Cardiomegaly is a catch-all term to refer to enlargement of the heart, and should not be confused with causes of enlargement of the cardiomediastinal outline, or enlargement of the cardiac silhouette.

Pathology

Etiology

There are many etiologies for cardiomegaly:

- congestive heart failure
- ischemic heart disease
- hypertension (with left ventricular hypertrophy)
- valvular disease
    - mitral regurgitation
    - tricuspid regurgitation
    - aortic stenosis
    - aortic regurgitation
    - subacute bacterial endocarditis
- cardiomyopathy
    - idiopathic cardiomyopathy
    - alcoholic cardiomyopathy
    - hypertrophic cardiomyopathy
    - drugs (numerous drugs are cardiotoxic)
- congenital heart disorders
    - ASD
    - VSD
    - PDA
    - coarctation of the aorta
    - Ebstein anomaly
    - tetralogy of Fallot
- pulmonary disease (leading to right-sided enlargement)
    - pulmonary embolism
    - COPD
    - cor pulmonale
    - primary pulmonary hypertension

- myocarditis
- systemic disease/physiology
    - normal “athletic” heart
    - pregnancy
    - renal failure
    - anemia
    - scleroderma
    - systemic lupus erythematosus
    - sickle cell disease
    - rheumatoid arthritis
    - Marfan syndrome
    - post-radiation

Radiographic features

In most cases, merely 'eye-balling' a chest x-ray will be sufficient in detecting cardiomegaly (as the heart is either clearly normal in size or clearly abnormally enlarged). In equivocal cases, the cardiothoracic ratio (CTR) can be easily calculated on a PA chest x-ray. The CTR measures the width of the cardiac silhouette and the thoracic cavity; a ratio greater than 0.5 is an abnormal finding.

Specific cardiac chamber enlargement can be recognized by cardiac contour changes, new or different interfaces with adjacent lung, and/or displacement of adjacent mediastinal structures. These are discussed separately:

- right atrial enlargement
- right ventricular enlargement
- left atrial enlargement
- left ventricular enlargement

Cardiomegaly is an umbrella designation for various conditions leading to heart enlargement, which usually remains undiagnosed until the symptoms ensue. It has become increasingly prevalent and carries a high mortality. Cardiomegaly means enlargement of the heart. The definition is when the transverse diameter of the cardiac silhouette is greater than or equal to 50% of the transverse diameter of the chest (increased cardiothoracic ratio) on a posterior-anterior projection of a chest radiograph or a computed tomography. This activity reviews the etiology, epidemiology, pathophysiology, signs and symptoms, evaluation, and management of cardiomegaly. It highlights the role of the interprofessional team in improving outcomes for patients with this condition.

Objectives:

- Identify the risk factors for developing cardiomegaly.
- Assess the typical presentation of a patient with cardiomegaly.

- Evaluate the treatment considerations in a patient with cardiomegaly.
- Communicate the importance of improving care coordination amongst the interprofessional team to enhance care delivery for patients affected by cardiomegaly.

Access free multiple choice questions on this topic.

Go to:

Introduction

Cardiomegaly means enlargement of the heart. The definition is when the transverse diameter of the cardiac silhouette is greater than or equal to 50% of the transverse diameter of the chest (increased cardiothoracic ratio) on a posterior-anterior projection of a chest radiograph or a computed tomography. It should not be confused with an enlargement of the cardiomediastinal outline. Cardiomegaly is usually a manifestation of another pathologic process and presents with several forms of primary or acquired cardiomyopathies. It may involve enlargement of the right, left, or ventricles or the atria. Many types of cardiomyopathy, such as dilated cardiomyopathy, are characterized by left ventricular dilation and systolic dysfunction, although right ventricular impairment and diastolic dysfunction can also develop.[1]

Go to:

Etiology

Several etiologies have been attributed to the development of cardiomegaly, resulting in either dilated or hypertrophic cardiomyopathy. These include the following:

- Coronary artery disease, including myocardial infarction and ischemia (most common cause)[2]
- Hypertensive heart disease[3]
- Valvular heart diseases, including stenosis or regurgitation of the aortic, mitral, pulmonary, or tricuspid valves and sub-acute bacterial endocarditis[4]
- Congenital heart disorders, including atrial septal defect, ventricular septal defect, patent ductus arteriosus, tetralogy of Fallot, Ebstein anomaly, and coarctation of the aorta
- Pulmonary diseases such as primary pulmonary hypertension, chronic obstructive pulmonary disease, obesity hypoventilation syndrome, and pulmonary embolism with cor-pulmonale[5]
- Infectious myocarditis secondary to viral infection (most common), HIV, Chaga disease[6]
- Infiltrative/deposition diseases, such as amyloidosis, sarcoidosis, hypothyroidism, acromegaly, and hemochromatosis[7]
- Toxin-induced cardiomyopathy (alcohol, cocaine, chemotherapeutic agents such as doxorubicin, cyclophosphamide, trastuzumab, and radiation)[8]
- Autoimmune cardiomyopathy, including eosinophilic myocarditis, idiopathic giant cell myocarditis, and collagen vascular disease
- Arrhythmia, including atrial fibrillation and flutter leading to tachycardia-induced cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy with the fibro-fatty replacement of RV

- Systemic diseases leading to a high output state, including anemia, hyperthyroidism, vitamin B1 deficiency (“beriberi”), and AV fistula[9]
- Physiologic conditions include stress cardiomyopathy, exercise-induced cardiomegaly or “athletic” heart, and pregnancy
- Familial cardiomyopathy, hypertrophic obstructive cardiomyopathy[10]
- Peripartum cardiomyopathy[11]
- Idiopathic cardiomyopathy[12][13][14]

Go to:

Epidemiology

Enlargement of the heart, both in the form of dilatation or hypertrophy, leads to a spectrum of clinical heart failure syndrome, with a prevalence of nearly 5.8 million people in the United States. Heart failure with preserved ejection fraction represents more than half of these cases. The incidence of heart failure increases with age, male gender, and African American race. About half of the people diagnosed with heart failure die within 5 years of diagnosis.[15] In adults, dilated cardiomyopathy is more prevalent in men than in women. In the pediatric population, the annual incidence is 0.57 cases per 100,000 per year (higher in boys than girls, in Blacks than Whites, and in babies less than 1 year than in children). Two-thirds of children have idiopathic disease.[16] Hypertrophic cardiomyopathy is a global disease, with cases in over 50 countries on all continents, affecting both sexes and of several ethnic and racial origins.[17] In diverse regions, such as the USA, Europe, China, Japan, and East Africa, hypertrophic cardiomyopathy is a common genetic cardiac disease, having a prevalence of around 1 in 500 in the general population.[18]

Go to:

Pathophysiology

The development of cardiac remodeling and hypertrophy is complex, with genetic and non-genetic components. The most critical pathophysiological changes leading to cardiomegaly include dilated hypertrophy, fibrosis, and contractile malfunction. Contractile dysfunction and abnormal myocardial remodeling can lead to hypertrophic cardiomyopathy or dilated cardiomyopathy. Mechanical stretching, circulating neurohormones, and oxidative stress are significant stimuli for the signal transduction of inflammatory cytokines and MAP kinase in cardiomyocytes. Signal transduction leads to changes in structural proteins and proteins that regulate excitation-contraction. Dilated cardiomyopathy mutations result in a reduced force of the sarcomere contraction and a reduction in sarcomere content. Hypertrophic cardiomyopathy mutations result in a molecular phenotype of hyperdynamic contractility, poor relaxation, and increased energy consumption.[19][20]

Pathophysiological mechanisms can vary depending on the underlying cause of cardiomyopathy. For instance, in diabetic cardiomyopathy, fatty acid metabolism is enhanced, glucose oxidation is suppressed, and intracellular signaling is modified, causing impairment in multiple steps of inefficient energy production, excitation-contraction coupling, and increased potential for ischemia/reperfusion injury. In alcohol-induced cardiomyopathy, cell death due to apoptosis ultimately leads to changes in various aspects of myocyte function.[21] In mitochondrial cardiomyopathy, multiple biochemical pathways involving mitochondria impair oxidative phosphorylation.[22] Peripartum cardiomyopathy is associated with genetic alterations, angiogenic imbalance, oxidative stress, and the production of a prolactin fragment.[23] In hypertrophic cardiomyopathy, ventricular hypertrophy results in a dynamic

pressure gradient across the left ventricular outflow tract, associated with further narrowing during systole. During this cardiac cycle, the mitral valve is pulled towards the septum by several proposed mechanisms: contraction of the papillary muscles, abnormal location in the outflow tract, and low pressure that occurs as blood is ejected at high velocity through a narrowed outflow tract (Venturi effect).[24]

