenario. Hence the scope for the presently proposed study.

A study from the Annals of Thoracic Medicine April 2014 looked at B lines in lung ultrasound and the presence of interstitial lung disease. They have assessed distance between the B lines in ultrasound and compared the same with high resolution computed tomography scans of the lung. With the same they differentiated interstitial lung disease and pulmonary fibrosis. But there has been no study that looks at breathlessness in general and no combination tool has been evaluated here.

METHODOLOGY

The study protocol was approved by the Institution Regional Board on 19/3/2013.

It was reviewed and approved of by the ethical board.

PATIENT POPULATION:

Patients where admitted to the emergency department of our hospital with acute or acute on chronic breathing difficulty, who fit into the inclusion criteria and gave written consent were included. As our hospital has patients from all over the country, consent was taken in the regional language.

INCLUSION CRITERIA:

A) Men and women who present to the emergency department with acute onset breathlessness or acute worsening of a chronic breathlessness.

B) Age above 18 years.

C) No other obvious non cardiac or non-pulmonary cause for breathlessness like trauma, organophosphorus poisoning or snake bite induced muscle weakness.

EXCLUSION CRITERIA:

1) Patients not requiring hospitalization, who get discharged from the emergency department.

2) Those who have an obvious non-cardiac, non-pulmonary cause for dyspnea like trauma induced, poisoning or snake bite induced muscular weakness.

3) Inability to perform peak expiratory flow rate.

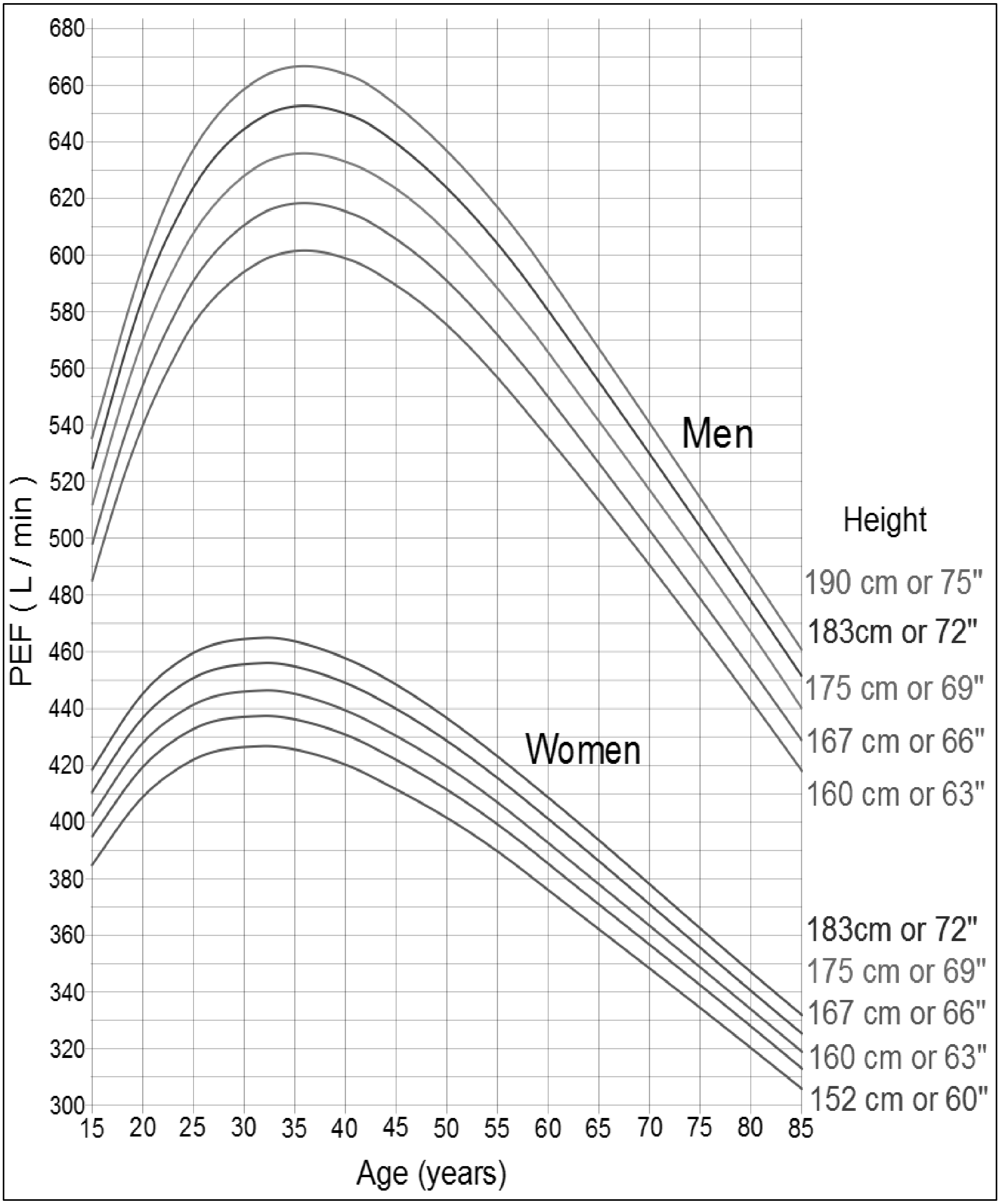
4) Patients who refuse consent.

Measurement of Dyspnea Discrimination Index:

As soon as patients were brought to either priority one or two from triage in the emergency department, they were at first seen by a casualty medical officer. Consent was taken from either the patient if stable enough or from the closest relative present at that point.

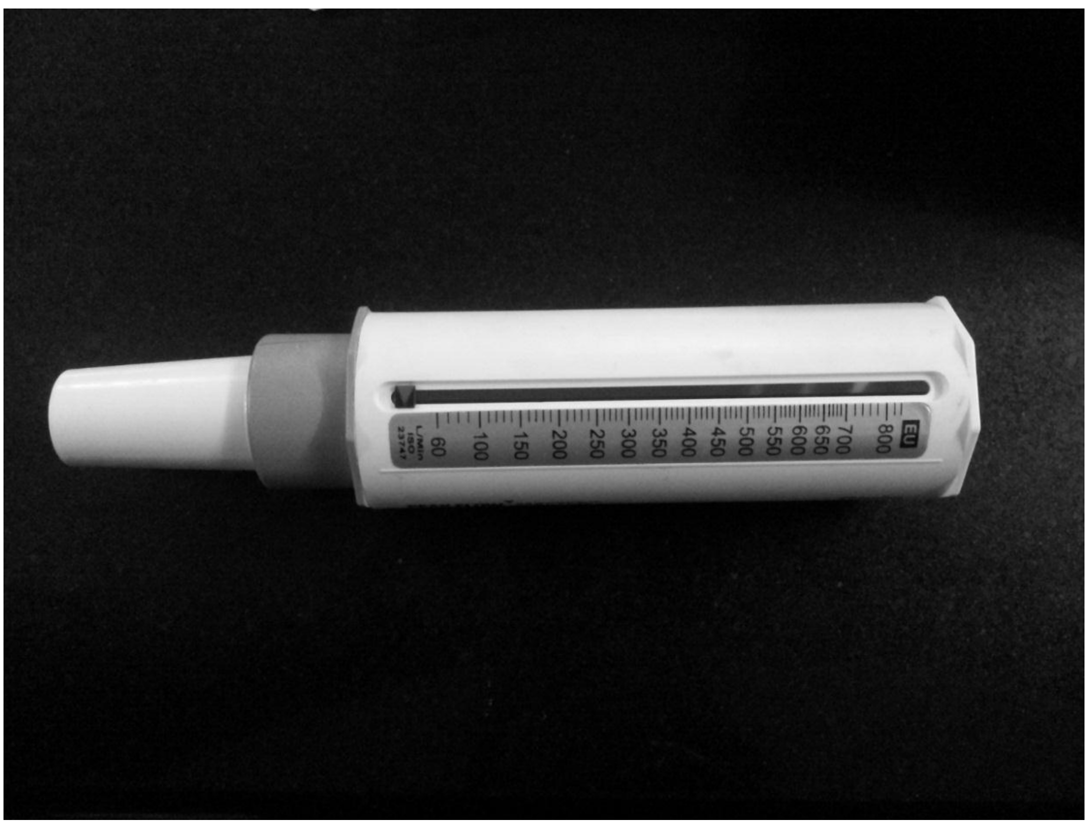
The patient was made to blow maximally into the peak flow meter. The reading was noted. Three such readings were taken and the best of three was chosen for the scoring tool. The percentage PEFR was calculated using normogram values which were standardized for the Indian population. These values were acquired from the pulmonary function lab of the hospital.

If the patient was not able to perform the peak expiratory flowmetry or they were too sick to withhold oxygen until the measurement is made, they were excluded.



PEFR Normogram

Simultaneously the casualty medical officer continued evaluation and medical management of the patient. An arterial blood gas was taken prior to administration of oxygen as is the protocol for any breathless patient who presents to the emergency. From the arterial blood gas the required values were taken note of. The patient's height was documented by either attaining the information from the relatives if they were aware of the same or from prior records if recorded or by measuring length with a measuring tape which was the closest possible approximation.



PEAK FLOW METER USED IN THE DDI STUDY

Lung Cardiac IVC screening

Within the first few hours of therapy the LCI ultrasound screening was performed. The machine used was a Sonosyte Turbo M. Only the primary investigator performed the scan. Cardiac mode was used for ECHO, IVC and lung ultrasound.

Validation of scan:

Prior to initiation of the study, the primary investigator was trained by a professional on the lung, cardiac and inferior vena cava ultrasonography techniques.

The classes were hands on and comprehensive. Images of all scans done were stored and 20% of the images were crosschecked for the purpose of validation of the scan.

IVC SCREENING:

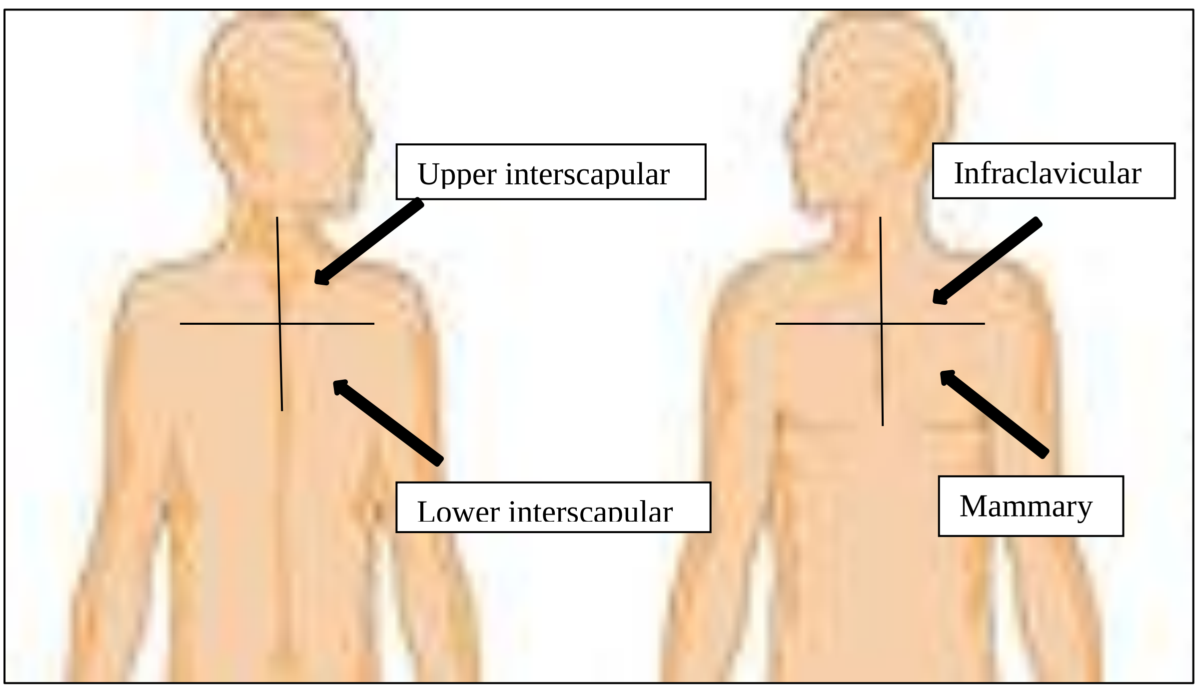
In the emergency department, the patient was first examined while lying flat. Initially the Inferior Vena Cava was visualized by placing the probe just below the lower margin of the xiphisternum. It was identified by the drainage of hepatic veins into the same and its final entry into the right atrium when traced further. Variability of the inferior vena cava with respiration was assessed qualitatively and opinion on whether it was less or more than 50% was documented.

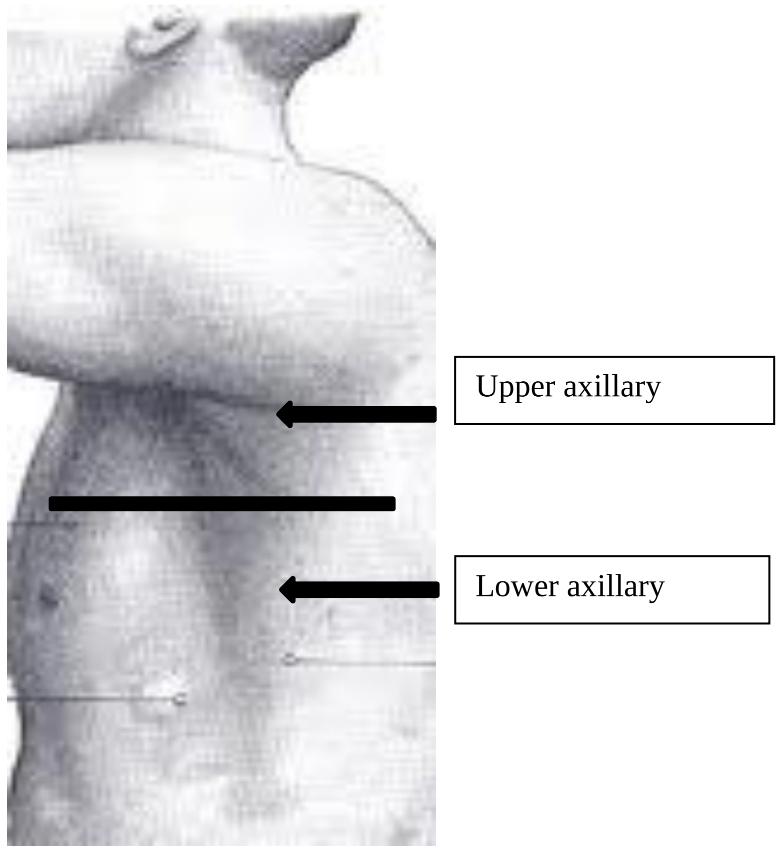
CARDIAC SCREENING:

The cardiac contractility was measured also in the supine position. Probe was placed in the second left intercostal space and the heart was visualized in the parasternal long axis view. The ejection fraction was calculated using the M mode method. Video clips of the cardiac contractility were taken and an image of the M mode calculation was stored. If there was difficulty visualizing the heart from this view, as is seen in patients with emphysematous lungs, the sub sternal view was used. If such were the case, ejection fraction was not calculated and approximate visual quantification of contractility was made.

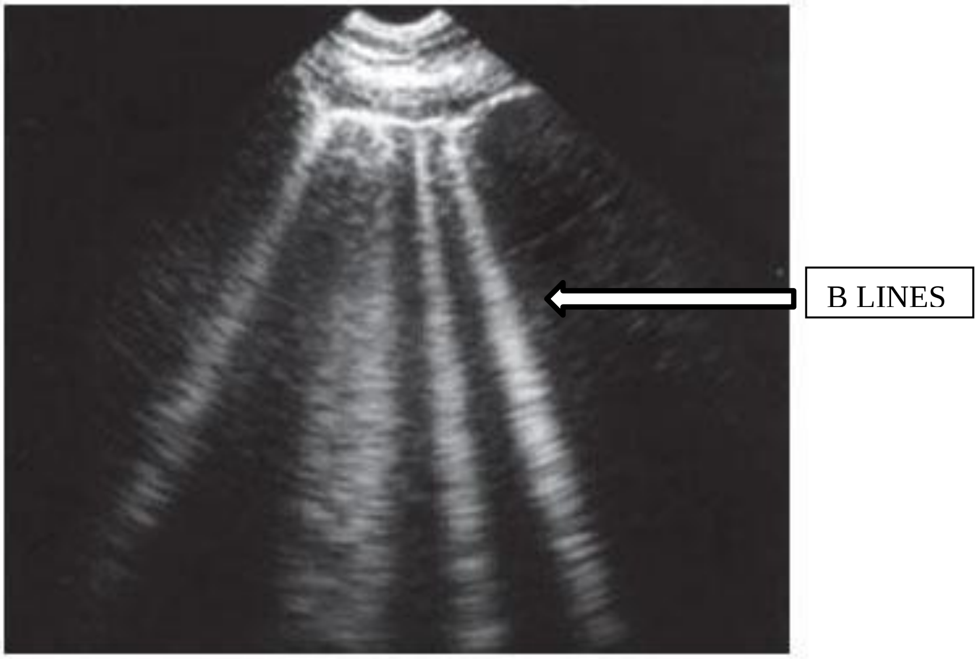
LUNG SCREENING:

The lung ultrasound was done in six specific positions. The infraclavicular, mammary, upper and lower axillary and the upper and lower interscapular regions were separately examined using the ultrasound probe.





All areas were imaged by ultrasound for all patients included in the study. Findings comprised of A lines, B lines, consolidations (air bronchogram), absent or present lung sliding, comet tails, pleural effusions and subpleural nodules. If the patient was not willing, imaging was not further continued.