Go to:

History and Physical

Many patients with cardiomegaly are asymptomatic, and the presence of symptoms alone is neither sensitive nor specific to diagnosis. The diagnosis of cardiomegaly is based on imaging, and history is only helpful in determining the cause of heart failure symptoms, resulting in systemic congestion and impaired organ perfusion.[25] A detailed history should elicit the presence or absence of the following:

- Shortness of breath on exertion or rest, orthopnea, and paroxysmal nocturnal dyspnea
- Peripheral edema and abdominal distension
- Fatigue and poor exercise tolerance
- Palpitations, lightheadedness, or syncope[26]
- Angina
- Anorexia, nausea, and early satiety
- Family history of cardiomyopathy
- Recent pregnancy/childbirth
- Comorbid illnesses, such as hypertension and diabetes mellitus

It is worth mentioning that cardiac function is adequate during rest and may become inadequate with exertion. Hence, it is not uncommon for patients to be asymptomatic at rest and experience symptoms only on exertion. The New York Heart Association classifies the severity of disease based on symptoms, where class I disease is asymptomatic with ordinary physical activity, and class IV denotes symptoms with rest. Perhaps the most specific sign of cardiomegaly is a displaced maximal impulse (PMI) point.[27] The precordial examination reveals a displaced PMI, usually below the 5th intercostal space, lateral to the midclavicular line, and palpable across 2 intercostal spaces. Sustained PMI is a sign of severe left ventricular hypertrophy. A sustained and prolonged left parasternal heave is indicative of right ventricular hypertrophy. Another physical finding observed in cardiomegaly is the holosystolic murmur of mitral or tricuspid regurgitation resulting from dilatation of the mitral annulus and displacement of papillary muscles with abnormal myocardial remodeling. Other exam findings may be seen depending on the presence or absence of decompensated heart failure. In such cases, a detailed physical exam may reveal the following abnormalities:

- Sinus tachycardia resulting from increased sympathetic drive
- Diminished pulse pressure reflecting reduced stroke volume
- Varying degrees of respiratory distress based on the severity of the disease
- Cool, cyanotic extremities secondary to peripheral vasoconstriction

- Jugular venous distension or positive abdominojugular reflex indicating elevated right-sided filling pressures
- Ascites, hepatomegaly, and peripheral edema result from increased pressure in the hepatic veins and systemic veins[28]
- Pulmonary crackles resulting from elevated left-sided filling pressure and transudation of fluid into alveoli
- S3 gallop in early diastole resulting from volume overload and systolic dysfunction; S4 gallop in late diastole resulting from diastolic dysfunction

Go to:

Evaluation

Diagnosis of cardiomegaly is primarily through imaging techniques that assess the heart's size and function. Diagnostic testing includes 1 of the following:

- A chest X-ray with an enlarged cardiac silhouette and a cardiothoracic ratio of more than 50% suggests cardiomegaly.[29] Further delineation of specific chamber enlargement is also possible. Right ventricle (RV) enlargement produces an upward deviation of the left apical margin, while left ventricle enlargement leads to a leftward displacement of the left heart border. Right atrial (RA) enlargement increases the right heart border convexity. Left atrial enlargement and its extension to the right leads to a "double density" sign.[30] Also, in heart failure, cephalization of the pulmonary vessels, Kerley B-lines, pulmonary edema, and pleural effusions are present.
- A transthoracic echocardiogram can assess the left ventricle, right ventricle, atrial size, and systolic/diastolic function. It can also determine valve structure and function and detect wall motion changes that suggest ischemia.
- Cardiac MRI is an emerging diagnostic modality for accurately evaluating left and right ventricle mass, size, and function. It can also characterize ischemic and non-ischemic causes such as myocarditis.
- An electrocardiogram (ECG) can reveal non-specific changes, including left ventricle/right ventricle hypertrophy, low voltage QRS in case of fibrosis/dilated cardiomyopathy, conduction abnormality, arrhythmia, premature ventricular complexes (PVCs), ST-T wave changes, and Q waves suggestive of prior myocardial infarction.
- Serum levels of brain natriuretic peptide (pro-BNP), troponin I and T, renal function, and liver function tests are helpful in the setting of heart failure.[31]
- Stress test or coronary angiogram to evaluate for coronary artery disease.
- Despite standard workup, the etiology of cardiomegaly is often unclear. In such cases, additional testing may be pursued to determine the underlying etiology.

Go to:

Treatment / Management

The treatment of mild cardiomegaly centers on the treatment of the underlying condition. Standard heart failure treatment guidelines also apply to moderate to severe cardiomegaly associated with heart failure.

- Patients at risk of cardiomyopathy benefit from risk factor modification such as smoking cessation, limiting alcohol intake, weight loss, exercise, and consuming a healthy diet. Recommendations include treating underlying risk factors such as hypertension, dyslipidemia, and diabetes. Other underlying conditions, including obstructive sleep apnea, arrhythmias, anemia, and thyroid disorders, also require treatment.[32]
- Patients with early onset cardiomyopathy who are asymptomatic are managed with risk factor modification and the addition of an angiotensin-converting enzyme (ACE) inhibitor or ARB (if intolerant to ACE) and beta-blocker if there is a history of myocardial infarction or reduced ejection fraction.[33]
- Patients with cardiomyopathy and symptoms of heart failure are managed with diuretics and salt restriction in addition to the above therapies.[34] All such patients should receive an ACE inhibitor or ARB (if intolerant to ACE) and a beta-blocker if they have reduced ejection fraction. An ARNI (ARB plus neprilysin inhibitor) is occasionally used instead of ACE/ARB to reduce hospitalization in heart failure and mortality. For patients with moderate to severe symptoms and reduced ejection fraction, the addition of aldosterone antagonists further reduces mortality. A hydralazine/nitrate combination, when added to ACE inhibitor, beta blocker, and diuretics, improves outcomes in Black patients. Digoxin is added in some patients to reduce the rate of hospitalization with heart failure; however, it does not impact outcomes. An ICD (implantable cardioverter defibrillator) is placed in patients with an ejection fraction of 35% or less to reduce mortality from sudden cardiac death. Cardiac resynchronization is performed with or without ICD in patients with an ejection fraction of 35% or less and moderate to severe symptoms with evidence of left bundle branch block.
- Patients with refractory heart failure should receive optimal medical management. Also, eligible patients can be considered for cardiac transplantation and bridge therapy, such as ventricle assist devices.[35]

Of special consideration is that no pharmacologic agent has shown benefits in heart failure with preserved ejection fraction. The mainstay of treatment is controlling underlying conditions such as hypertension, heart rate in patients with atrial fibrillation, ischemia with medication or coronary intervention, and diuretics for fluid overload. Patients with asymptomatic hypertrophic obstructive cardiomyopathy can be safely monitored. Patients with symptoms of heart failure and left ventricular outflow tract obstruction may benefit from negative inotropes such as beta-blockers, calcium channel blockers, or dipyridamole. Vasodilators and diuretics should be avoided in such patients. Some novel treatment strategies are being studied through recent evidence favoring the supplementation of endogenous antioxidants for managing diabetic cardiomyopathy. These strategies include gene therapy targeting the phosphoinositide 3-kinase signaling pathway and miRNA dysregulation. A future strategy could be to target redox stress and protective protein signaling pathways for combating the ever-rising incidence of heart failure in patients with diabetes.[36]

Go to:

Differential Diagnosis

Differentials of cardiomegaly include disorders that can result in an enlarged cardiomediastinal silhouette on a frontal (or posteroanterior) chest X-ray. These include:

- Pericardial effusion
- Anterior mediastinal mass
- Prominent epicardial fat pad
- Mediastinal widening secondary to pulmonary/aortic pathology
- Expiratory radiograph
- AP projection
- Thymus tumor[37]
- Cardiac neoplasms
- Myocarditis

Go to:

Prognosis

Despite the advent of new therapies, mortality remains high in patients with symptomatic heart failure. Roughly, 1-year mortality is 30%, while 5-year mortality is 50%. The severity of symptoms, advanced age, and heart failure hospitalization are significant predictors of mortality in heart failure.[38] Overall, the prognosis of patients with dilated cardiomyopathy is guarded. Most patients eventually end up with chronic heart failure. Many become candidates for a heart transplant or an assist device, which also adds morbidity. Almost 50% of patients are dead within 5 years. Mortality rates of 1% to 4% have been reported in patients with hypertrophic cardiomyopathy, but these numbers have greatly improved in the past 2 decades. Even though most patients have no symptoms, the first clinical presentation is often sudden death from malignant arrhythmias. The highest mortality is in young people.