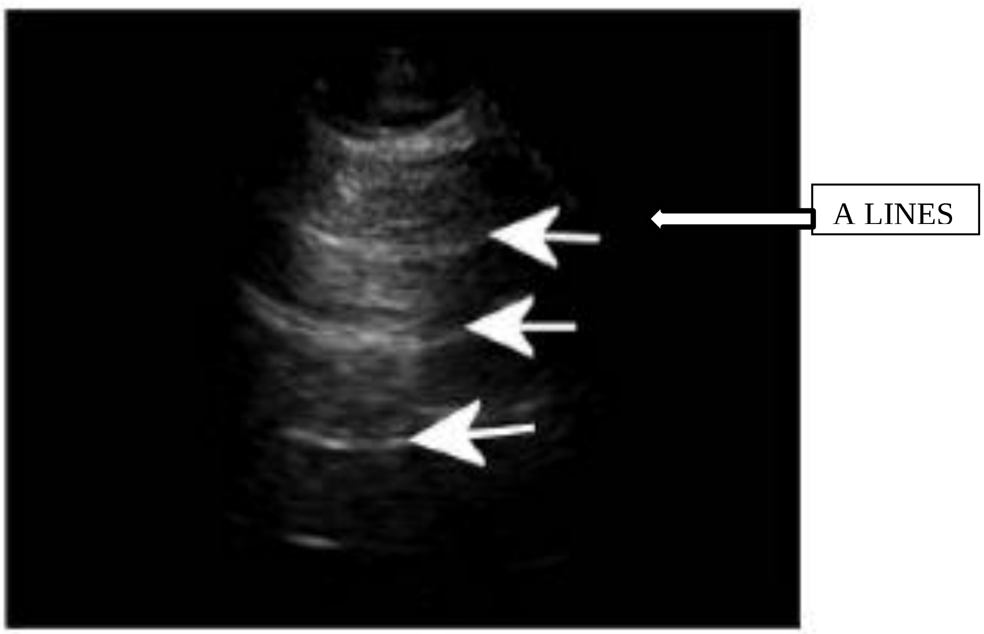
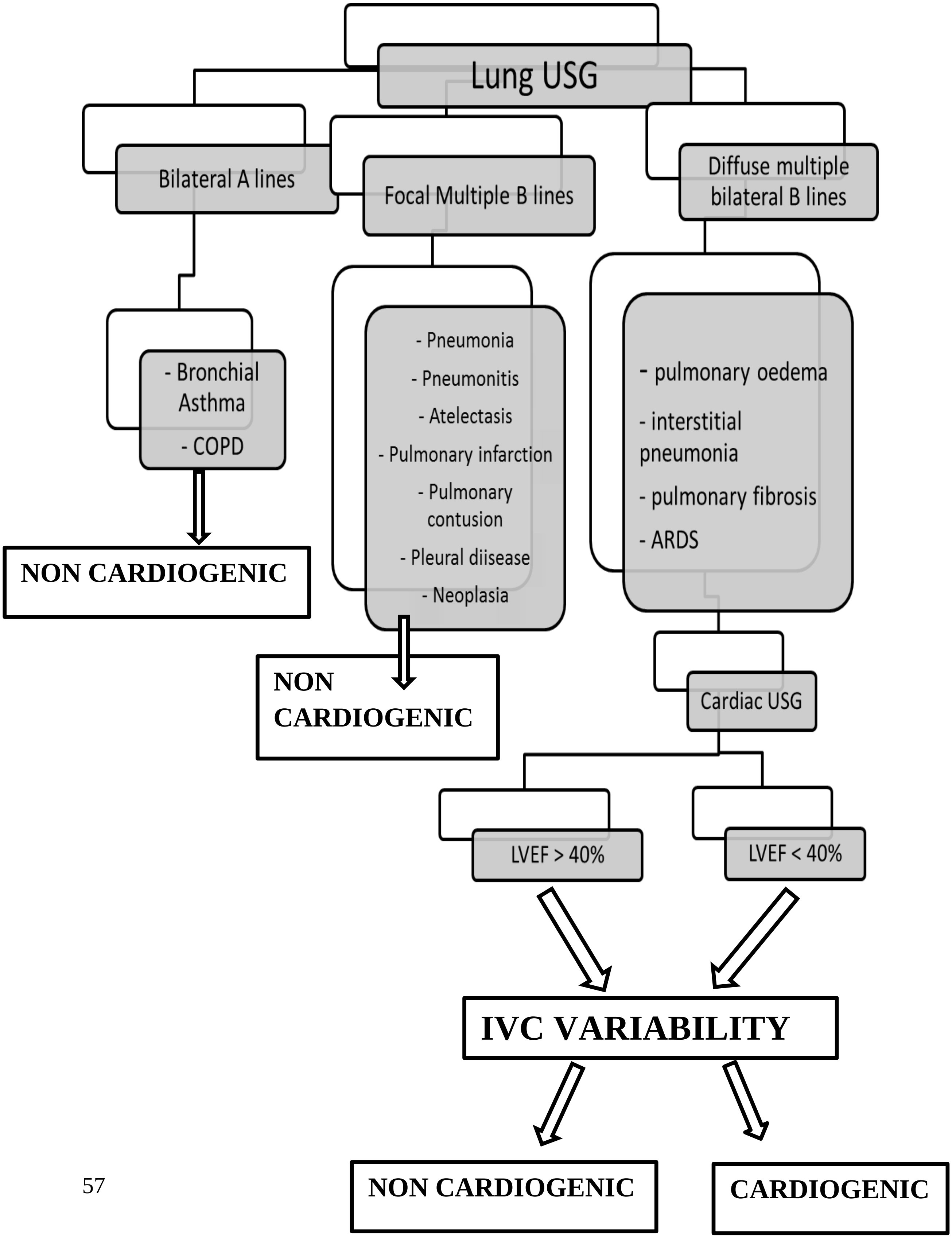


Figure 1: B lines diffusely present

Figure 2: A lines (Reverberation artifact)

With the findings of the ultrasound tool the following algorithm was followed and a diagnostic impression was made



Patients were treated in the emergency department by the casualty medical officer and medications optimized as per their diagnosis and protocol. The presumed diagnosis was taken note of. It was also taken note of if the patient had any prior diagnosis of cardiac or pulmonary disease. Other comorbidities, addictions were also tabulated.

The patient was admitted in the main medicine wards and intensive care unit based on need. The patient was followed up at discharge and final diagnosis was made note of. Investigations were also followed up over a period of a few months and echocardiography, pulmonary function tests were taken note of which would help with the conglomerate final diagnosis which is the gold standard to compare out diagnostic tool with.

Patients who presented to casualty with breathlessness and were treated there itself and discharged were excluded from the study. There were also patients who presented with breathlessness post trauma and lung contusion, muscular dystrophy and with weakness post organophosphorus poisoning who were excluded.

The integrated information was then analyzed with the help of the statistician who was also a part of the co-investigator team. Images were cross-checked by an experienced intensivist validation of the imaging was done by cross assessing 20% of the images taken. All other images were stored in case of later requirement.

SAMPLE SIZE CALCULATION:

Sample size was calculated from the formula 4pq/d2.

From previous studies, sensitivity and specificity was found to be 82% and 74% respectively. The precision of the estimate (d) was kept at ± 8 for the calculation of 95% confidence interval (CI). Using these values, we calculated a sample size of 115 patients.

QUANTITATIVE VARIABLES:

PEFR % = (Measured Peak expiratory flow rate / Predicted Peak expiratory flow rate) x 100

PaO2 = partial pressure of oxygen as per arterial blood gas value on room air

PaCO2 = partial pressure of carbon dioxide as per arterial blood gas value on room air

DDI: Dyspnea discrimination Index is a product of two simple parameters to assess the etiology of the same

DDI = PEF x PaO2/1000

DDI% = PEF% x PaO2/1000

LVEF (Left ventricular ejection fraction and Inferior Vena Cava collapsibility) as per USG documentation

STATISTICAL ANALYSIS:

1. Sensitivity, specificity, negative and positive predictive value and likelihood ratio were calculated for PEFR, %PEFR, DDI and %DDI.

2. To discriminate the variables in the two groups a non-parametric test; Wilcoxon rank sum test was used.

3. Receiver Operator Characteristic curves were made and area under the curve was calculated.

4. Best cut off points were taken from the receiver operator characteristic curves.

5. Ultrasound LCI tool was analyzed for sensitivity, specificity and positive and negative predictive values.

6. Discriminative analysis: To see which were the variables that discriminate between the groups when adjusted simultaneously in the discriminate model.

7. Sensitivity analysis to see if the acquisition of the emergency medicines own ultrasound machine had increased the accuracy of diagnosis of the casualty medical officers.

RESULTS:

Figure 1:

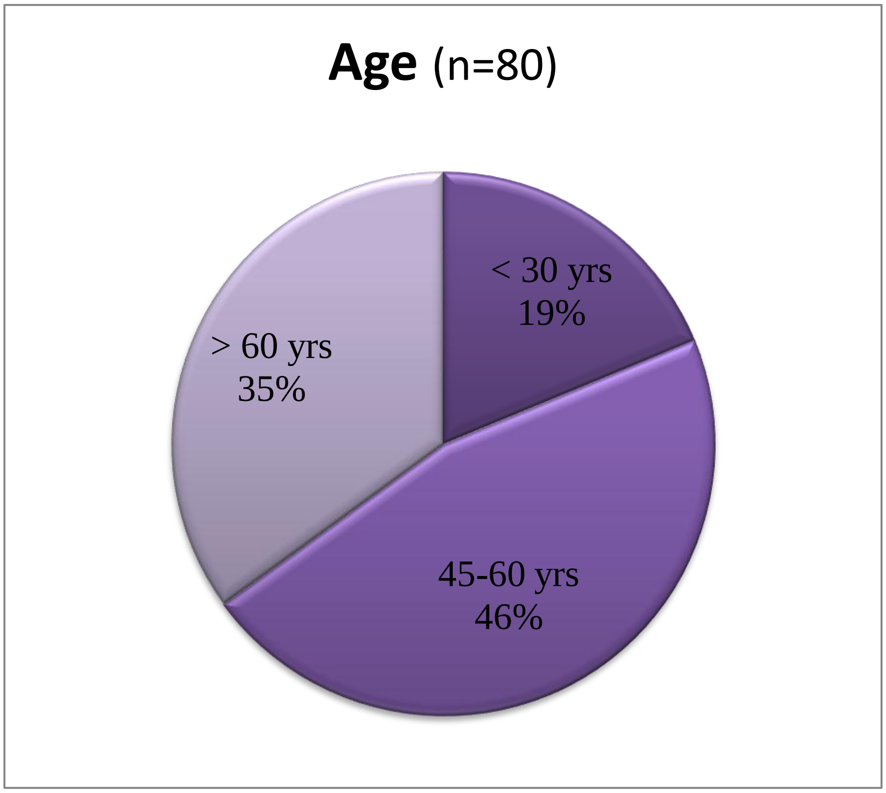


Figure 1: Represents the percentage of people in each age group among the study population

This pie chart represents the age group of the people who were evaluated in this study. The age groups were divided arbitrarily into three namely, less than thirty, thirty to forty five and the largest number fell in the middle age group from 45 to 60 years.

Figure 2:

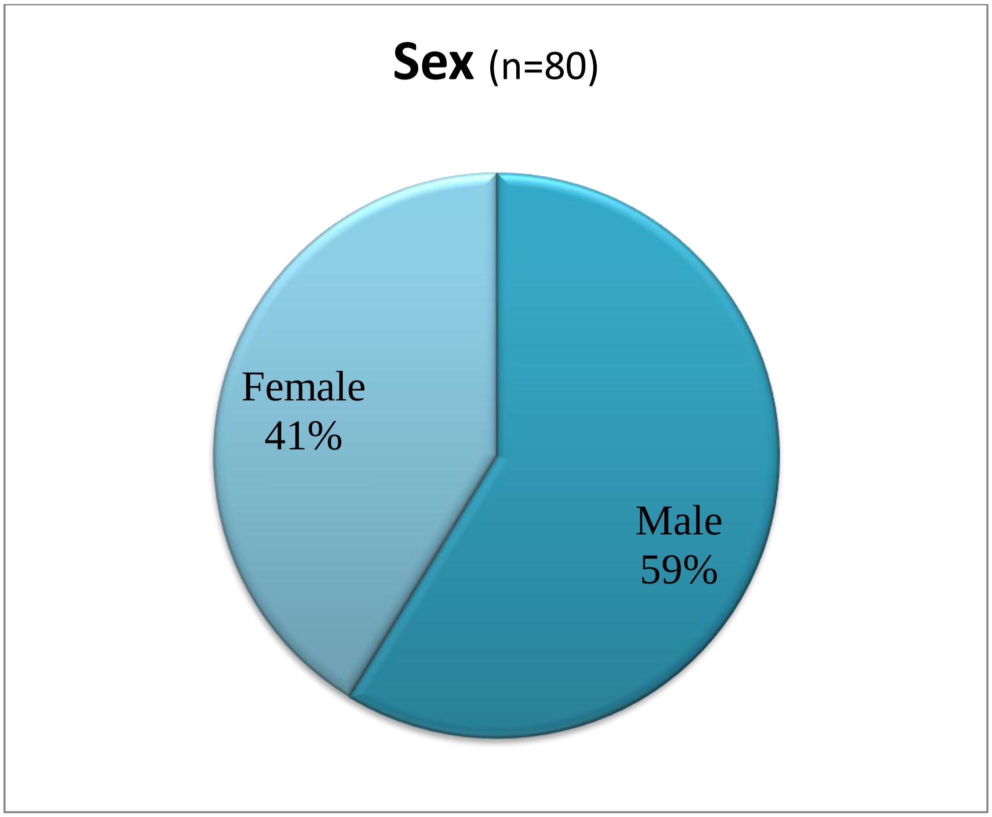


Figure 2: shows the sex distribution of the cases evaluated

This pie chart represents the gender distribution of the patients in the study. There were more men than women overall.

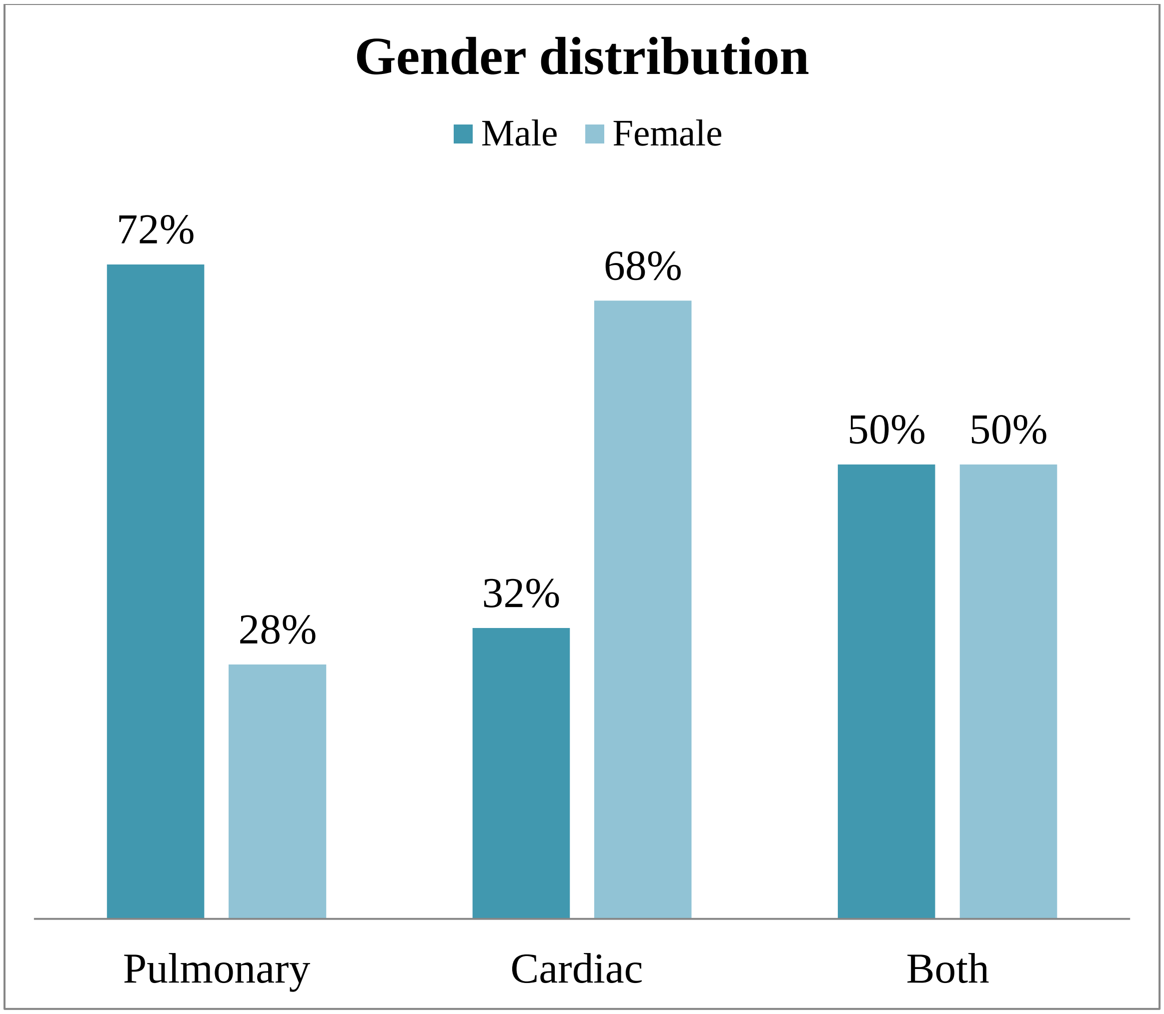


Figure 3: Bar graph of gender distribution among the three groups

There were more women in the group that presented with breathlessness because a cardiac pathology and clearly more in that presented with a pulmonary cause of breathlessness. The group with both cardiac and pulmonary problems actually had an equal distribution among men and women.