Go to:

Complications

As cardiomegaly can be secondary to various underlying pathologies, resulting complications tend to vary a great deal as well. The following are a few important complications to be aware of:

- Decompensated heart failure
- Sudden cardiac death and malignant ventricular arrhythmias[39]
- Thromboembolism secondary to mural thrombi

Go to:

Deterrence and Patient Education

Patient education regarding medication compliance, dietary restrictions, and regular follow-up is critical to achieving the best outcomes. In addition, families should go through an investigative procedure when someone is found to have hypertrophic obstructive cardiomyopathy.

Go to:

Pearls and Other Issues

Cardiac transplantation is an emerging treatment for patients with refractory end-stage heart failure. Patients undergo cardiopulmonary assessment and prognostication using specific scoring systems to determine their candidacy for transplant. Patients with systemic illness, life expectancy under 2 years, active substance and alcohol abuse, and non-compliance with medical therapy are considered poor candidates for cardiac transplantation. Patients should have a robust psychosocial support system to qualify. A risk-benefit assessment is necessary before the patient qualifies for the transplant list. Patients who are not candidates for a cardiac transplant can qualify for a durable ventricular assist device.[40]

Go to:

Enhancing Healthcare Team Outcomes

Heart failure readmissions account for a majority of national healthcare expenditures. Support programs are operating nationwide to minimize the number of congestive heart failure-related hospitalizations and reduce the economic strain. These programs utilize a collaborative approach with many integrated disciplines and providers. Some inpatient strategies include guideline-based care, discharge support by nurses, patient education, medication reconciliation by the pharmacist, and early post-discharge follow-up. A board-certified cardiology pharmacist can assist clinicians in selecting medications for blood pressure control and other factors where medication can provide ancillary benefits. Cardiology-specialized nurses are also valuable interprofessional team members, coordinating activities between various specialists and other clinicians and providing patient counseling. Promising outpatient strategies include interprofessional team engagement in heart failure clinics and disease management programs that make in-person contact with patients and provide individualized education.[41] Cardiomegaly and heart failure require an interprofessional team approach that includes physicians and specialists, specialty-trained nurses, pharmacists, and therapists working collaboratively to make optimal therapeutic choices that lead to the best possible patient outcomes. This interprofessional approach requires open communication between all members of the care team and accurate, updated documentation to be effective.

ABSTRACT

A chest x-ray is the most commonly used modality for detecting cardiomegaly, and the cardiothoracic ratio (CTR) has been used as an important tool for estimating the heart size. The main aims of the present study were to determine the distribution of cardiomegaly in normal adults in Saudi Arabia and to evaluate the correlation between the presence of cardiomegaly and age. Data was collected from King Abdulaziz Hospital, Jeddah. A conventional x-ray machine was used for obtaining the x-rays, and CTR was calculated for each patient. Our study included 59 participants (24 females, 40.7%; 35 males, 59.3%) who were examined by posteroanterior (PA) chest x-rays; their age range was 15–79 years. Descriptive analyze were performed using SPSS. The results of our study showed that 38 (64.4%) patients were normal, while 21 (35.6%) patients had cardiomegaly. Of the patients with cardiomegaly, 14 were males (66.7%) and 7 were females (33.3%). The age distribution of these patients was as follows: 15–25 years, 2 patients; 26–36 years, 3 patients; 37–47 years, 5 patients; 48–58 years, 5 patients; 59–69 years, 4 patients; and 59–69 years, 2 patients. The results revealed that cardiomegaly occurs more commonly in males than in females and is particularly observed in the middle-aged group.

1. Introduction

Chest x-rays are generally used to diagnose many conditions involving the chest wall; thoracic bones; and structures contained within the thoracic cavity, including the lungs, heart, and great vessels (Kelly & Frauenfelder, 2019). Pneumonia and congestive heart failure are very commonly diagnosed by chest x-rays (Sabatine & Cannon, 2015). However, for some chest conditions, chest x-rays are effective in screening but not in diagnosis (S. Ellis & Aziz, 2016). When a condition is suspected on the basis of chest radiography, additional chest imaging can be required for reaching a definitive diagnosis or for obtaining evidence in favor of the diagnosis suggested by the initial chest radiography. Unless a fractured rib is suspected of being displaced and therefore likely to cause damage to the lungs and other tissue structures, a chest x-ray is not necessary (S. Ellis & Aziz, 2016). The main areas wherein a chest x-ray can identify problems can be summarized as 'ABCDEF' by their first letters: airways (hilar adenopathy or enlargement), breast shadows or bones (including rib fractures and lytic bone lesions), cardiac silhouette (cardiac enlargement), costophrenic angles (pleural effusions), diaphragm (evidence of free air, edges such as apices indicative of fibrosis, pneumothorax, pleural thickening, or plaques), extrathoracic tissues, fields (lung parenchyma or evidence of alveolar filling), and failure (alveolar air space disease with prominent vascularity with or without pleural effusions) (H. Ellis & Mahadevan, 2018). While chest radiography is a cheap and relatively safe method for investigating chest diseases, there are various serious chest conditions that may be associated with a normal chest x-ray (Kelly, 2007). For example, a patient with an acute myocardial infarction may have a completely normal chest x-ray (Tsakok & Gleeson, 2018). Therefore, additional assessment may be necessary to reach a definitive diagnosis.

Cardiomegaly occurs when the heart is >50% bigger than the inner diameter of the rib cage. It can be caused by many conditions, including coronary artery disease, kidney disease, hypertension, inherited disorder, infection, and cardiomyopathy (Amin & Siddiqui, 2019). Thus, early detection of cardiomegaly results from the diagnosis of underlying symptoms (Ebenezer & Rao, 2017). The assessment of the heart size via chest x-rays remains an important and useful diagnostic parameter (Mensah et al., 2015). The cardiothoracic ratio (CTR) can be easily calculated using a chest x-ray to detect the increase in the heart size and predict cardiomegaly with a 95.8% accuracy (Ebenezer & Rao, 2017). In our study, cardiomegaly was assessed by calculating CTR using chest x-rays of normal adults in Saudi Arabia. The aims of our study were to determine the distribution of cardiomegaly in males and females and to evaluate the correlation between the presence of cardiomegaly and age.

2. Materials and methods

2.1. Participants

Participants were randomly selected from patients who had received a chest x-ray in King Abdulaziz Hospital, Saudi Arabia, Jeddah. The patients' samples were randomly selected through the PACS in the radiology department of the hospital. The first 100 ceases of chest x-ray were chosen chronologically. Our research was restricted for one month (from October to November 2019), therefore we had this limited number of chest x-ray. The main selection criteria were as follows: adult who received chest x-ray; having no chronic diseases; having an erect PA position; and having a PA chest x-ray with good image contrast, with full inspiration, and without artifacts. Of the 100 participants considered initially, children, patients with supine, rotation or AP chest x-rays, those with chest x-rays with artifacts and those with PA chest x-rays without full inspiration were excluded from the analysis. In total, only 59 participants met the inclusion criteria. Of these, 35 were males (59.3%) and 24 were females (40.7%).

2.2. Radiographic technique

Chest x-rays were obtained using digital x-ray machine from Siemens, with the following scanning parameters: 120–140 kV and 200–220 mAs. The x-ray tube specification was as follows: focal spot, 0.5–0.7 mm; anode heat dissipation, 400 HU/second; and anode heat storage capacity, 4.0 MHU. The cassette size was selected to be 35 × 43 cm or 35 × 35 cm depending on the size of the patient. The orientation of the larger cassette depended of the size of the patient.

The patient was positioned erect, facing the cassette, with the chin extended, and resting on the top of the cassette. The median sagittal plane was adjusted perpendicular to the middle of the cassette, with the patient's arms encircling the cassette. Alternatively, the dorsal aspects of the hands were placed behind and below the hips to allow the shoulders to be rotated forward and pressed downward in contact with the cassette. The thorax was positioned symmetrically relative to the film.

The horizontal central beam was directed at a right angle to the cassette at the level of the 8th thoracic vertebra (i.e. the spinous process of T7). The surface markings of the T7 spinous process could be assessed using the inferior angle of the scapula before pushing the shoulders forward. Exposure was performed on arrested full inspiration.