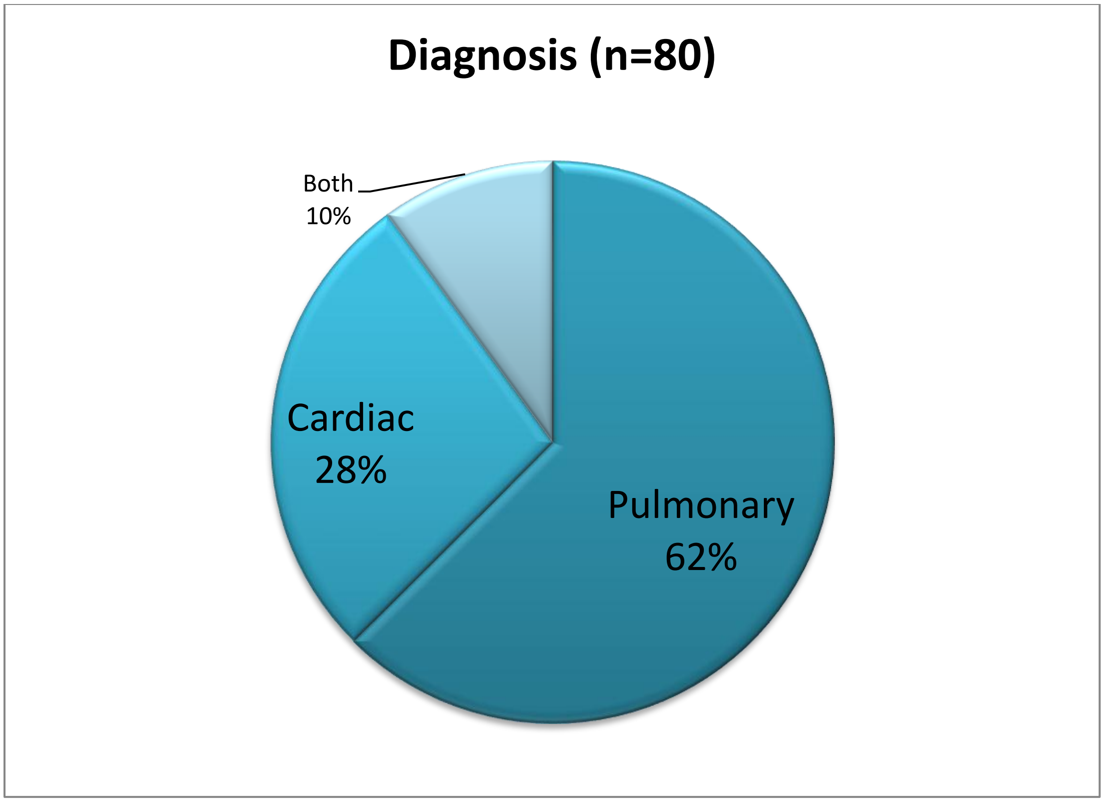
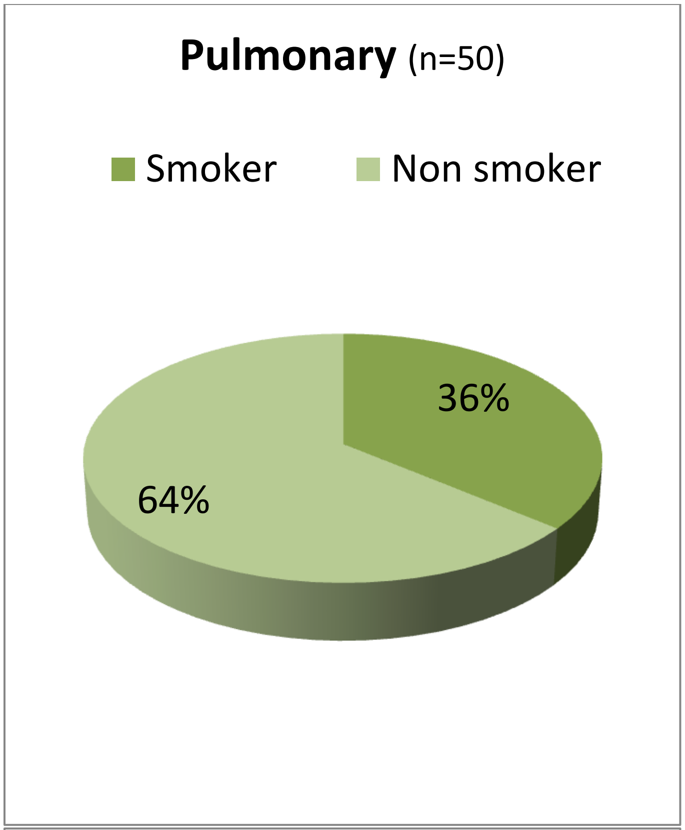


Figure 4: Pie chart showing the final diagnosis, cardiac, pulmonary or both.

The final diagnosis categorized all the patients into three, namely the cardiac, pulmonary and both groups. There were a larger percentage of people with pulmonary cause of breathlessness who were seen in the emergency and there were only a few with both together.



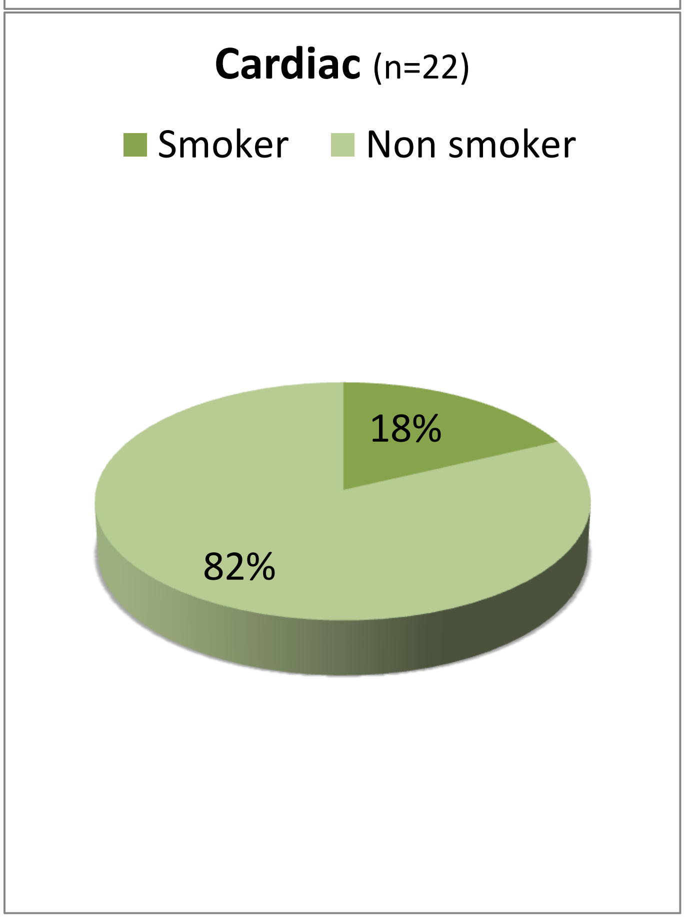


Figure 5a/5b: Pie chart showing the percentage of smokers among those with cardiac or pulmonary disease.

On looking at the number of patients with each diagnosis who smoke, it was noted that a larger percentage of those who smoke had pulmonary cause for breathlessness. 36% of those with pulmonary cause for breathlessness smoke, while only 18% of those with cardiac cause do the same.

In smokers with chronic obstructive pulmonary disease it was noted that cardiac imaging was difficult. As emphysematous lung obscures imaging, left ventricular ejection fraction could not be assessed in the parasternal long axis view. In such patients the sub sternal view helps visualize the heart better and ejection fraction is approximated based on visual impression.

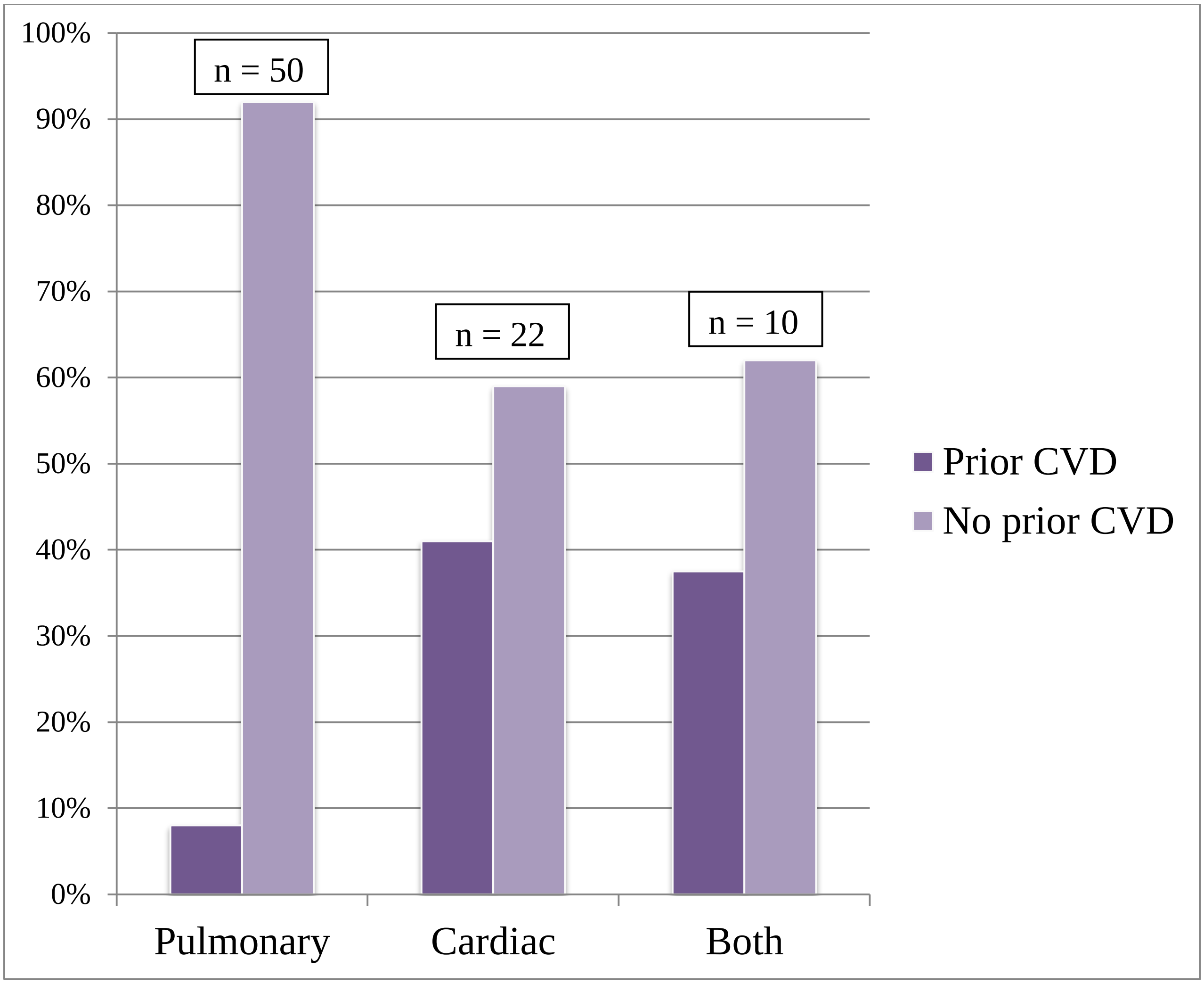


Figure 6: Bar graph of the percentage of those with prior cardiovascular disease

Of a total of fifty patients with pulmonary cause for breathlessness, only four patients (8%) have had prior cardiac disease. In the cardiac group, nine patients, that is 41% have had prior cardiac disease. Hence a noted difference is present in this respect

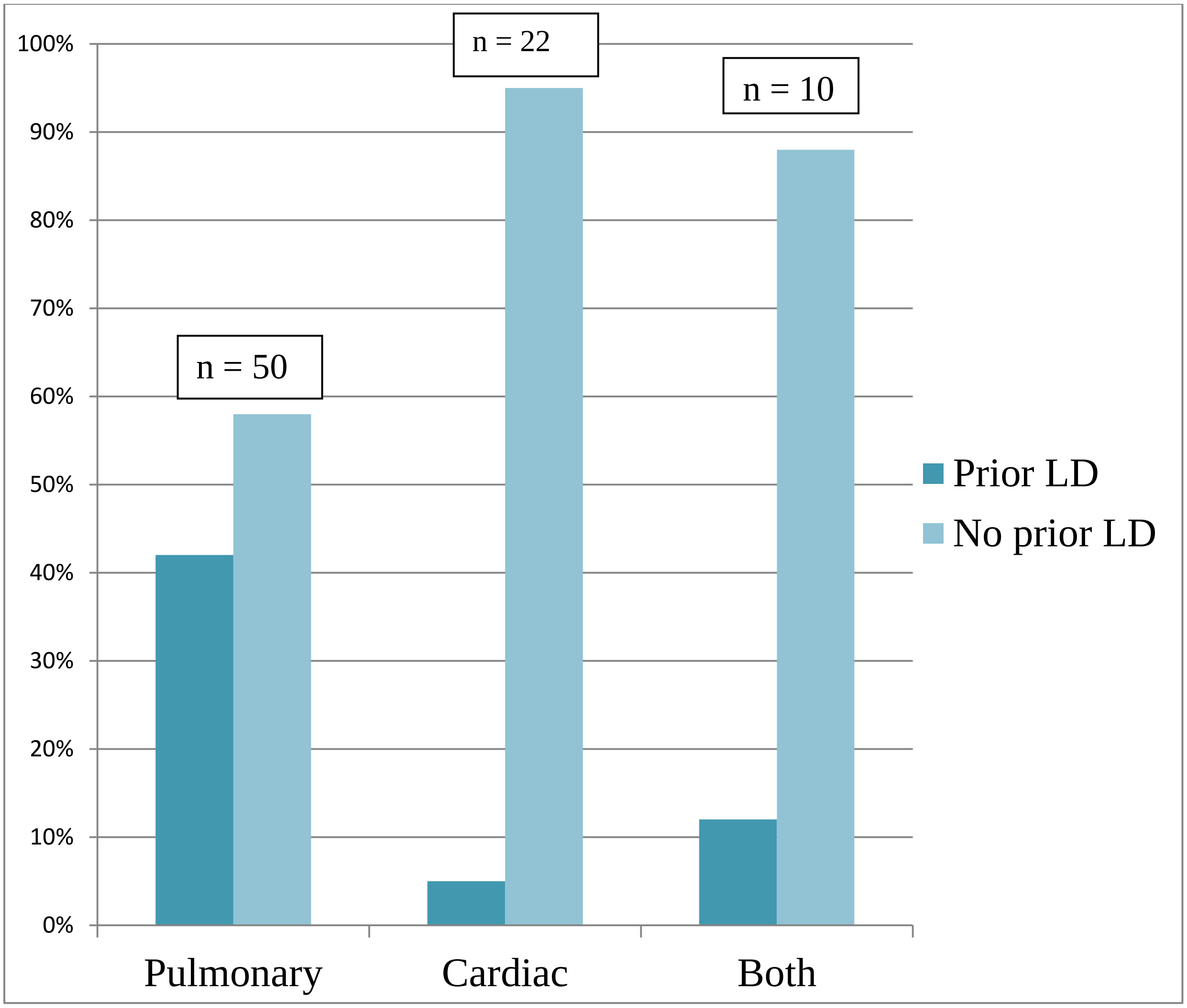


Figure 7: Bar graph of patients with prior known lung disease (LD - lung disease)

The above graph represents the percentage of patients with prior lung disease. 42% of patients in the pulmonary group have had earlier lung disease which is known to them. Common conditions noted were chronic obstructive pulmonary disease or bronchial asthma, prior tuberculosis, bronchiectasis and obstructive sleep apnea. Only 4% of patients in the cardiac group have had prior lung disease.

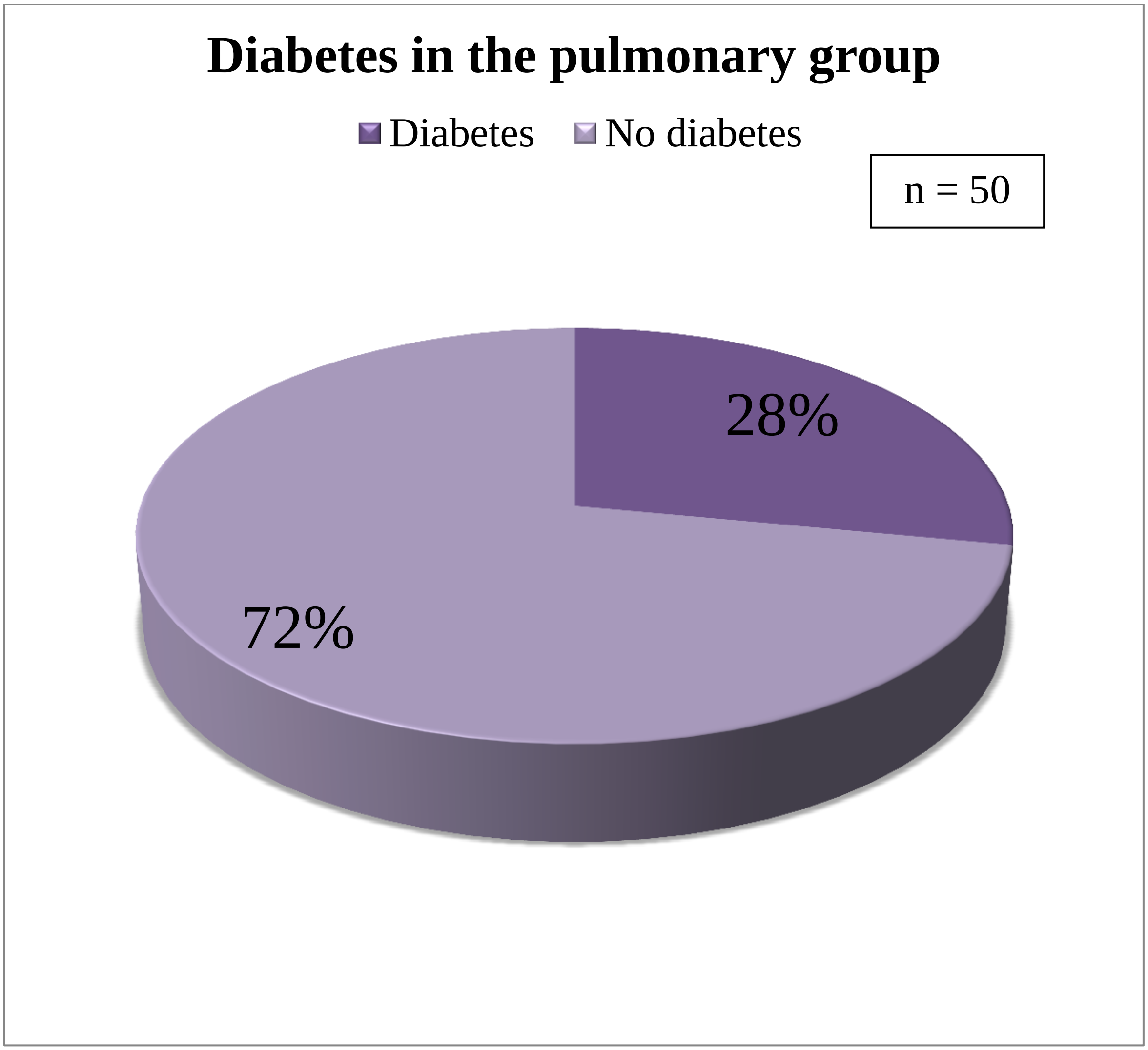


Figure 8a: Shows the percentage of patients with pulmonary cause for dyspnea who are diabetic.