The ideal PA chest x-ray for the heart and aorta should demonstrate the following:
the clavicles symmetrical to and equidistant from the spinous processes, the mediastinum and heart center defined sharply, the costophrenic angles and diaphragm outlined clearly, and full lung fields with the scapula projected laterally away from the lung fields.

2.3. Technical considerations

A PA marker is normally used to identify the right or left side of the patient. Care should be taken to select the correct marker in order to avoid misdiagnosis. In our study, the kilovoltage was adjusted to enable adequate penetration with the bodies of the thoracic vertebrae visible through the heart.

For comparison purposes, records of exposure factors used, such as focal field distance (FFD), should be maintained for follow-up examinations. Care should be taken in case of postoperative patients who have underwater seals and intravenous drips. The examination time should also be kept to a minimum. A normal PA x-ray can also be considered in patients with a permanent in situ pacemaker.

2.4. Image interpretation

On chest x-rays, the heart could be seen as a pear-shaped structure with soft tissue density, with its apex and inferior wall being adjacent to the diaphragm and its narrower upper base overlying the spine. The size and shape of the heart varied with the build of the participants, respiration, and the position and clinical state of the participants.

2.5. Radiographic measures

Measurements were performed by the researchers and reviewed by a radiologist committee at the University of Jeddah in the Department of Medical Imaging and Radiation Sciences. The heart size was estimated from the PA chest x-ray by calculating CTR, i.e. the ratio between the maximum transverse diameter of the heart and the maximum width of the thorax above the costophrenic angles measured from the inner edges of the ribs. CTR was calculated manually and documented for each patient, as shown in Figure 1. In adults, the normal CTR is 0.5 at the most (Whitley et al., 2015). The following equation was used to calculate CTR:

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Figure 1. PA chest x-ray showing CTR (a = the distance from the right heart border to the midline, b = the distance from the left heart border to the midline, and c = the maximum thoracic diameter).

where a = the distance from the right heart border to the midline, b = the distance from the left heart border to the midline, and c = the maximum thoracic diameter (TD) above the costophrenic angles from the inner borders of the ribs (Whitley et al., 2015).

The protocol used in our study has been commonly used as the gold standard technique for estimating cardiomegaly in previous studies (Halilu et al., 2017; Mensah et al., 2015; Sinha et al., 2013). To apply the manual measurements of CTR, we required a good PA erect chest x-ray with no rotation or artifacts. In our study, an independent committee of radiologists from King Abdulaziz Hospital, Saudi Arabia, Jeddah has reviewed the accuracy and precision of CTR measurements on chest x-ray. This committee has signed off the measurements by the research team.

2.6. Data collection

The following information was collected for each patient: sex, age, and CTR.

2.7. Statistical analyses

Descriptive analyses and Pearson correlation were performed using the Statistical Package for the Social Sciences (SPSS) software, version 20.0 (IBM Corp., Armonk, NY, USA). All tests with $P \leq 0.05$ (two-tailed) were considered statistically significant.

2.8. Ethical considerations

Special consideration was given to the right of confidentiality for all the participants. Privacy was ensured by using numbers to denote participants in order to provide a link between the collected information and the participants. Permission for conducting the study was obtained from the head of the radiology department at King Abdulaziz Hospital, Saudi Arabia, Jeddah. A consent form was obtained from each participant before participating in the study.

3. Results

The present study showed that of the 59 participants who were examined by chest radiography, 35 were males (59.3%) and 24 were females (40.7%) (Figure 2). The age distribution of the participants was as follows: 15–25 years, 12 participants; 26–36 years, 8 participants; 37–47 years, 20 participants; 48–58 years, 11 participants; 59–69 years, 5 participants; and 59–69 years, 3 participants (Figure 3). Further, 21 participants (35.6%) had cardiomegaly, while 38 participants (64.4%) had a normal heart size (Figure 4).

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Figure 2. Gender distribution of study participants.

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Figure 3. Age distribution of study participants.

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Figure 4. Distribution of normal individuals and patients with cardiomegaly.

Of the patients with cardiomegaly, 7 were females and 14 were males (Figure 5). The age distribution of patients with cardiomegaly was as follows: 15–25 years, 2 patients; 26–36 years, 3 patients; 37–47 years, 5 patients; 48–58 years, 5 patients; 59–69 years, 4 patients; and 59–69 years, 2 patients (Figure 6).

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Figure 5. Gender distribution of patients with cardiomegaly.

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Figure 6. Age distribution of patients with cardiomegaly.

As shown in Table 1, there was a significant correlation between age and the distance from the left heart border to the midline, the distance between both heart borders, TD, and CTR in all the patients, ($P < 0.05$ for all). There was a significant correlation between age and CTR in all the patients ($P = 0.028$).

The scatter plot in Figure 7 shows the relationship between age and CTR. In addition, Figure 8 illustrates the scatter plot of the relationship between age and the distance from the right and left heart borders to the midline. Similarly, Figure 9 shows the scatter plot of the relationship of age with the distance between both heart borders and TD.

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Figure 7. Scatter plot showing the relation between age and cardiothoracic ratio (CTR).

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Figure 8. Scatter plot showing the relation between age and the distance from the right and left heart borders to the midline.

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Figure 9. Scatter plot showing the relation of age with the distance between both the heart borders and thoracic diameter (TD).

4. Discussion

The present study demonstrated that the percentage of male patients with a positive result for cardiomegaly (66.7%) was twice that of female patients (33.3%). The age group that had the highest distribution of cardiomegaly was 37–58 years.

The average CTR differed for different genders and age groups. Previous studies have shown that CTR was higher in females than in males (Brakohiapa et al., 2017; Mensah et al., 2015). In contrast, our results revealed that CTR was higher in males than in females. This might be due to the differences in the study population. Our study was conducted among normal adults in Saudi Arabia, where the prevalence of cardiovascular diseases is high, especially in males (Ibrahim et al., 2014).

In line with previous studies (Brakohiapa et al., 2017; Mensah et al., 2015), there was a significant correlation between age and CTR in all the patients. The highest value was found in the middle-aged group (37–58 years). In addition, there was a direct relationship between age and the distance from the left heart border to the midline. However, no significant relationship was observed between age and CTR in patients with cardiomegaly.

Our results showed a significant correlation between the distance of both the heart borders and CTR in all the patients ($P < 0.001$). A similar correlation was found between the distance between both the heart borders and TD ($P < 0.001$). Thus, TD has a significant correlation with CTR, which is in agreement with the results of a previous study by Mensah et al. (2015).

5. Conclusion

In the present study, 35.6% of the participants who received a chest x-ray had cardiomegaly (CTR > 0.5), with most being middle-aged (37–58 years), in Saudi Arabian population. In particular, our results demonstrated that males are more affected by cardiomegaly than females. Our study recommends the use of a PA chest x-ray to accurately measure CTR and estimate the cardiomegaly in larger sample size. In addition, anatomical differences of the heart between genders should be taken into consideration during measurements.

Acknowledgments

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Abstract

Objectives

The cardiothoracic ratio (CTR) is a useful technique to investigate the prevalence of cardiomegaly, an important clinical manifestation of several cardiovascular diseases. The aim of this study was to

determine the relationship between various macroscopic measurements of heart size on postmortem chest X-rays and CTR as well as develop a new CTR threshold or scoring system to improve reliability of CTR in forensic settings.

Materials and methods

We selected 131 forensic autopsy cases aged more than 18. The heart length and width, wall thicknesses, chamber diameters, and heart weights were measured during autopsy. The postmortem CTR was measured in an anteroposterior chest radiography. In autopsy cases among the Thai population, two groups were defined: normal and overweight heart, with cut-off values based on average heart weight + 1SD.

Results

The results showed that the wall thickness and chamber diameter were not related to CTR, but the heart length and width were. A multivariable analysis was performed and showed good discriminating power, with an area under the ROC curve of 0.88. A new formula was developed, which included age, BMI, and CTR. The recommend cut-off score was 122 for the diagnosis of cardiomegaly, in which the sensitivity and specificity were 78.3% and 72.9%.

Conclusions

The findings of increased CTR cannot be equated to cardiac wall hypertrophy and chamber enlargement. This study suggests that a combination of CTR, BMI, and age of the deceased improves the level of discrimination between the condition of normal heart and cardiomegaly before autopsy.

Introduction

In clinical practice, the cardiothoracic ratio (CTR) is a useful screening technique to detect cardiomegaly [1,2]. This method has been used for many years, first in chest X-rays and later computed tomography (CT) [3,4]. CTR is calculated by dividing the maximum horizontal cardiac diameter by the maximum horizontal thoracic diameter, with a value of more than 0.5 defining cardiomegaly. Also, CTR may be helpful in determining the cause of death, particularly when the results are compared to an autopsy [5].

The rate of traditional autopsies has declined dramatically worldwide. Currently in US hospitals, the autopsy rate, inclusive of forensic cases is only 8% whereas in the 1940s and 1950s, it was approximately 50% [6]. The main reasons for this trend are a decreasing request rate and an increase in the difficulty to obtain permission from family members. Diagnostic technology has also reduced the need for diagnostic autopsies [7]. In postmortem examinations, CTR can be used to investigate the prevalence of cardiomegaly and therefore the cause of death in relation to cardiovascular diseases [4,5,8,9]. Previous literature have looked at CTR studies on postmortem CT (PMCT) [4,[8], [9], [10]], however, plain X-ray investigations still play a crucial role in routine forensic practice in Thailand due to their easy accessibility and cost-effectiveness. Currently, all district hospitals in Thailand have general radiographic services, but CT machines are only available in a general hospital. Data obtained from postmortem plain radiographs are particularly useful to investigate the cause of death when findings are considered together with postmortem examinations or in comparison to clinical radiography [5]. Therefore, postmortem chest radiographs might be helpful in a forensic scenario if they could reveal enough information regarding heart size to evaluate cardiomegaly independently of an autopsy and, consequently, the potential cause of death of the deceased.

In this study, we aimed to address two important issues. The first goal was to investigate the relationship between various macroscopic measurements of cardiac size and the CTR on postmortem plain chest X-rays. The second goal was to establish an adjusted CTR-based score to predict cardiomegaly from postmortem plain chest X-rays.

Results

A total of 131 autopsy cases were evaluated in this study. The descriptive results of all variables in autopsy cases by heart weight group are illustrated in Table 1. The subjects were divided as follows: 28 (21.4%) females and 103 (78.6%) males. The male to female ratio in this study was 3.68:1. There were 12 women (43%) and 34 men (33%) with cardiomegaly. The mean (±SD) age of all subjects was 46.89 (±15.6), with the cardiomegaly group having a higher average than the non-cardiomegaly group.

Discussion

The first aim of this study was to determine the reliability of postmortem CTR to predict abnormal heart size by comparing CTR values to various cardiac parameters in forensic autopsy cases. To the best of our knowledge, this was the first study to assess the ability of postmortem CTR to predict cardiac size using direct measurements of cardiac walls and chambers. The results demonstrated a low positive, but statistically significant correlation between postmortem CTR, heart length, and heart

Conclusions

In summary, this study evaluated the reliability of CTR in postmortem chest X-rays to discriminate between normal and overweight hearts. Measuring the CTR with postmortem chest X-ray is easy to do and reproducible. We found that the findings of increased CTR cannot be equated to cardiac wall hypertrophy and chamber enlargement. The postmortem CTR alone is unable to diagnose cardiomegaly. Hence, it would be better to take into account BMI and age of the deceased in this new scoring system.

OBJECTIVE

Recently, many AI methods have been proposed to detect cardiomegaly on chest X-rays (CXRs) by measuring cardio-thoracic ratios (CTRs). However, accurate measurement of CTRs on CXRs with pulmonary abnormalities is challenging due to the corrupted lung regions. Here, we propose a new AI model to address this problem.

MATERIALS & METHODS

931 CXRs from Indonesian hospitals, confirmed as not having any chest abnormality (i.e., normal CXRs), were annotated by three radiologists who measured CTRs for each CXR based on the boundaries of heart and lung regions. These were later split for AI training and testing. 170 CXRs, confirmed as having at least one of four abnormalities (i.e., cardiomegaly, effusion, opacity, and pneumothorax), were collected from a Vietnam hospital and annotated.Two AI models (baseline and proposed) were trained and evaluated by calculating mean absolute errors (MAEs) of CTR measurement. The baseline network was trained using the normal CXRs without any pulmonary abnormalities. The proposed network was trained using the normal and synthetic CXRs with pulmonary abnormalities (e.g., effusion, opacity, etc.) which were generated from the normal CXRs via another AI.

RESULTS

When we tested both AIs on normal CXRs (from Indonesia), a marginal improvement of CTR measurement was observed in the proposed network (MAE: 0.013 for proposed; 0.014 for baseline; p-value=0.028). On the other hand, when testing on CXRs with abnormalities (from Vietnam), the proposed network outperformed the baseline (MAE: 0.022 for proposed; 0.026 for baseline; p-value=0.001).

CONCLUSION

The proposed AI can accurately measure CTR values on CXRs with pulmonary abnormalities.

ABSTRACT

A chest x-ray is the most commonly used modality for detecting cardiomegaly, and the cardiothoracic ratio (CTR) has been used as an important tool for estimating the heart size. The main aims of the present study were to determine the distribution of cardiomegaly in normal adults in Saudi Arabia and to evaluate the correlation between the presence of cardiomegaly and age. Data was collected from King Abdulaziz Hospital, Jeddah. A conventional x-ray machine was used for obtaining the x-rays, and CTR was calculated for each patient. Our study included 59 participants (24 females, 40.7%; 35 males, 59.3%) who were examined by posteroanterior (PA) chest x-rays; their age range was 15–79 years. Descriptive analyze were performed using SPSS. The results of our study showed that 38 (64.4%) patients were normal, while 21 (35.6%) patients had cardiomegaly. Of the patients with cardiomegaly, 14 were males (66.7%) and 7 were females (33.3%). The age distribution of these patients was as follows: 15–25 years, 2 patients; 26–36 years, 3 patients; 37–47 years, 5 patients; 48–58 years, 5 patients; 59–69 years, 4 patients; and 59–69 years, 2 patients. The results revealed that cardiomegaly occurs more commonly in males than in females and is particularly observed in the middle-aged group.

1. Introduction

Chest x-rays are generally used to diagnose many conditions involving the chest wall; thoracic bones; and structures contained within the thoracic cavity, including the lungs, heart, and great vessels (Kelly & Frauenfelder, 2019). Pneumonia and congestive heart failure are very commonly diagnosed by chest x-rays (Sabatine & Cannon, 2015). However, for some chest conditions, chest x-rays are effective in screening but not in diagnosis (S. Ellis & Aziz, 2016). When a condition is suspected on the basis of chest radiography, additional chest imaging can be required for reaching a definitive diagnosis or for obtaining evidence in favor of the diagnosis suggested by the initial chest radiography. Unless a fractured rib is suspected of being displaced and therefore likely to cause damage to the lungs and other tissue structures, a chest x-ray is not necessary (S. Ellis & Aziz, 2016). The main areas wherein a chest x-ray can identify problems can be summarized as 'ABCDEF' by their first letters: airways (hilar adenopathy or enlargement), breast shadows or bones (including rib fractures and lytic bone lesions), cardiac silhouette (cardiac enlargement), costophrenic angles (pleural effusions), diaphragm (evidence of free air, edges such as apices indicative of fibrosis, pneumothorax, pleural thickening, or plaques), extrathoracic tissues, fields (lung parenchyma or evidence of alveolar filling), and failure (alveolar air space disease with prominent vascularity with or without pleural effusions) (H. Ellis & Mahadevan, 2018). While chest radiography is a cheap and relatively safe method for investigating chest diseases, there are various serious chest conditions that may be associated with a normal chest x-ray (Kelly, 2007). For example, a patient with an acute myocardial infarction may have a completely normal chest x-ray (Tsakok & Gleeson, 2018). Therefore, additional assessment may be necessary to reach a definitive diagnosis.

Cardiomegaly occurs when the heart is >50% bigger than the inner diameter of the rib cage. It can be caused by many conditions, including coronary artery disease, kidney disease, hypertension, inherited disorder, infection, and cardiomyopathy (Amin & Siddiqui, 2019). Thus, early detection of cardiomegaly results from the diagnosis of underlying symptoms (Ebenezer & Rao, 2017). The assessment of the heart size via chest x-rays remains an important and useful diagnostic parameter (Mensah et al., 2015). The cardiothoracic ratio (CTR) can be easily calculated using a chest x-ray to detect the increase in the heart size and predict cardiomegaly with a 95.8% accuracy (Ebenezer & Rao, 2017). In our study, cardiomegaly was assessed by calculating CTR using chest x-rays of normal adults in Saudi Arabia. The aims of our study were to determine the distribution of cardiomegaly in males and females and to evaluate the correlation between the presence of cardiomegaly and age.