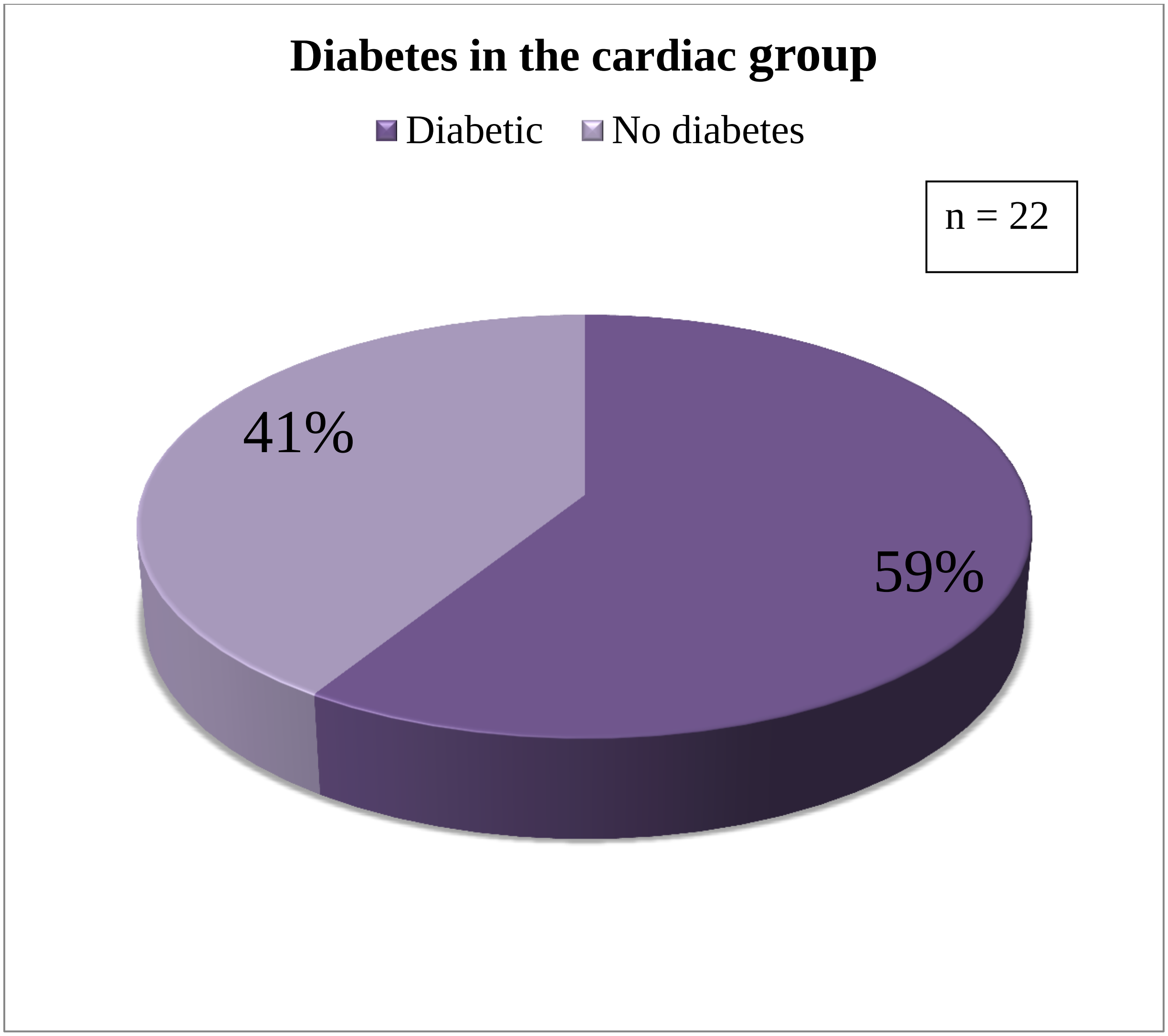


Figure 8b: Shows the percentage of patients with cardiac cause for dyspnea who are diabetic.

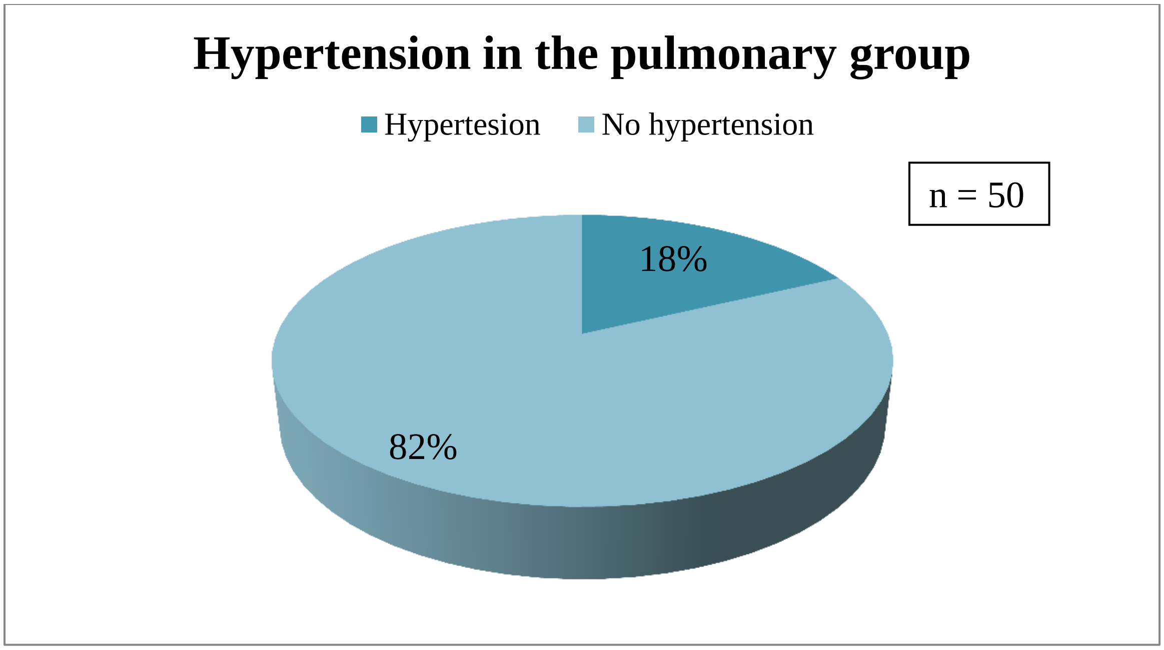


Figure 9a: Shows the percentage of patients with pulmonary cause for dyspnea who are hypertensive.

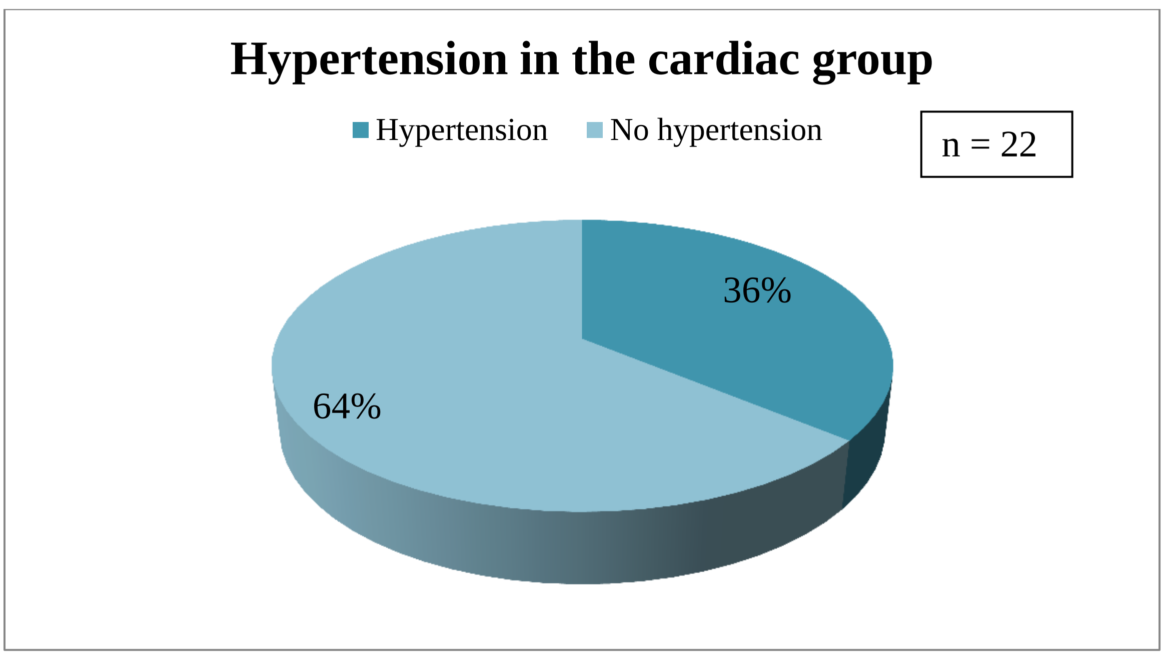


Figure 9b: Shows the percentage of patients with cardiac cause for dyspnea who are hypertensive.

The initial two pie charts represent the percentage of diabetics in each group of breathless patients. Of the people with pulmonary cause for dyspnea, 14(28%) out of 50 were diabetic. In the group with breathlessness due to a cardiac cause, 13(59%) out of 22 were diabetic. Hence there is a large difference in percentage of people with diabetes in both groups.

Patients presented with very high sugars which required insulin therapy for correction even if history suggested good glycemic control in the past. There were two patients who presented with hypoglycemia in the setting of acute worsening of the illness.

The next two pie charts explain hypertension in the patients who were studied for dyspnea in the emergency department. Out of the fifty patients who were breathless because of a pulmonary pathology, only 9(18%) were hypertensive. In the cardiac group, out of 22 patients 8(36%) were hypertensive. Hence hypertension and diabete were seen more in the patients with cardiac cause for dyspnea.

Despite the prior diagnosis of hypertension, some patients who presented to the emergency department had low blood pressures and persisted to be in shock despite fluid resuscitation. In contrast there were others who had very high blood pressures at presentation when acutely ill. They were treated by the emergency medicine medical officer with diuretics and occasionally nitroglycerine and blood pressures were hence brought under control.

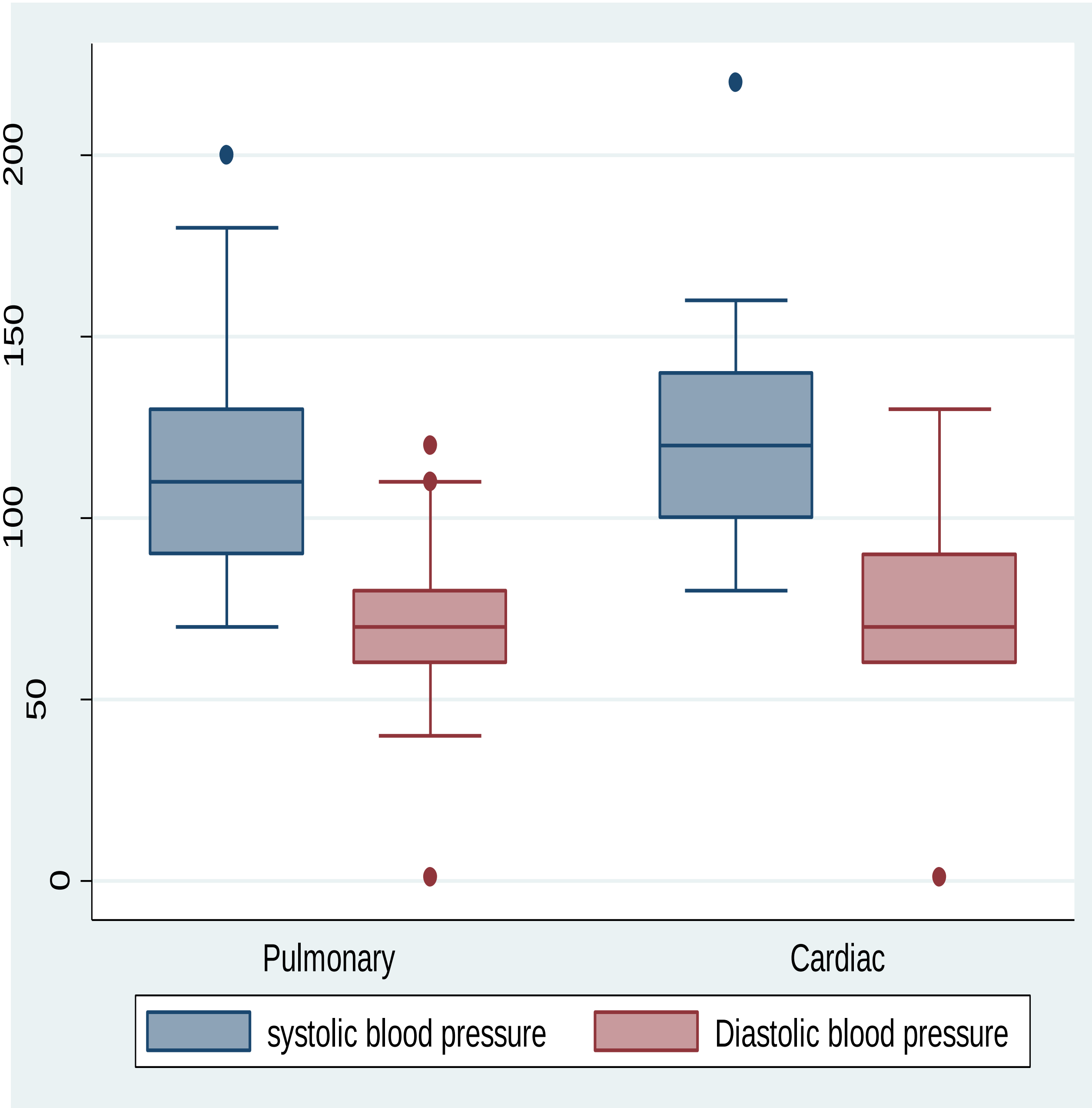


Figure 10: Graph representing the systolic and diastolic blood pressure median and range in both the cardiac and pulmonary dyspnea groups

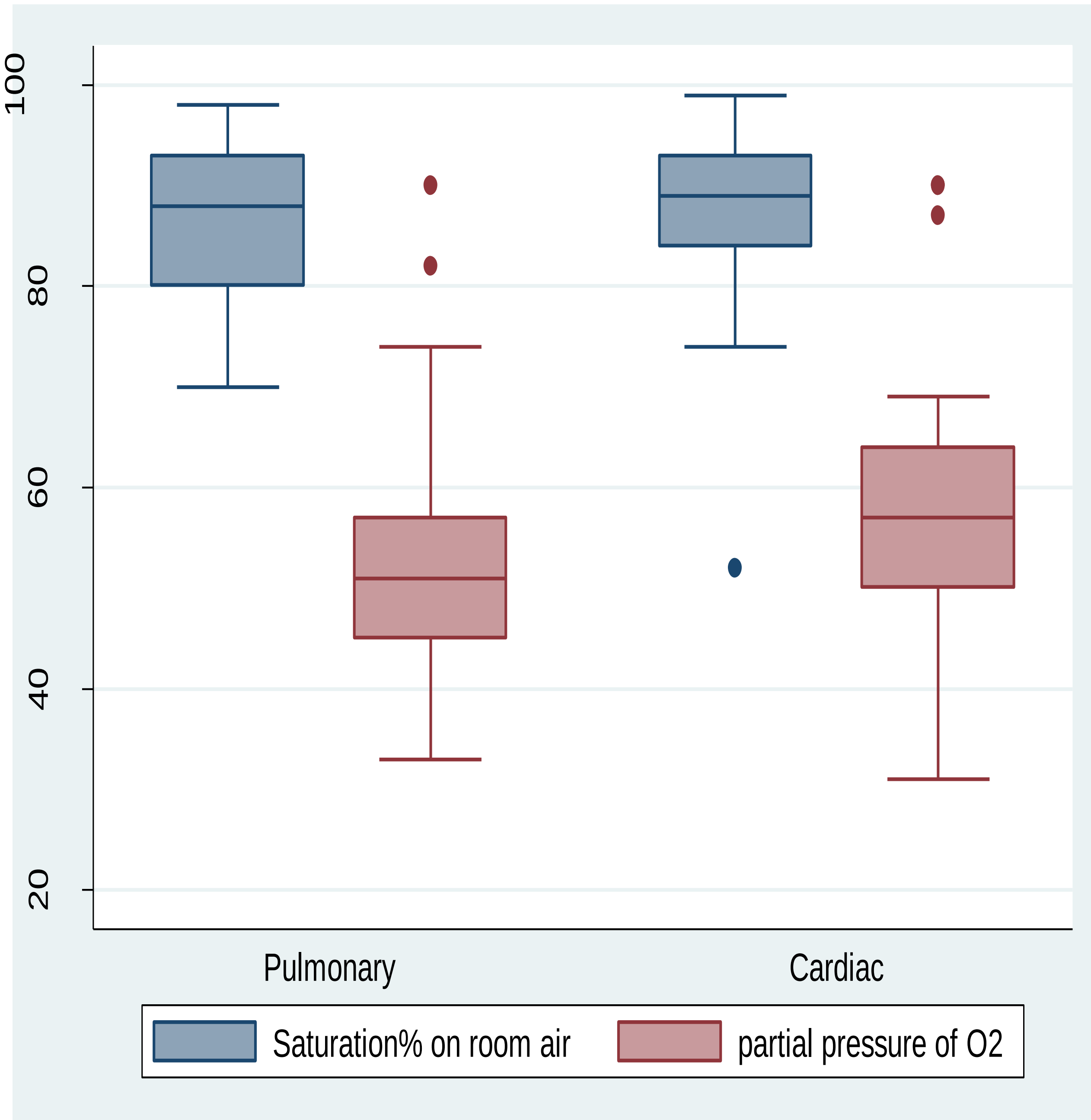


Figure 11: Graph representing the range and median values of saturation and partial pressure of oxygen in both the cardiac and pulmonary dyspnea groups

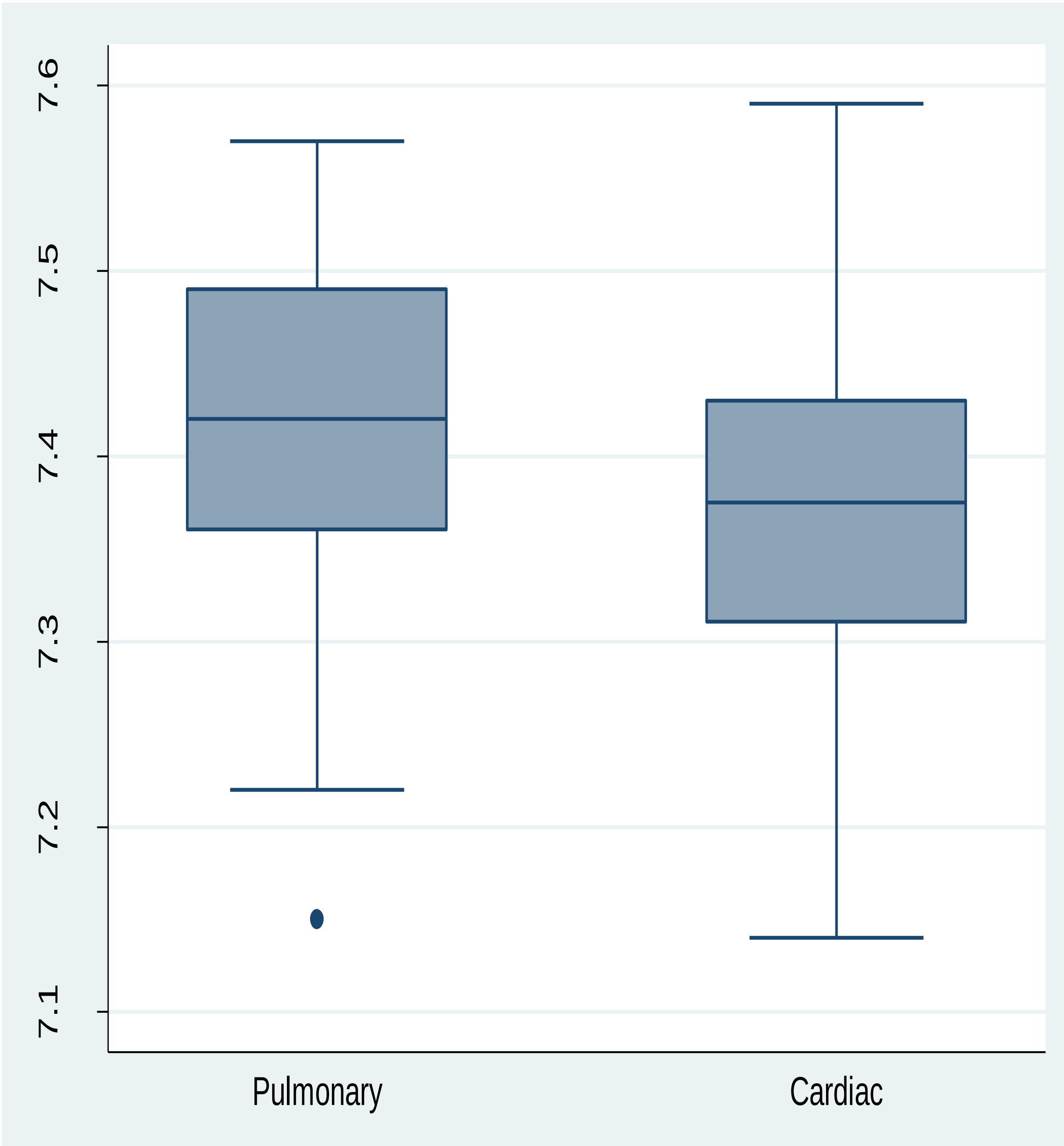


Figure 12: Graph representing the range and median values of the PH of arterial blood gas in both the cardiac and pulmonary dyspnea groups

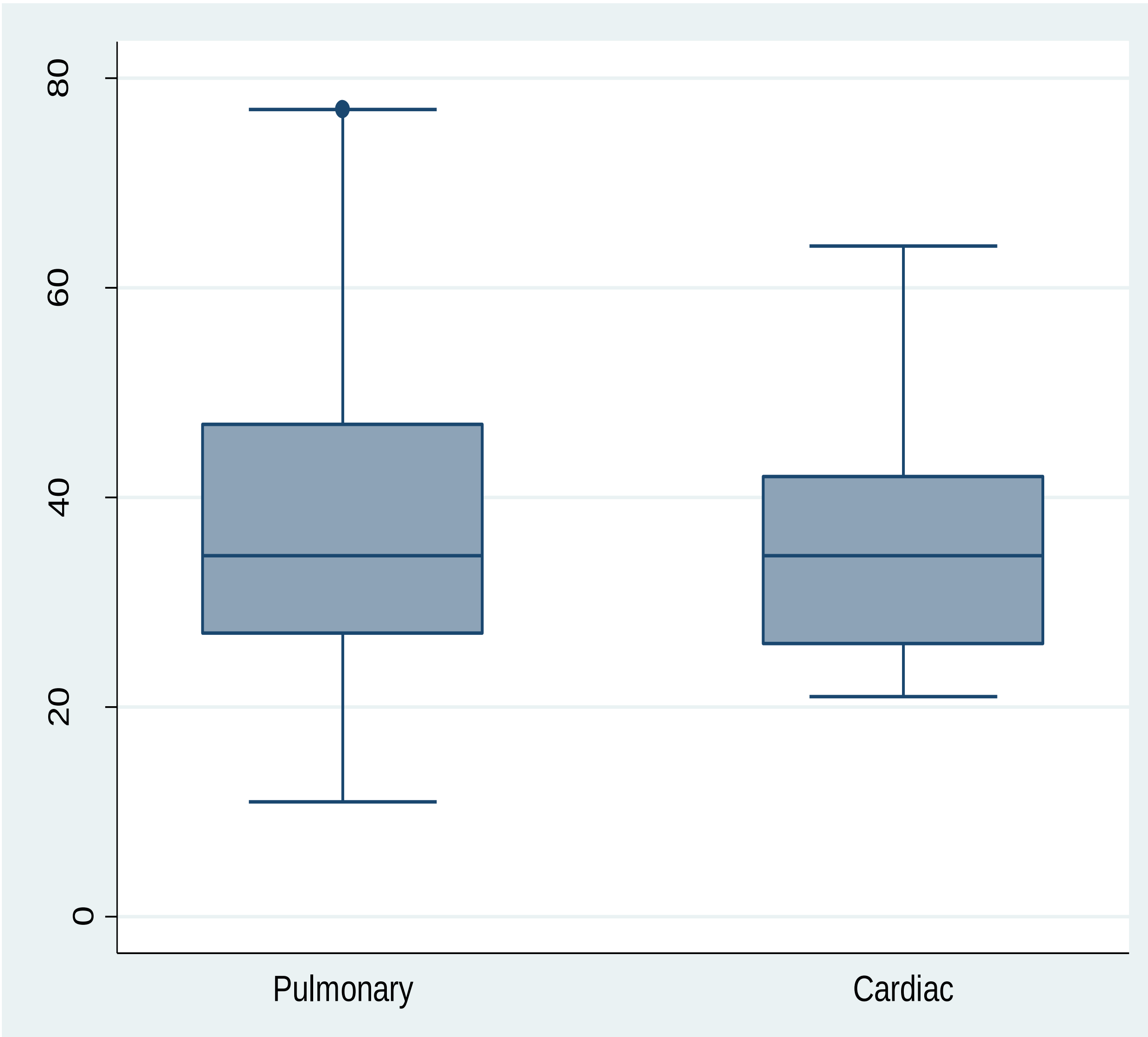


Figure 13: Graph representing the range and median values of partial pressure of carbon dioxide in both the cardiac and pulmonary dyspnea groups

The above four graphs represent various important parameters which were assessed for the breathless patients as they presented in the emergency department.

The systolic and diastolic blood pressures were measured at onset. The pulmonary group had a mean systolic blood pressure reading of 115.2 +/- 31, while that of the pulmonary group was 121.36 +/- 33.

Diastolic blood pressures likewise for the pulmonary group consisted of a mean of 69.2 +/- 19 and in the cardiac group 73.2 +/- 25.

The other parameters looked at were the saturations at presentation and it they were noted to have a similar distribution the cardiac and the pulmonary group. The partial pressure of carbon dioxide had a larger variation in the pulmonary group ranging from below 20 to above 70 mm of Hg

VARIABLE	PULMONARY (n = 50)	CARDIAC (n = 22)	BOTH (n = 8)
AGE			
<30	9 (18)	5 (22.7)	0
30 - 45	9 (18)	1 (4.5)	2 (25)
45 - 60	15 (30)	8 (36.36)	3 (37.5)
> 60	17 (34)	8 (36.36)	3(37.5)
SEX			
MALE	36 (72)	7 (31.82)	4 (50)
FEMALE	14 (28)	15 (68.18)	4 (50)

Table 1: Baseline characteristics of patients in the cardiac, pulmonary and overlap groups

VARIABLE	PULMONARY (n = 50)	CARDIAC (n = 22)	BOTH (n = 8)
SMOKING	18 (36)	4 (18.2)	3 (37.5)
PRIOR CVD	4 (8)	9 (41)	3 (37.5)
PRIOR KNOWN ILD	21 (42)	1 (4.6)	1 (12.5)
HTN	9 (18)	8 (36.4)	3 (37.5)
DM	14 (28)	13 (59.1)	3 (37.5)
SBP	115.2 +/- 31	121.36 +/- 33	106.25 +/- 11
DBP	69.2 +/- 19	73.2 +/- 25	68.8 +/- 8
SATURATION	86.6 +/- 7	87 +/- 10.3	83.25 +/- 9.6
PH	7.41 =/- 0.09	7.38 +/- 0.11	7.37 +/- 0.07

Table 1 (continued): Baseline characteristics of patients in the cardiac, pulmonary and overlap groups

Pulmonary dyspnea

VARIABLE	n	MEAN	S.D.
DDI	50	5.47	+/- 2.82
DDI%	50	1.31	+/- 0.68
Pco2	50	37.64	+/- 13.74
Po2	50	52.72	+/- 11.75
PEFR	50	101.80	+/- 37.51
PEFR%	50	24.38	+/- 10.72

Table 2: Table showing univariate analysis of the various parameters assessed in the study in the pulmonary group

As values were looked at separately for those with cardiac and pulmonary causes for breathlessness, it was noticed that there was a difference in range of values of DDI, % DDI and % PEFR. These values were tabulated and mean calculated. The lowest value for DDI noted was 1.65 with a maximum value of 13.12. The median was calculated to be 5.

For percentage DDI the mean value was 1.31 with a minimum value of 0.42 and a maximum of 3.39. The median value was calculated to be 1.10.

Mean for PEFR as elucidated in the table was 101.80 with a minimum value of 50, maximum of 200 and a median of100. Likewise PEFR percentage had a mean of 24.38 with a minimum value of 10.22 and maximum of 56. The median for the same was 22.26.

Final comparison of values had to be performed using a non-parametric because of the type of data obtained.

Cardiac dyspnea

VARIABLE	n	MEAN	S.D.
DDI	22	8.34	+/- 3.75
DDI%	22	2.34	+/- 1.14
Pco2	22	35.77	+/- 11.07
Po2	22	58.77	+/- 15.19
PEFR	22	145.00	+/- 58.70
PEFR%	22	40.67	+/- 16.82

Table 3: Table showing univariate analysis of the various parameters assessed in the study in the cardiac group

Univariate analysis done on the patients with dyspnea because of a cardiac cause was also assessed as given in the above table. For DDI the mean value was 8.34, with a minimum value of 2.80 and a maximum value of 16.10. The median value was 7.80.

For DDI% the mean value was calculated to be 2.34 with a minimum value of 0.77 and a maximum of 5.58. The median value here was 2.09.

PEFR was found to have a mean of 145, with a minimum value of 60 and a maximum of 260. The median was 150. For PEFR% the mean as tabulated above is 40.67 with a minimum value of 13.83 and a maximum value of 90. The median for the same was calculated to be 40.

Cardiac plus pulmonary dyspnea

VARIABLE	n	MEAN	S.D.
DDI	8	6.39	+/- 3.64
DDI%	8	1.53	+/- 0.73
Pco2	8	49.88	+/- 21.58
Po2	8	47.63	+/- 10.94
PEFR	8	132.50	+/- 76.86
PEFR%	8	31.88	+/- 14.90

Table 4: Table showing univariate analysis of the various parameters assessed in the study in the pulmonary plus cardiac group

Only eight patients studied had cardiac and pulmonary reasons for breathlessness. For DDI the mean value was 6.39, with a minimum value of 1.36 and a maximum value of 11.76. The median value was 5.83.

For DDI% the mean value was calculated to be 1.53 with a minimum value of 0.42 and a maximum of 2.55. The median value here was 1.58.

PEFR was found to have a mean of 132.5, with a minimum value of 40 and a maximum of 280.

The median was 110. For PEFR% the mean as tabulated above is 31.88 with a minimum value of 12.56 and a maximum value of 60.67.

The median for the same was calculated to be 30.40. The values for the mixed group were actually noted to be between those for cardiac and pulmonary.

VARIABLE	PULMONARY	CARDIAC	P VALUE
PCO2	37.64 +/- 13.74	35.77 +/- 11.07	0.75
PO2	52.72 +/- 11.75	58.77 +/- 15.19	0.06
PEFR	101.8 +/- 37.51	145 +/- 58.70	0.003
%PEFR	24.38 +/- 10.72	40.67 +/- 16.82	0.0001
DDI	5.47 +/- 2.82	8.34 +/- 3.75	0.001
%DDI	1.31 +/- 0.68	2.34 +/- 1.14	0.0001

Table 5: Wilcoxon rank sum test to comparing the two groups

Otherwise known as the Mann-Whitney test, the Wilcoxon rank sum test is a non-parametric test used to compare the two groups.

The results for PEFR, %PEFR, DDI and %DDI were all noted to have a significant difference. Hence the benefit in use of this tool in the emergency setting. After attaining these results we proceeded to calculate sensitivity and specificity for these parameters.

The difference between PEFR in the two groups had a p value of 0.003, for % PEFR it was 0.001.

For DDI it was noted to be 0.001 and for % DDI it was 0.0001.

The PO2 and PCo2 of the patients in the two groups was also compared. There was a difference but it was not statistically significant.

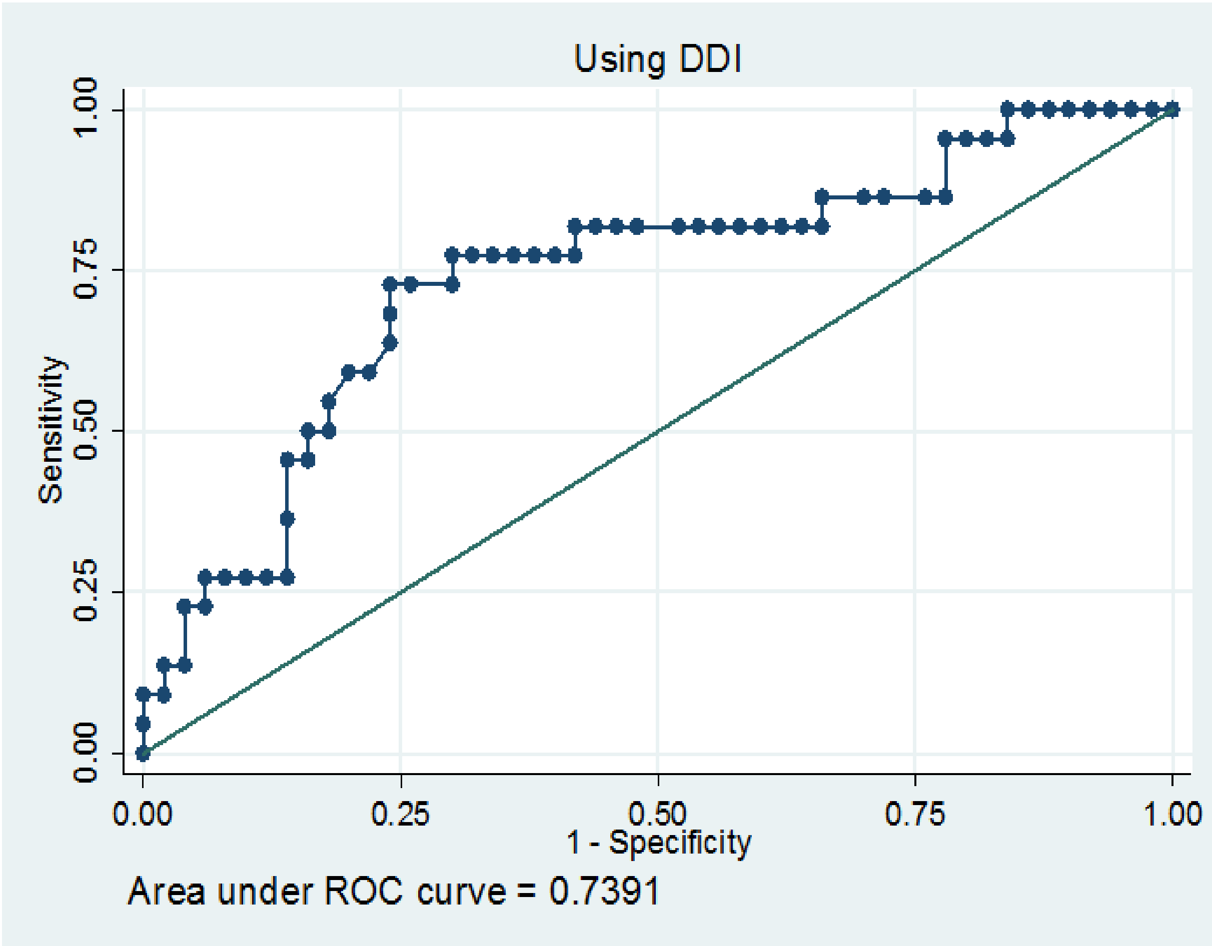


Figure 14: Receiver operator characteristic curve for Dyspnea discrimination index

With the values calculated for each patient for DDI, a receiver operator curve was drawn. The point of maximum sensitivity along with specificity was chosen from this curve as cut off.