2. Materials and methods

2.1. Participants

Participants were randomly selected from patients who had received a chest x-ray in King Abdulaziz Hospital, Saudi Arabia, Jeddah. The patients' samples were randomly selected through the PACS in the radiology department of the hospital. The first 100 ceases of chest x-ray were chosen chronologically. Our research was restricted for one month (from October to November 2019), therefore we had this limited number of chest x-ray. The main selection criteria were as follows: adult who received chest x-ray; having no chronic diseases; having an erect PA position; and having a PA chest x-ray with good image contrast, with full inspiration, and without artifacts. Of the 100 participants considered initially, children, patients with supine, rotation or AP chest x-rays, those with chest x-rays with artifacts and those with PA chest x-rays without full inspiration were excluded from the analysis. In total, only 59 participants met the inclusion criteria. Of these, 35 were males (59.3%) and 24 were females (40.7%).

2.2. Radiographic technique

Chest x-rays were obtained using digital x-ray machine from Siemens, with the following scanning parameters: 120–140 kV and 200–220 mAs. The x-ray tube specification was as follows: focal spot, 0.5–0.7 mm; anode heat dissipation, 400 HU/second; and anode heat storage capacity, 4.0 MHU. The cassette size was selected to be 35 × 43 cm or 35 × 35 cm depending on the size of the patient. The orientation of the larger cassette depended of the size of the patient.

The patient was positioned erect, facing the cassette, with the chin extended, and resting on the top of the cassette. The median sagittal plane was adjusted perpendicular to the middle of the cassette, with the patient's arms encircling the cassette. Alternatively, the dorsal aspects of the hands were placed behind and below the hips to allow the shoulders to be rotated forward and pressed downward in contact with the cassette. The thorax was positioned symmetrically relative to the film.

The horizontal central beam was directed at a right angle to the cassette at the level of the 8^{th} thoracic vertebra (i.e. the spinous process of T7). The surface markings of the T7 spinous process could be assessed using the inferior angle of the scapula before pushing the shoulders forward. Exposure was performed on arrested full inspiration.

The ideal PA chest x-ray for the heart and aorta should demonstrate the following:
the clavicles symmetrical to and equidistant from the spinous processes, the mediastinum and heart center defined sharply, the costophrenic angles and diaphragm outlined clearly, and full lung fields with the scapula projected laterally away from the lung fields.

2.3. Technical considerations

A PA marker is normally used to identify the right or left side of the patient. Care should be taken to select the correct marker in order to avoid misdiagnosis. In our study, the kilovoltage was adjusted to enable adequate penetration with the bodies of the thoracic vertebrae visible through the heart.

For comparison purposes, records of exposure factors used, such as focal field distance (FFD), should be maintained for follow-up examinations. Care should be taken in case of postoperative patients who have underwater seals and intravenous drips. The examination time should also be kept to a minimum. A normal PA x-ray can also be considered in patients with a permanent in situ pacemaker.

2.4. Image interpretation

On chest x-rays, the heart could be seen as a pear-shaped structure with soft tissue density, with its apex and inferior wall being adjacent to the diaphragm and its narrower upper base overlying the spine. The size and shape of the heart varied with the build of the participants, respiration, and the position and clinical state of the participants.

2.5. Radiographic measures

Measurements were performed by the researchers and reviewed by a radiologist committee at the University of Jeddah in the Department of Medical Imaging and Radiation Sciences. The heart size was estimated from the PA chest x-ray by calculating CTR, i.e. the ratio between the maximum transverse diameter of the heart and the maximum width of the thorax above the costophrenic angles measured from the inner edges of the ribs. CTR was calculated manually and documented for each patient, as shown in Figure 1. In adults, the normal CTR is 0.5 at the most (Whitley et al., 2015). The following equation was used to calculate CTR:

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Figure 1. PA chest x-ray showing CTR (a = the distance from the right heart border to the midline, b = the distance from the left heart border to the midline, and c = the maximum thoracic diameter).

where a = the distance from the right heart border to the midline, b = the distance from the left heart border to the midline, and c = the maximum thoracic diameter (TD) above the costophrenic angles from the inner borders of the ribs (Whitley et al., 2015).

The protocol used in our study has been commonly used as the gold standard technique for estimating cardiomegaly in previous studies (Halilu et al., 2017; Mensah et al., 2015; Sinha et al., 2013). To apply the manual measurements of CTR, we required a good PA erect chest x-ray with no rotation or artifacts. In our study, an independent committee of radiologists from King Abdulaziz Hospital, Saudi Arabia, Jeddah has reviewed the accuracy and precision of CTR measurements on chest x-ray. This committee has signed off the measurements by the research team.

2.6. Data collection

The following information was collected for each patient: sex, age, and CTR.

2.7. Statistical analyses

Descriptive analyses and Pearson correlation were performed using the Statistical Package for the Social Sciences (SPSS) software, version 20.0 (IBM Corp., Armonk, NY, USA). All tests with $P \leq 0.05$ (two-tailed) were considered statistically significant.

2.8. Ethical considerations

Special consideration was given to the right of confidentiality for all the participants. Privacy was ensured by using numbers to denote participants in order to provide a link between the collected information and the participants. Permission for conducting the study was obtained from the head of the radiology department at King Abdulaziz Hospital, Saudi Arabia, Jeddah. A consent form was obtained from each participant before participating in the study.

3. Results

The present study showed that of the 59 participants who were examined by chest radiography, 35 were males (59.3%) and 24 were females (40.7%) (Figure 2). The age distribution of the participants was as follows: 15–25 years, 12 participants; 26–36 years, 8 participants; 37–47 years, 20 participants; 48–58 years, 11 participants; 59–69 years, 5 participants; and 59–69 years, 3 participants (Figure 3). Further, 21 participants (35.6%) had cardiomegaly, while 38 participants (64.4%) had a normal heart size (Figure 4).

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Figure 2. Gender distribution of study participants.

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Figure 3. Age distribution of study participants.

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Figure 4. Distribution of normal individuals and patients with cardiomegaly.

Of the patients with cardiomegaly, 7 were females and 14 were males (Figure 5). The age distribution of patients with cardiomegaly was as follows: 15–25 years, 2 patients; 26–36 years, 3 patients; 37–47 years, 5 patients; 48–58 years, 5 patients; 59–69 years, 4 patients; and 59–69 years, 2 patients (Figure 6).

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Figure 5. Gender distribution of patients with cardiomegaly.

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Figure 6. Age distribution of patients with cardiomegaly.

As shown in Table 1, there was a significant correlation between age and the distance from the left heart border to the midline, the distance between both heart borders, TD, and CTR in all the patients, ($P < 0.05$ for all). There was a significant correlation between age and CTR in all the patients ($P = 0.028$).

Table 1. Correlations between age, RT and LT heart border to midline, both heart boarders, TD and CTR in all patients (n = 59).

Correlations							
Empty Cell	Empty Cell	**Age**	**RT heart border to midline**	**LT heart border to midline**	**Both**	**TD**	**CTR**
Age	Pearson Correlation	1	0.075	0.258*	0.215	0.050	0.285*
	P-value	-	0.571	0.049	0.102	0.706	0.028
RT heart border to midline	Pearson Correlation	0.075	1	0.354**	0.708**	0.471**	0.657**
	P-value	0.571	-	0.006	0.0001	0.0001	0.0001
LT heart border to midline	Pearson Correlation	0.258*	0.354**	1	0.816**	0.767**	0.580**
	P-value	0.049	0.006	-	0.0001	0.0001	0.0001
Both heart borders	Pearson Correlation	0.215	0.708**	0.816**	1	0.752**	0.855**
	P-value	0.102	0.0001	0.0001		0.0001	0.0001
TD	Pearson Correlation	0.050	0.471**	0.767**	0.752**	1	0.324*
	P-value	0.706	0.0001	0.0001	0.0001	-	0.012

Correlations							
Empty Cell	Empty Cell	**Age**	**RT heart border to midline**	**LT heart border to midline**	**Both**	**TD**	**CTR**
CTR	Pearson Correlation	0.285*	0.657**	0.580**	0.855**	0.324*	1
	P-value	0.028	0.0001	0.0001	0.0001	0.012	-

*. Correlation is significant at the p value < 0.05 level (2-tailed).

**. Correlation is significant at the p value < 0.01 level (2-tailed).

TD: Thoracic Diameter, CTR: Cardiothoracic Ratio, RT: Right, LT: Left.