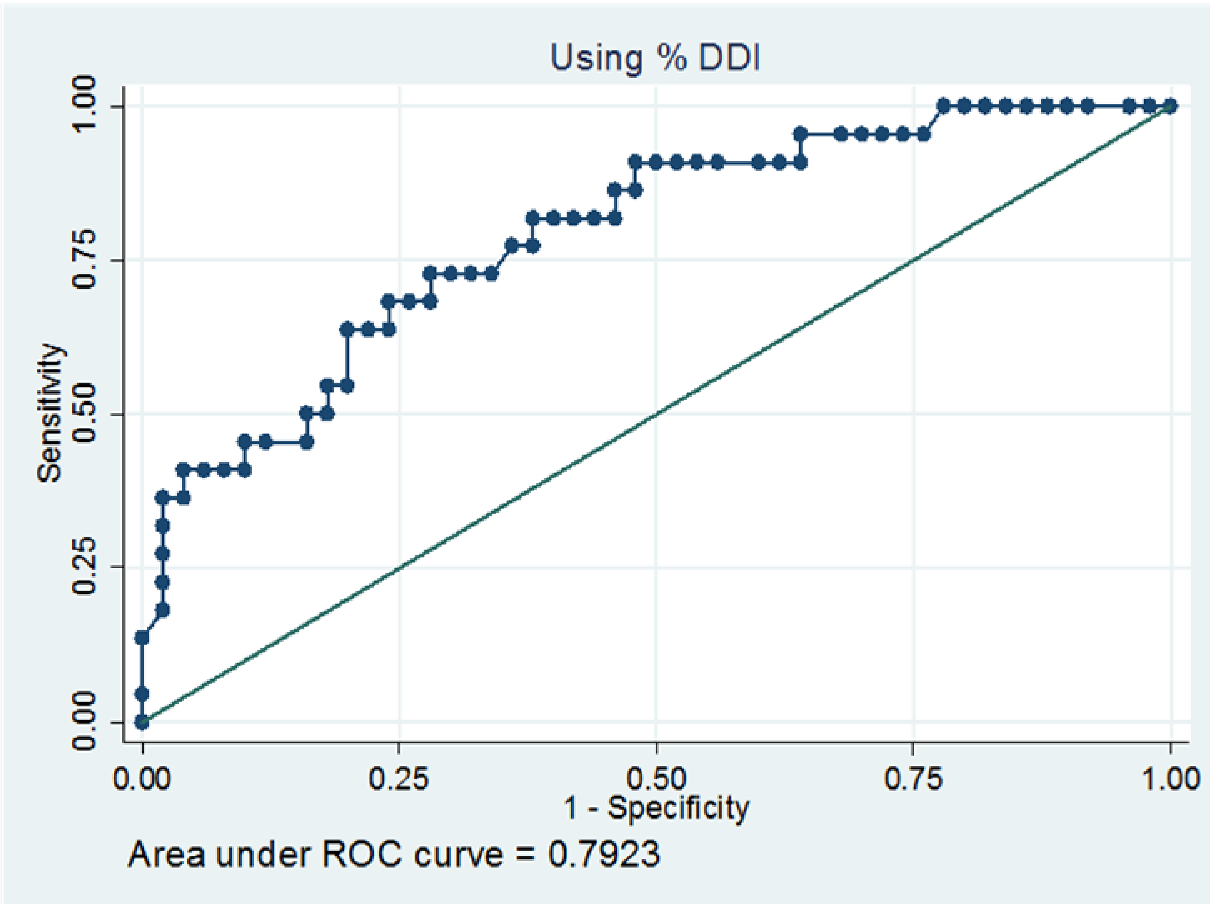


Figure 15: Receiver operator characteristic curve for percentage dyspnea discrimination index

Here also the point closest to the 'y' axis with maximum sensitivity and specificity was chosen and a cut off value was chosen. Area under the curve was calculated to be 0.79.

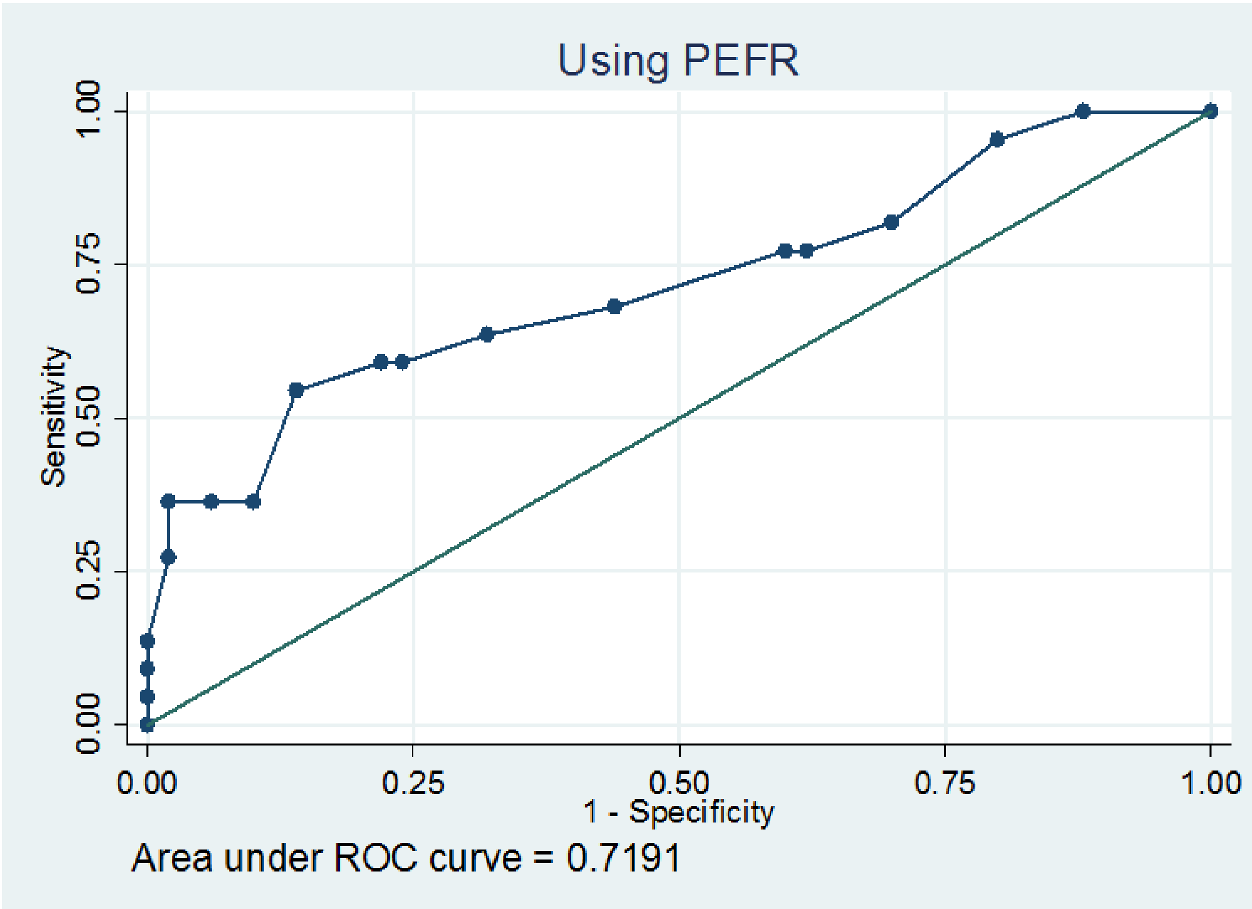


Figure 16: Receiver operator characteristic curve for peak expiratory flow rate

The area under the curve was calculated from this receiver operator curve to be 0.719. The point chosen with the best sensitivity and specificity was 140.

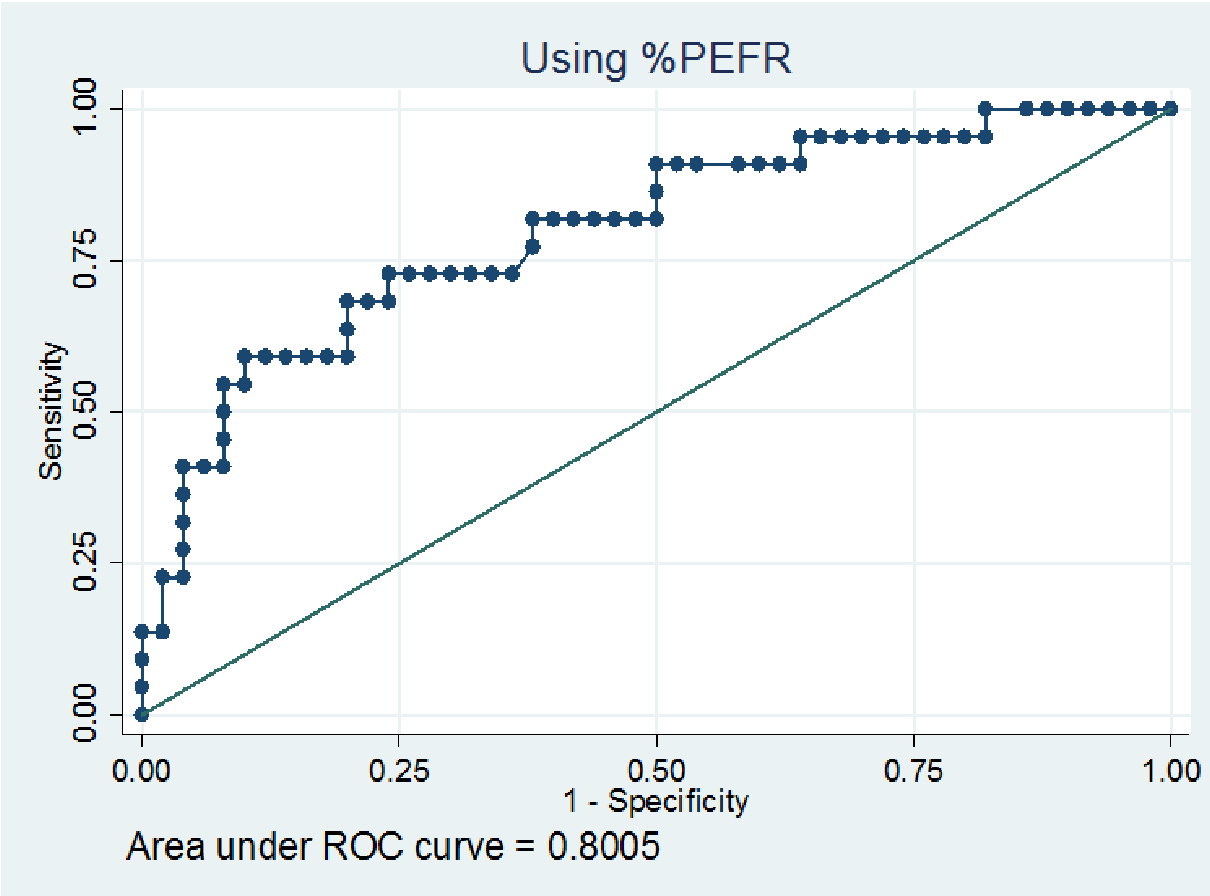


Figure 17: Receiver operator characteristic curve for percentage peak expiratory flow rate

The area under the curve was calculated from this receiver operator curve to be 0.8005. The point chosen with the best sensitivity and specificity was 31.11.

PEFR	140
PEFR %	31.11
DDI	6.3
DDI%	1.67

Table 6: Cut offs calculated from ROC curve

VARIABLE	SENSITIVITY %	SPECIFICITY %
PEFR	59.1	78
PEFR%	72.7	76
DDI	77.3	70
DDI%	72.7	72

Table 7: Sensitivity and specificity of DDI, %DDI, PEFR, %PEFR

The sensitivity and specificity of the tool was studied as a whole and PEFR as a separate component was also evaluated.

Sensitivity was 77.3% for DDI which was the documented highest of the scores while specificity was 70. DDI% improved on the specificity which was 72% and a sensitivity of 72.7%. The PEFR and PEFR percentage were less sensitive but both had higher specificities of 78% and 76% respectively. These values are similar to those published in the study done in Cleveland on their population.

VARIABLE	LR +	LR-	PPV%	NPV%
PEFR	0.685	2.69	54.2	81.3
PEFR%	3.03	0.359	57.1	86.4
DDI	2.58	0.325	53.1	87.5
DDI%	2.6	0.379	53.3	85.7

Table 8: Likelihood ratios, positive and negative predictive values of DDI, %DDI, PEFR, %PEFR

The other parameters calculated were positive and negative likelihood ratio, positive predictive value and negative predictive value.

%PEFR, DDI and %DDI were found to have good positive likelihood ratios with an adequately high negative predictive value, but a poor positive predictive value.

	Pulmonary	Cardiac	Both
Pulmonary	49(98%)	1(4.5%)	0
Cardiac	1(2%)	21(95.5%)	0
Both	0	0	8(100%)

Table 9: Represents the comparison between the diagnosis by ultrasound and the gold standard which is diagnosis at discharge

The above table elaborates the diagnosis made using the ultrasound machine, in comparison to the final diagnosis as gold standard. There was only one case in each group that was falsely diagnosed as the other. The diagnosis of a mixed cardiac and pulmonary condition was 100% correct.

Ultrasound is a very accurate tool. Difficulties arise only if there are lung problems like severe chronic obstructive pulmonary disease, where the visualization of the heart in the parasternal long axis view is difficult. Hence the difficulty is differentiating the cause of breathlessness.

The above table shows that the tool is accurate in diagnosing pathologies with both cardiac and pulmonary causes for breathlessness. If there were larger numbers in that group, results could have been interpreted with more significance.

SENSITIVITY %	98	89.4 – 99.9
SPECIFICITY %	95.5	77.2 – 99.9
LIKELIHOOD RATIO +	21.6	3.18 - 146
LIKELIHOOD RATIO -	0.021	0.003 – 0.146
PPV	98	89.4 – 99.9
NPV	95.5	77.2 – 99.9

Table 10: Table of sensitivity, specificity, positive and negative predictive values of USG as a tool to diagnose cause of dyspnea

The above table shows a sensitivity of 98% with a narrow confidence interval and a specificity of 95.5%. This also results in a positive likelihood ratio of 21.6 which makes the post test probability very high. The test also has a very high positive and negative predictive value of 98 and 95.5. Hence ultrasound has been proven to be very useful in discriminating cardiac and pulmonary cause for dyspnea.

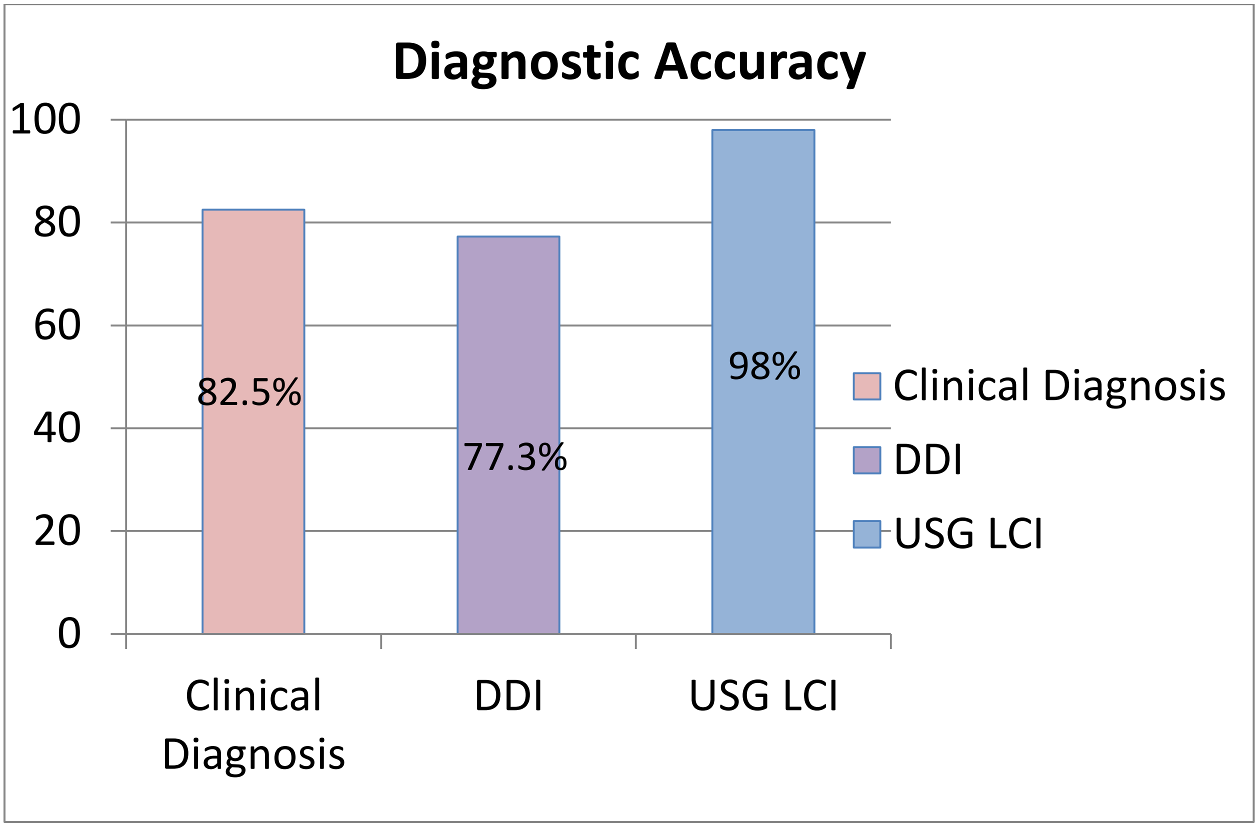


Figure 18: Graph representing diagnostic accuracy of the various methods studied

The diagnostic accuracy in the emergency department was calculated to be 82.5%, much higher than in studies published from elsewhere. As the sensitivity of DDI and associated scores was only 77% or less, in a situation where clinical diagnostics has better accuracy, these scores render no assistance. The ultrasound on the other hand has very high discriminative power and would be a useful tool in the emergency set up.

SENSITIVITY ANALYSIS

The following graph represents the spilt analysis of diagnostic accuracy of the casualty medical officers. The department ultrasound machine was availed of in July 2014. Hence this was done to see if there was a difference prior to acquisition of the same.

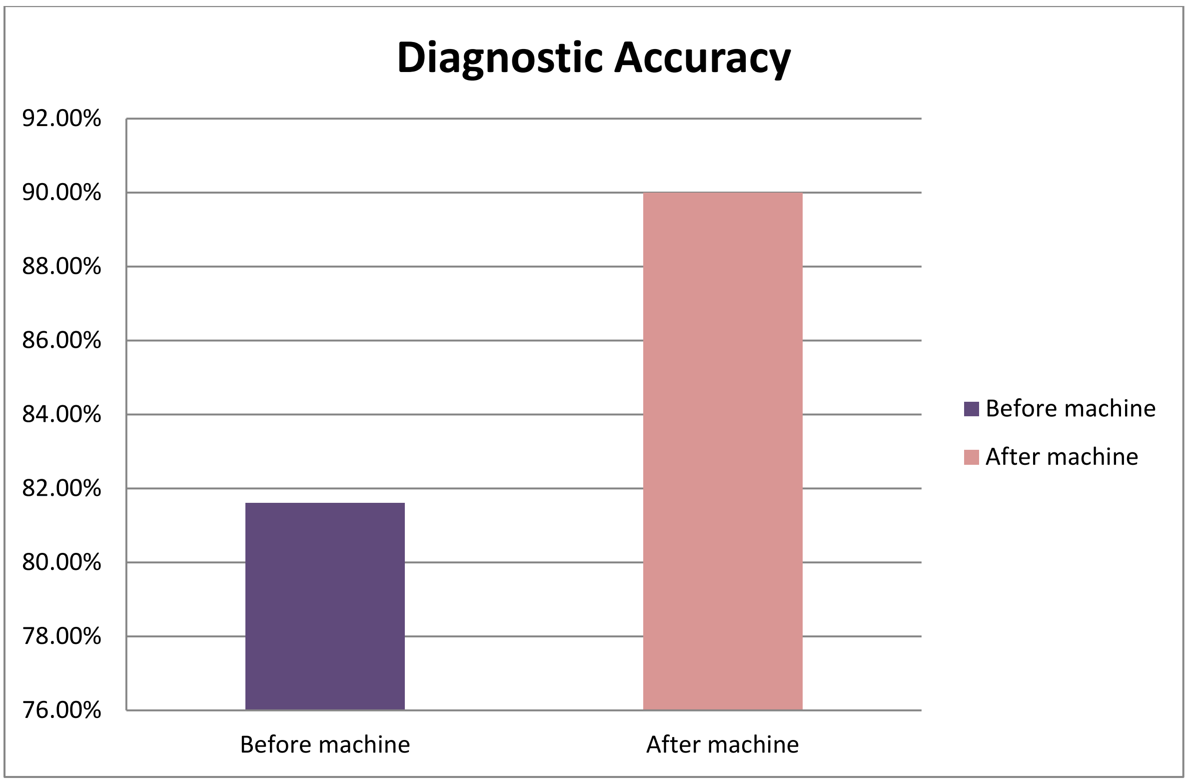


Figure 19: Bar graph of the diagnostic accuracy prior to and after the emergency department's acquisition of the ultrasound machine

Prior to July diagnostic accuracy was 81.6% and after the same it was noted to be 90%

Discriminate Model

Multivariate analysis that looks at the various parameters studied in combinations to see if another permutation of the same may be a more sensitive test.

On analysis of **partial pressure of carbon dioxide along with percentage PEFR**:

Out of 50 patients with pulmonary cause for breathlessness, 40 were diagnosed with this combination correctly while 10 were diagnosed falsely as a cardiac cause.

Out of the 22 patients with a cardiac cause for breathlessness this score diagnosed 15 correctly, but 7 were diagnosed falsely as pulmonary.

Hence the sensitivity of PCo2 along with %PEFR = 68.75%.

This hence has a lesser sensitivity than the original tool, discriminative power hence being poor.

The other combination looked at was **partial pressure of carbon dioxide with dyspnea discrimination index.**

Out of 50 patients with pulmonary cause for breathlessness, 41 were diagnosed with this combination correctly while 9 were diagnosed falsely as a cardiac cause.

Out of the 22 patients with a cardiac cause for breathlessness this score diagnosed 13 accurately, but 9 were diagnosed falsely as pulmonary.

Hence the sensitivity of PCo2 along with DDI = 67.5%.

This also has a lesser sensitivity than the original tool.

DDI% along with partial pressure of carbon dioxide as a scoring tool:

Out of 50 patients with pulmonary cause for breathlessness39 were diagnosed with this combination correctly while 11 were diagnosed falsely as a cardiac cause.

Out of the 22 patients with a cardiac cause for breathlessness this score diagnosed 14 correctly, but 8 were diagnosed falsely as pulmonary.

Hence the sensitivity of PCo2 along with %DDI = 66.25%.

This also has a lesser sensitivity than the original tool. As values in combination with partial pressure of carbon dioxide were lower than without the same, no further permutations and combinations were attempted.

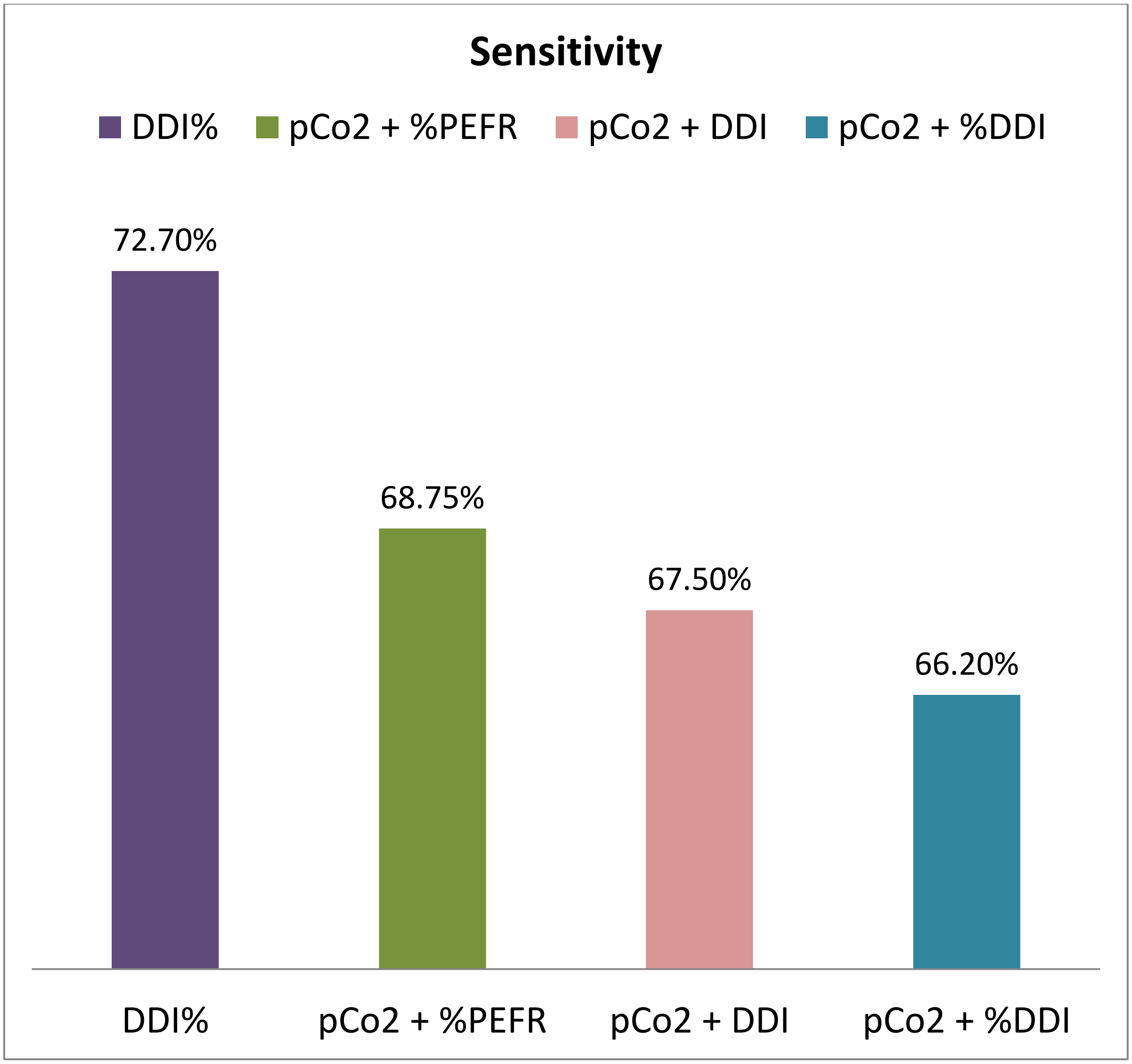


Figure 20: Discriminate model analysis

IMAGES FROM PATIENTS INCLUDED IN THE STUDY:

PHOTO 1: Liver with base of lung showing B lines

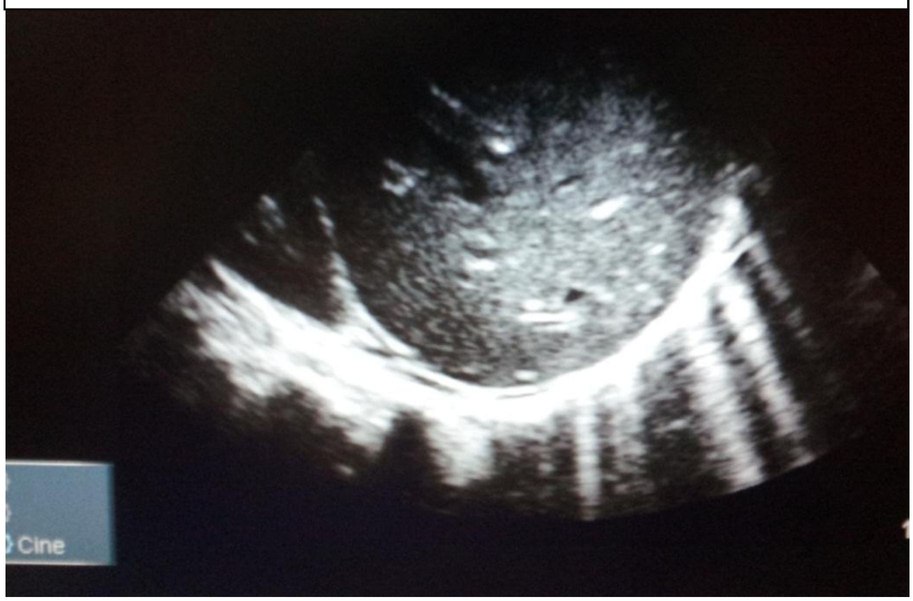


PHOTO 2: Diffuse B lines

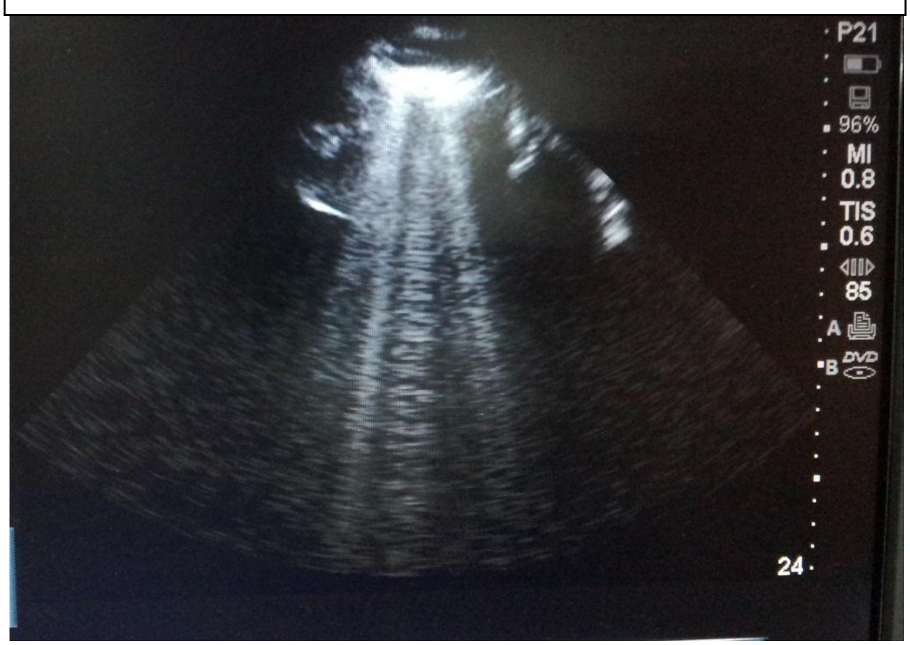


PHOTO 3: Liver with base of lung showing pleural effusion

PHOTO 4: Hepatic vein draining into the inferior vena cava

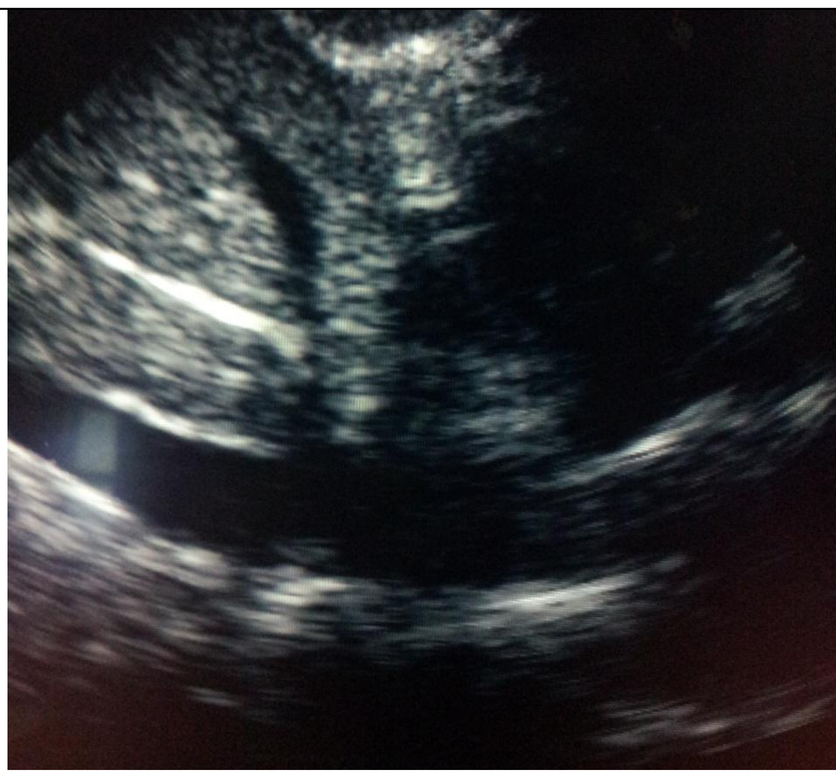


PHOTO 5: M mode for measurement of ejection fraction

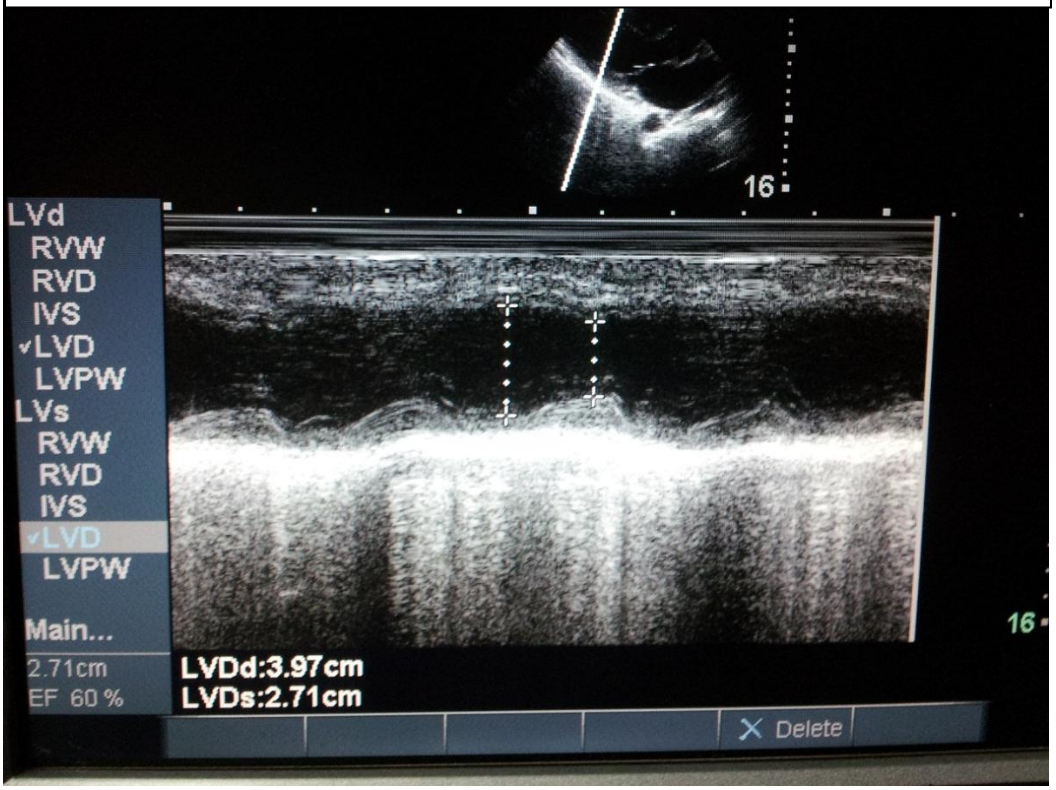
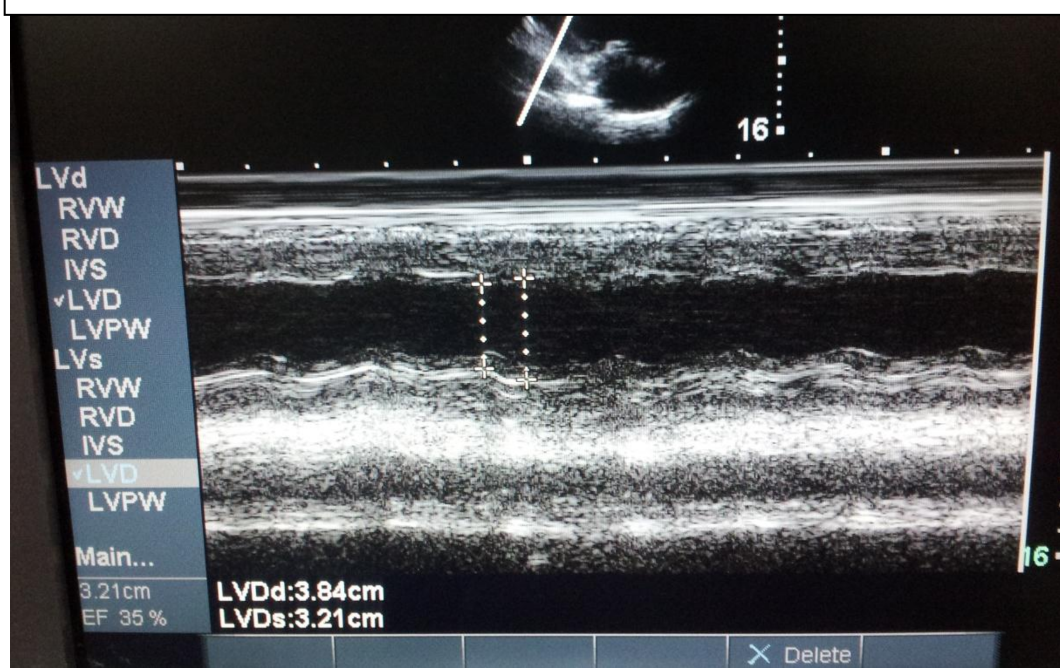


PHOTO 6: M mode for measurement of ejection fraction



DISCUSSION

This is the first ever study done in India evaluating a tool used in the emergency department to differentiate between a pulmonary and a cardiac cause for acute onset breathlessness. The study looked at two different bedside methods to assess breathlessness. The first is an index that includes a peak flow meter reading and the partial pressure of oxygen. In combination the test has been proven elsewhere to help in discrimination. These two entities were chosen in the score as they were thought to have the maximum difference in patients with cardiac and pulmonary causes for breathlessness. Hence in combination they were postulated to have an additive effect to diagnostic accuracy.