The scatter plot in Figure 7 shows the relationship between age and CTR. In addition, Figure 8 illustrates the scatter plot of the relationship between age and the distance from the right and left heart borders to the midline. Similarly, Figure 9 shows the scatter plot of the relationship of age with the distance between both heart borders and TD.

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Figure 7. Scatter plot showing the relation between age and cardiothoracic ratio (CTR).

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Figure 8. Scatter plot showing the relation between age and the distance from the right and left heart borders to the midline.

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Figure 9. Scatter plot showing the relation of age with the distance between both the heart borders and thoracic diameter (TD).

4. Discussion

The present study demonstrated that the percentage of male patients with a positive result for cardiomegaly (66.7%) was twice that of female patients (33.3%). The age group that had the highest distribution of cardiomegaly was 37–58 years.

The average CTR differed for different genders and age groups. Previous studies have shown that CTR was higher in females than in males (Brakohiapa et al., 2017; Mensah et al., 2015). In contrast, our results revealed that CTR was higher in males than in females. This might be due to the differences in the study population. Our study was conducted among normal adults in Saudi Arabia, where the prevalence of cardiovascular diseases is high, especially in males (Ibrahim et al., 2014).

In line with previous studies (Brakohiapa et al., 2017; Mensah et al., 2015), there was a significant correlation between age and CTR in all the patients. The highest value was found in the middle-aged group (37–58 years). In addition, there was a direct relationship between age and the distance from the left heart border to the midline. However, no significant relationship was observed between age and CTR in patients with cardiomegaly.

Our results showed a significant correlation between the distance of both the heart borders and CTR in all the patients ($P < 0.001$). A similar correlation was found between the distance between both the heart borders and TD ($P < 0.001$). Thus, TD has a significant correlation with CTR, which is in agreement with the results of a previous study by Mensah et al. (2015).

5. Conclusion

In the present study, 35.6% of the participants who received a chest x-ray had cardiomegaly (CTR > 0.5), with most being middle-aged (37–58 years), in Saudi Arabian population. In particular, our results demonstrated that males are more affected by cardiomegaly than females. Our study recommends the use of a PA chest x-ray to accurately measure CTR and estimate the cardiomegaly in larger sample size. In addition, anatomical differences of the heart between genders should be taken into consideration during measurements.

Cardiomegaly on chest radiographs (CXR) in pediatric patients leads to multiple tests. We aimed to determine the positive predictive value (PPV) of cardiomegaly on CXR in predicting subsequent heart disease and to assess the utility of obtaining a B-type Natriuretic Peptide level (BNP) and/or electrocardiogram (EKG) in such patients. We hypothesized that an echocardiogram may not be appropriate in all cases of cardiomegaly on CXR, particularly in a patient with a normal EKG and BNP level.

Methods

We performed a retrospective cohort study of pediatric patients with cardiomegaly on their initial CXR between January 2015–December 2017. Patients without a subsequent echocardiogram or known congenital heart disease were excluded. A patient was deemed to have heart disease if they had structural abnormalities, functional abnormalities or a pericardial effusion on echocardiogram. The PPV of CXR and the PPV/NPV of the other tests (EKG, BNP) were calculated using contingency tables.

Results

Four hundred and eighty nine patients met inclusion criteria. The PPV of cardiomegaly on CXR alone without any other diagnostic testing in predicting subsequent heart disease was 15%. The PPV increased if there was either an abnormal EKG or a BNP >100 pg/ml and further increased if both of these were present. The PPV values were higher in patients <1 year of age.

Conclusions

Cardiomegaly on CXR can often predict the presence of heart disease, particularly in infants. Further testing with EKG and BNP can better predict who may have heart disease, but it may not eliminate the need for echocardiography.

Introduction

The Appropriate Use Criteria (AUC) for Initial Transthoracic Echocardiography in Outpatient Pediatric Cardiology has rated an abnormal chest radiograph (CXR) suggestive of cardiovascular disease as an "Appropriate" indication for obtaining an echocardiogram (AUC indication # 51) [1]. However, the AUC guidelines are mostly based on expert consensus. The rates of CXR performance vary by pediatric emergency departments (ED) and their location. A study performed in a pediatric ED showed that a CXR was ordered on ~ 6% of patients [2]. Cardiomegaly on CXR in pediatric patients often leads to multiple tests including blood work, electrocardiograms (EKG) and echocardiograms. Previous studies have investigated the utility of CXR when evaluating children with potential heart disease [[3], [4], [5]], but very few studies have focused on whether current criteria for cardiomegaly by CXR can accurately predict disease [6]. A false positive diagnosis of cardiomegaly on CXR is quite frequent in children and an enlargement of the cardiac silhouette may not always indicate heart disease. "Pseudo-cardiomegaly" may be related to thoracic wall abnormalities, technical factors, mediastinal abnormalities or pulmonary conditions [7]. A prior study suggested that a thorough physical examination and an EKG evaluation by a pediatric emergency care physician has an excellent rate of detection of cardiac-related causes, however, this was limited to patients with chest pain [8]. In addition, while an abnormal EKG may indicate heart disease, especially in adults, it may not be specific for cardiac disease in the pediatric population. One study demonstrated that only 2% of EKG abnormalities were related to the underlying cardiac abnormality [9]. On the other hand, elevation of B-type Natriuretic Peptide (BNP) may be seen with diseases that cause left ventricular volume and right ventricular volume or pressure overload, with complex congenital heart diseases having greater elevations of BNP as compared to simple cardiac defects [10]. An echocardiogram can provide qualitative, and both accurate and reproducible quantitative, measurements of cardiac chamber size and function [11]. However, an echocardiogram is expensive, more time consuming, and has limited availability compared to a CXR.

Our goal was to determine the positive predictive value (PPV) of cardiomegaly on CXR in predicting subsequent heart disease and to assess the utility of obtaining a BNP and/or EKG in such patients. We hypothesized that an echocardiogram may not be appropriate in all cases of cardiomegaly on CXR, particularly when a patient also had a normal EKG and a normal BNP level.

Patients and methods

We performed a retrospective chart review of all pediatric patients (0–21 years) with cardiomegaly on an initial CXR between January 2015–December 2017 in a tertiary care pediatric hospital, including the ED, the outpatient clinics and the inpatient setting. Patients without a subsequent echocardiogram either at the same encounter as the CXR or within 30 days of that encounter were excluded. Additionally, those with known congenital heart disease were excluded. The institutional review board at

Results

There were 282,618 patients with a CXR during the study timeframe, with 1544 having cardiomegaly on their initial CXR. Of these, 1055 patients were excluded (909 patients did not get a subsequent echocardiogram, 109 patients had known congenital heart disease and 37 patients did not meet criteria for cardiomegaly when measured by a blinded observer). Ultimately, 489 patients met

inclusion criteria (Table 1). Additional testing included an EKG in 275 patients, a BNP level in 176, and both tests

Discussion

We hypothesized that an echocardiogram may not be appropriate in patients with cardiomegaly on CXR and a normal EKG and a normal BNP level. Our study demonstrates that cardiomegaly on CXR in pediatric patients is an overall rare finding. However, when present it may predict the presence of heart disease, particularly in infants. Our findings suggest that it may be appropriate to consider an echocardiogram in this patient population with cardiomegaly on CXR and particularly in those with an

Conclusions

Cardiomegaly on CXR is an overall rare finding. However, when present, it often predicts the presence of structural or functional heart disease, particularly in infants. Further testing with EKG and BNP can better predict who may have heart disease. However, a normal EKG and a normal BNP level may not eliminate the need for echocardiography. This remains true even in patients with a normal cardiovascular physical examination.

Summary

Perforation of the heart is a rare, but life-threatening complication of chest tube thoracostomy. We report the very unusual case where right-sided insertion of a Matthys catheter (6 F) due to pleural effusion resulted in a left atrium perforation. Heart injury was immediately considered as a continuous flow of bright red blood emerging through the chest drain. Diagnosis was confirmed by computertomography also revealing a massive cardiomegaly due to pre-existing mitral valve regurgitation. In two consecutive thoracotomies, first the Mathys drain was removed and the heart defect closed and then the mitral valve was replaced by a bio prosthesis. The extent of the cardiomegaly and the position of the left atrium were not detected pre-operatively by chest X-ray or ultrasonic device. Despite a nosocomial pneumonia, the patient fully recovered. This case shows that extreme caution is necessary when inserting chest tubes in patients where thorax imaging by X-ray or ultrasonic device does not provide a clear anatomical site. In order to minimise complications, a blunt puncturing procedure or Seldinger technique should be used and assisted by a Doppler ultrasonic device. Also early imaging by CT and Doppler ultrasonic technique should be attempted. This may reduce incidence of severe complications as in this case.