Among the patients that presented to our emergency department, there were more males than females. The largest number of people were in the age group between forty five and sixty years. There were more men than women who presented with pulmonary cause of breathlessness and more women than men who presented with cardiac cause for breathlessness. The group with both cardiac and pulmonary pathologies had equal number of men and women. There was larger number of patients with pulmonary cause of breathlessness which consisted of 62% of the patients assessed in this study. 28% were diagnosed to have a cardiac pathology and the remaining 10% had a combined cardiac and pulmonary pathology. On assessing some of the risk factors associated with breathlessness it was noticed that there were 36% smokers among those who presented with a pulmonary cause for breathlessness and 18% among those with cardiac cause for the same. 41% of those with cardiac cause of breathlessness had prior cardiac disease while 42% of those with pulmonary cause for breathlessness had prior lung disease.

A large percentage of the patients studied were diabetics. 59% of the cardiac dyspnea group were diabetic while 28% of the pulmonary dyspnea group were diabetic. There were less patients with hypertension than diabetes. 18% percent of the people in the pulmonary group and 36% of the people in the cardiac group were known to be hypertensive.

Other parameters looked at individually like the presenting saturation, arterial blood gas PH, partial pressure of oxygen and blood pressures at arrival as represented in the earlier mentioned table were similar between the two groups with vales varying based on severity of breathlessness and underlying individual pathology.

The Dyspnea discrimination index was assessed and there was a good difference noted between the cardiac and the pulmonary group. The mean value in the pulmonary group was 5.47 +/- 2.82 and in the cardiac group it was a higher value of 8.34 +/- 3.75. Using the Wilcoxon Rank Sum test the difference was noted to be significant with a p value of 0.001. Likewise for percentage DDI the values were 1.31 +/- 0.68 in the pulmonary group and 2.34 +/- 1.14 in the cardiac group with a significant difference (p value of 0.0001). ROC curves were drawn for the values and best cut offs were calculated. Using these cut offs the cause of breathlessness was tabulated with respect to the scores. Hence the sensitivity and specificity of the score in differentiation of cause of breathlessness was assessed. The sensitivity of Dyspnea discrimination index was 77.3% and the specificity was 70%. Percentage dyspnea discrimination index had a sensitivity of 72.7% and a specificity of 72%.

This tool was initially studied in Cleveland many years ago where the casualty medical officers' diagnostic accuracy with clinical assessment and basic available tests was only 69%. In our setting the casualty diagnostic accuracy is 82.5%. The reason for the same may be the casualty set up itself as the department is a medical department based team and there are medicine consultants on the floor at all times to aid in assessment and treatment. There is also the open system where all other departments are called in to help with assessment. It may be that with the opinion of the super specialist as a guide, the casualty medical officers diagnostic accuracy was higher than it would have been on its own. This still ultimately leads to the conclusion that the dyspnea discrimination index, though it does help differentiate a cardiac and pulmonary cause of breathlessness in the emergency department, will not be very useful in settings were clinical diagnostics are very good.

Other entities on their own were looked at using the same Wilcoxon Rank Sum Test to see if there was any statistical significance in their discriminatory ability. Peak expiratory flow rate had a mean of 101.8 +/- 37.51 in the pulmonary group and 145.00 +/- 58.70 in the cardiac group. The difference between the two also was found to be significant with a p value of 0.003. Percentage PEFR was also studied in the same manner and found to have a mean of 145.00 +/- 58.70 in the pulmonary group and 40.67 +/- 16.82 in the cardiac group. On assessing in a likewise manner with the Wilcoxon rank sum test the difference in percentage PEFR between the two groups it was found to be significant with a p value of 0.0001. These values were also plotted to formulate a ROC curve and the best cut offs were taken. The sensitivity of the PEFR was found to be 59.1% and the specificity was 78%. The sensitivity of %PEFR was 72.7% and specificity was

76%. Hence the PEFR on its own was not adequately sensitive whereas the PEFR% was more sensitive and specific on its own.

But none of these values were adequate to be used as a tool to improve diagnostic accuracy in the emergency department.

Advantages of the scoring tool

- The tool is easy to use and there is no expertise required to use it. It would actually serve well for use in a peripheral set up where experience may be less and facility also may be limited. It can be measured even by the nurses or technicians in the emergency department.

- It is inexpensive and disposable mouth pieces can be used so that the same peak flow meter can be used multiple times.

- It is a light weight instrument that can be carried around for use, especially in ambulance facilities and as a part of the outreach programs.

- The other component of the scoring tool is partial pressure of oxygen and is a part of standard of care in the management of patients with breathlessness. Hence it does not add any additional costs to what was already to be done for primary management.

- The score is easy to interpret with a simple cut off value.

Advantages of this tool may imply that its use in the peripheral set up where there are poor facilities and there are financial constraints, may be beneficial. One problem they may face though is the requirement of a blood gas analyzer. This facility may not be available in a remote set up.

Hence on looking back at the sensitivity and specificity of the individual values of the score it is obvious that %PEFR on its own is very good and can be used instead of the DDI tool as the advantage over the former is only a minimal increase in sensitivity.

Disadvantages of the scoring tool

- Moderate sensitivity and specificity. Hence not the ideal tool to enhance diagnostic accuracy.

- Very breathless patients cannot blow into the peak flow meter and hence values cannot be assessed for them. In such patients withholding oxygen until PEFR is measured is not justified and hence they cannot be assessed by this tool.

Hence in a tertiary care hospital this tool would not help adequately to discriminate between cardiac and pulmonary causes for breathlessness in the emergency department.

Discriminate Model:

The discriminate model analysis looked at other combinations other than peak expiratory flow rate along with partial pressure of oxygen from the arterial blood gas. Various permutations and combinations were attempted with partial pressure of carbon dioxide along with the dyspnea discrimination index or along with peak expiratory flow rate on its own.

This analysis revealed that combinations with partial pressure of carbon dioxide had poor discriminative power as per this model. On assessing all the possible combinations it was concluded that the entities with the maximum discriminative ability were peak expiratory flow rate and partial pressure of oxygen.

Ultrasound 'Lung Cardiac Inferior Vena Cava' screening tool

In the entire study done on 80 patients in the emergency department only two ultrasound diagnoses were not accurate. Hence the sensitivity was found to be 98% and the specificity was 95.5%. This was comparable to the study done by Kajimoto on this screening tool. Imaging findings of A lines, B lines and air bronchogram are simple and can be taught to all emergency physicians. The ejection fraction calculation is a slightly more complex measurement but also can be taught through short ultrasound training courses. After repeated scanning experience the ejection fraction can actually be approximated visually. The tool is ideal for tertiary and secondary care where diagnostic accuracy can be increased to almost a hundred percent. In some secondary care facilities there may not be an x ray machine. An ultrasound as it is cheaper than setting an x ray facility can help tide over that deficiency with respect to lung and cardiac imaging. Presently many peripheral hospitals already have an ultrasound machine which is used for obstetric purposes. The idea of extending the facility to assess the lung and the heart can be propagated among these people.

The likelihood ratios, the positive being 21.6 and the negative being 0.021 implies that whatever be the pretest probability, the post test probability will be very high.

Advantages of the LCI ultrasound screening tool

- Extremely good sensitivity and specificity in discriminating a cardiac and pulmonary cause for breathlessness.
- Minimal training is required to be able to do the scan
- Simple algorithmic method to finally come to a diagnosis
- The tool not only differentiates cardiac and pulmonary cause of breathlessness but is accurate with respect to the exact diagnosis itself.
- The ultrasound machine required to assess all that has been assessed as a part of the LCI screen is a simple hand held tool and there is no need for a complex device.
- Can be done immediately and there is no need for technical help, hence no waiting time.
- Can be done for the sickest of patients as they do not need to exert for the procedure.

Disadvantages of the LCI ultrasound screening tool

- Requires training before use.
- The ultrasound facility is required in the hospital where this is to be used.
- Cannot be transported as easily as the PEFR meter.
- In patients with emphysematous chest it is difficult to visualize the heart and hence the ejection fraction is visually approximated. This can cause errors if assessed by a less experienced person.
- A tool also looking at the right heart may help better in assessing disease like pulmonary embolism.

The advantages of this tool out way the disadvantages and hence confirm that it would benefit the emergency department to invest in an ultrasound machine that would help with diagnostics.

This is the first study done in the emergency set up in India which looks at the ultrasound as a tool for assessing cause of breathlessness.

Our emergency department availed of its own ultrasound machine midway through the study and the emergency department physicians also went for a training course on basic ultrasonography of the chest. They were not taught the LCI screening tool but were capable of assessing the lung and cardiac parameters on their own. Hence the doubt arose if the diagnostic accuracy was so high among the physicians because they were using their machine on their own in their initial assessment. To look at the difference between diagnostic accuracy before and after the day the ultrasound machine was procured, a sensitivity analysis was done.

Sensitivity analysis revealed that in the first part of the study when the Emergency department ultrasound machine was not available, the accuracy of diagnosis made by the casualty medical officer was 81.6%. In the second part, after the medical officers went for the critical course on ultrasound use the accuracy of diagnosis was 90%. Hence a difference was noted between the two time frames. This only reiterates the fact that ultrasound use in the emergency department will improve diagnostic accuracy by heaps and bounds and that will aid in accurate and fast treatment, hence benefiting mortality.

Hence ultimately comparing the three diagnostic modalities it was noted that that of the dyspnea discrimination index was lowest, clinical assessment of the casualty medical officer was a little better and the best and most accurate tool was the ultrasound screening.

The Indian scenario

There have been no Indian studies on ultrasound tools to looks at cause for breathlessness. There are a few publications from critical care units looking at ultrasound in shock and ultrasound assessment of the lung alone. A study published in Indian Journal Of Critical Care Medicine in April 2014 only looked at ultrasound in assessment of extravascular fluid volume among patients with shock in the intensive care unit(43). In this study they primarily looked at B lines found in all lung fields. There was another study published in Annals of Thoracic Medicine April 2014, which looked at B lines in lung ultrasound and the presence of interstitial lung disease. They have assessed distance between the B lines in ultrasound and compared the same with high resolution computed tomography scans of the lung. It was concluded that closely placed B lines suggest interstitial lung disease while B lines which are further apart are seen in pulmonary fibrosis(44)

There are no studies in India that look at heart assessment in the diagnosis of cause of breathlessness. This is surprising because echocardiography was far more utilized than lung ultrasound. These tools have been underutilized in the emergency department and this realization is what has triggered the Western studies that look at ultrasound assessment tools. It started off with algorithms involving only lung ultrasound. They eventually combined lung and cardiac ultrasound. Finally the algorithm used in this study with lung, inferior vena cava and cardiac imaging was postulated and studied. The evaluation of valvular heart lesions may aid in improving diagnosis but may need more training and can be time consuming. Hence studies with and without the assessment of the same may tell us if it is required.

Conclusion

The bedside tools assessed in this study showed good discriminative power between cardiac and pulmonary causes of breathlessness. As the diagnostic accuracy in our emergency department is good, the dyspnea discrimination index may not help differentiate the cause further. The ultrasound tool on the other hand has a very high sensitivity and specificity and will be ideal in a tertiary care emergency set up where it can be used in the emergency department to identify the exact cause for breathlessness.

Limitations

- A larger sample size with more patients assessed in each group would have given better results.
- As the emergency department procured an ultrasound machine during the course of the study, the accuracy of diagnosis of emergency physicians changed to a small extent.

Suggestions for future analysis

- Studies looking at LCI score along with assessment of valvular heart lesions may increase the diagnostic accuracy of the proposed ultrasound scan. But the evaluation should compare the new tool with the present LCI screen to see if benefit with respect to time and learning curve is present or not.

- The dyspnea discrimination index could be assessed as first line evaluation in the ambulance units that treat patients with some immediate care before reaching the hospital. It may be found useful in planning mode of therapy.

Clinical Application

The studied tools are useful in two different scenarios. The dyspnea discrimination index will help in a rural or peripheral health care setting to differentiate the cause of breathlessness and hence plan early management. On the other hand the ultrasound screening is a useful tool in a tertiary care set up where it will provide the exact diagnosis for which the appropriate therapy can be initiated without delay.

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Annexure

1. **Informed consent form**
2. **Thesis performa**
3. **Data sheet**

Christian Medical College, Vellore

Department of General medicine

INFORMED CONSENT FORM

Contact Information:

Dr. Gina Maryann Chandy

Department of General medicine

Christian medical college, Vellore- 632004

Purpose of Subject information & Consent form:

The purpose of this form is to inform you about this research study. If you sign this form, it means that you have agreed to take part in this study. The form describes the purpose, procedures, benefits, risks and side effects of the research study. It may contain words that you do not understand. Please ask the study doctor or personnel to explain any words or procedures that you do not clearly understand. You may also want to discuss this with your family and/or friends. You may refuse to take part or withdraw from this study at any time. This will not affect your medical care at the Christian Medical College (CMC) hospital.

Introduction:

You are being asked to participate in this study because you have come to the emergency department with the primary complaint of breathlessness which can be because of various causes. The usual dilemma is whether the original pathology is in the heart or the lungs. This study helps assess a tool which would make this discrimination easier. Advantage of this is that the accurate treatment will be started earlier which has been shown to improve outcomes.

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Purpose of the study:

The purpose of the study is to is to find a simple method which can differentiate breathing difficulty of cardiac and pulmonary etiology.

Procedures:

You will be asked to undergo the following tests when you come to the emergency department.

Peak expiratory flow recording:

You will be asked to blow fast through this device thrice to check your lung function. The best value will be taken for the study.

Arterial blood gas analysis:

You will undergo Allen's test which will be explained by your doctor, followed by arterial blood sampling using an ABG syringe with 26 G needle from the radial artery & the sample will be sent for blood gas analysis.

Measurement of NT pro BNP:

Along with the baseline parameters usually checked on a patient who presents with breathing difficulty, an additional biochemical marker will be sent called NT pro BNP which also helps pinpoint the cause of breathlessness. The sample taking will not cause any extra discomfort and there are no additional risks involved.

Potential Risks & Discomforts:

This study does not involve any new drugs or treatment. It involves adding additional tests for the diagnosis of breathing difficulty & tests currently used. The risks are mainly related to procedures ; arterial blood gas (ABG) that is done routinely for the diagnosis of your condition outside of this trial as well. The most common problems from ABG include temporary soreness, bruising & rarely bleeding, numbness of hand, where the needle is inserted.

Potential benefits:

Your participation may provide the medical community a new, simple rapid test to find the cause for breathing difficulty in the emergency department , which will help us administer better care.

Confidentiality:

All of the information that we obtain during this research will be kept confidential. No one other than the study investigators will know your identity from our files. The results of this research study may be presented at meetings or in scientific publications; however, your identity will not be disclosed in any of these presentations. As part of this study, we will request your authorization to access information from your medical files from the CMC hospital. The ethics committee of CMC Vellore may also access your medical files.

Voluntary participation & withdrawal:

It is entirely your choice whether or not you participate in this research study. If you decide not to participate, your current and future medical care at the CMC will not be affected by this choice. You may decide to withdraw from this study at any time. Your participation in this study may be terminated by you, or your study investigators.

Legal Rights:

You are not waiving any of your legal rights by participating in this study or by signing this consent form. This includes, for example, the right to seek damages under law for any research related injury.

SUBJECT INFORMED CONSENT:

1. I understand that this is a research study.

2. I have read all the pages of the consent form. The research personnel have explained the information and procedures involved in the study. I have had the opportunity to ask questions and my questions have been answered satisfactorily. I have been given time to consider the information carefully and to decide whether or not to participate in this study.

3. I have been informed that my participation in this study is entirely voluntary and that I may refuse to participate, or withdraw at any time, without any consequences to my ongoing and future medical care at this institution.

4. I authorize the release of my medical records to the study investigators as well as the ethics committee of CMC Vellore for purposes of this study only. This authorization will be valid for a period of 5 years.

5. I understand that I will be given a copy of this informed consent form to keep for my own information, once it is signed. I have been informed that a copy of this consent form will be placed in my medical chart so that health care providers at this institution will know that I am participating in a study and what is involved.

6. I understand that I do not give up any of my legal rights by signing this form nor am I freeing the investigators, sponsors, or the health establishment where the study takes place from their civil and professional responsibilities.

1. My signature below indicates that I voluntarily agree to take part in this study.

__________________________ ________________ _____________

Subject's signature Name (in block letters) Date

__________________________ _______________ ______________

Signature of Person Date

Administering Informed Consent Name (in block letters)

I confirm having met with the subject at the time of enrolment and have I have answered his/her questions about this study.

Investigator or Project coordinator's signature

Name (in block letters) Date

Dyspnea Discrimination Index (DDI) study:

Performa:

1. Name of the patient:
2. Age (In years):
3. Sex: (1-male, 2- female)
4. Hospital number:
5. History:
   - Smoking: (1- Yes, 2- No)
   - If yes, Pack years:

   [No. of pack-years = (No. of cigarettes smoked per day × No. of years smoked)/20] (1 pack has 20 cigarettes)

   - Alcohol: (1- Yes, 2- No)
   - Past history of Myocardial infarction: (1-Yes, 2- No)
   - Diabetes: (1-Yes, 2- No)
   - Hypertension: (1-Yes, 2- No)

6. Vitals at admission:
   - Pulse: /min
   - Blood pressure: mm Hg
   - Respiratory rate: /min
   - Saturation: %(Room air)

7. Diagnosis in ED:

8. Height (in cm) or length(in cm):

9. Predicted PEFR:
10. % PEFR:
    Trial i)
    Trial ii)
    Trial iii)

11. ABG values:

pH	PCO2	PO2	HCO3	Lactate	BE

12. DDI: (PEFR* PaO2)÷1000=
13. Ultrasound:
    a. Lung USG:(1- A lines, 2- B lines, 3- consolidation, 4- absent lung sliding, 5- pleural effusion)

	Right	left
Infraclavicular		
mammary		
Upper axillary		
Lower axillary		
Upper interscapular		
Lower interscapular		

    b. Cardiac USG:
    LV function- (nomal-1, dysfunction-2),
    EF: %
    c. IVC: Variability- (yes-1, No-2)

12. ECG: (1-Sinus tachycardia, 2- AF, 3- ACS, 4- Bundle branch blocks, 5- Heart block, 6- VT/V.fib, 7-Ventricular hypertrophy)

13. Chest X ray:

14. Cardiac markers:

Time of sampling	CK-MB	Troponin T

15. Final diagnosis:

16. Condition at discharge: (1-Discharged, 2- Death)