Introduction

Chest tube thoracostomy is a common procedure for treating pneumothorax and draining the pleural space after operation, trauma or in patients with pleural effusion or empyaema.1, 2, 3, 4, 5

The complication rate of this procedure may reach 30%, but severe incidents are rare in the hand of experienced physicians.6, 7, 8 They include malpositioning of the chest tube with injury to the lung, liver, diaphragm, stomach, spleen and intercostal or intrathoracic blood vessels which may result in major bleeding. Phrenic nerve lesions, traumatic arteriovenous fistula and pulmonary infarction due to excessive suction have also been reported.9, 10, 11

A far more serious, but very rare complication is the perforation of the heart with consecutive pericardial tamponade or haemothorax. There are only few cases in the literature where this severe complication was reported.12, 13, 14, 15, 16 The typical clinical background for this life-threatening

incident is an emergency situation such as trauma, anatomical abnormalities or a massive pre-existing cardiomegaly.

Here we report the very rare case of a 72-year-old female patient where right-sided tube thoracostomy, performed to drain a pleural effusion, resulted in perforation of the left atrium. This complication occurred due to excessive cardiomegaly, the extent of which was not evident in chest X-ray and ultrasonic examination. The patient survived this severe complication after several therapeutic interventions, and we present and discuss the clinical course and draw conclusions for safe chest tube placement.

Section snippets

Case report

A 72-year-old female patient was admitted in the afternoon to the emergency room of our hospital with severe dyspnoea increasing over a period of 4 days. Mitral valve regurgitation with chronic heart failure (NYHA III), tachyarrhythmia over many years and a post-thrombotic syndrome were reported in her medical history. Medication consisted of furosemide, digoxin and phenprocoumon orally.

Clinical examination of the conscious patient revealed orthopnoea and attenuated breathing sounds over the

Discussion

Chest tube thoracostomy may be associated with severe and well-known complications such as lung, liver, spleen injury or major bleeding.6, 7, 8, 9, 10, 11 On the other hand, iatrogenic perforation of the heart is a very rare and dramatic incident. We presented the very unusual case where insertion of a chest tube into the right pleural space resulted in a life-threatening perforation of the left atrium.

There are only few reports in the literature about injuries of the heart due to chest tube

Cardiomegaly is among the disorders categorized by a structural enlargement of the heart by any of the situations including pregnancy, resulting in damage to heart muscles and causing trouble in normal heart functioning. Cardiomegaly can be defined in terms of dilatation with an enlarged heart and decreased left or biventricular contraction. The genetic origin of cardiomegaly is becoming more evident due to extensive genomic research opening up new avenues to ensure the use of precision medicine. Cardiomegaly is usually assessed by using an array of radiological modalities, including computed tomography (CT) scans, chest X-rays, and MRIs. These imaging techniques have provided an important opportunity for the physiology and anatomy of the heart. This review aims to highlight the complexity of cardiomegaly, highlighting the contribution of both ecological and genetic variables to its progression. Moreover, we further highlight the worth of precise clinical diagnosis, which comprises blood biomarkers and electrocardiograms (EKG ECG), demonstrating the significance of distinguishing between numerous basic causes. Finally, the analysis highlights the extensive variation of treatment lines, such as lifestyle modifications, prescription drugs, surgery, and implantable devices, although highlighting the critical need for individualized and personalized care.

Introduction

The word 'cardiomegaly' refers to an enlarged heart seen in every X-ray of the chest.[1] Cardiomegaly is left or bi-ventricular dilation and reduced contraction.[2] Cardiomegaly is triggered by mutations in genes encoding sarcomere and desmosome structural components.[3] Myocardium inflammation can result from infection, allergens, toxins, medication, and systemic endocrine or autoimmune

disorders. The heterogeneity of Cardiomegaly makes accurate diagnosis difficult due to its clinical appearance.[4] Cardiomyopathies are conditions affecting the heart muscle, leading to impaired mechanical and electrical function, which can manifest as either dilated, hypertrophic, or restrictive pathophysiological changes[5] (Fig. 1).

Echocardiography and other imaging techniques are used to evaluate ventricular dysfunction and adverse myocardial modifications, and when inflammation or infection is assumed, immunological and histological analyses are recommended.[6,7] Cardiomegaly is a condition causing impaired contractility and is typically treated first-line to prevent heart failure. Life-threatening arrhythmias prevention, cardiac resynchronization therapy, and implantable cardioverter-defibrillators may be necessary. Customized treatments can improve prognosis by identifying the cause of cardiomegaly.[8] Personalized clinical care and Improved etiology-driven cardiomegaly patients will benefit from radiological diagnostic tools like echocardiography and CT angiography, enabling early diagnosis and treatment.[9,10] Cardiomegaly is a swollen heart symptom, not an illness. Moderate cardiomegaly is less extreme and may not be noticeable. In some cases, cardiomegaly is temporary and healing on its own, while others can have irreversible cardiomegaly. In avoiding heart damage, it is crucial to treat the symptom and its underlying cause, which involves improvements in medicine, surgery, and lifestyle.[11,12]

Cardiomyopathy is a disorder that affects the heart muscle or myocardium and causes cardiomegaly.[5] There are three main types of cardiomegaly (Table 1, Fig. 2).

Dilated cardiomyopathy (DCM) is a complex and impairing cardiac disease described as the left ventricle's hypertrophy and a gradual loss of pumping capacity.[40,41] DCM is a common cause of heart failure, affecting millions of people globally. It has a substantial negative impact on the lives of those who are diagnosed with the disease as well as on healthcare systems. Poor left ventricular function (main pumping cavity) is known as DCM.[42] As a non-ischemic heart muscle illness, DCM is not related to ischemic heart disorders like myocardial infarction; rather, its fundamental causes are different from those linked to coronary artery blockages or myocardial infarction.[43] Conversely, DCM is primarily distinguished by anomalies in both structure and function seen in the myocardium, the heart's muscle tissue, which eventually lead to impaired cardiac function. These anomalies may have serious, possibly fatal effects if they are not addressed. DCM is the main cause of cardiac hypertrophy and heart failure.[12]

Coronary artery disease or irregular load circumstances cannot account for DCM in ischemic cardiomyopathy (ICMP). DCM can grow at any age and is more common in men, accounting for about 60 % of all cases of cardiomyopathy in children.[44,45] The disease is a heterogeneous condition involving inappropriate ventricular hypertrophy or dilation of ventricles, which develops gradually and can lead to compensatory heart failure.[46,47] Our aim in exploring the complexities of DCM is to bring together current knowledge, emphasize recent advances, and identify areas where our comprehension is needed. This review paper functions as a comprehensive reference for healthcare experts, researchers, and those interested in gaining a deeper insight into DCM. Our goal as we explore the various aspects of DCM is to actively contribute to ongoing efforts aimed at improving patient care and outcomes in the challenging field of cardiovascular diseases.

DCM can be caused by heart muscle issues intrinsic to it. Approximately 48 percent of cases are inherited.[48] Genetic defects have been reported that affect the structural elements of cardiomyocytes, ion channels, cytoskeletons, and mitochondria.[49,50] DCM can be influenced by systemic factors like inflammation, malnutrition, and infectious diseases, with alcoholism accounting for 21–36 % of cases in high-income countries like the UK.[51,52] The risk of developing DCM due to

alcohol dependence is impaired by several susceptibility factors, including race and genetic factors.[51,53]

Heart genetic defects include muscle protein, A/C laminin, heavy chain β-myosin, troponin T, myosin binding, C protein, myosin, alpha sodium channel unit, and phosphate lamb. Neuromuscular genetic defects include muscular dystrophy of Duchenne, Baker, mitochondrial disorders, Bart syndrome, contagious viruses, fungi, parasites, rickettsia, protozoa, autoimmune myocarditis, Churg-Strauss syndrome, polyangiitis granuloma, systemic lupus, and toxic alcohol of Sarcos.[51,54] Drug-induced anti-tumor and psychiatric medications, along with other medications, can cause various health issues such as hypoplasia, hyperactivity, Cushing's disease, Addison's disease, pheochromocytoma, acromegaly, diabetes, perinatal cardiomyopathy, fatty acid oxidation, and congenital metabolic errors.[55] Genetic predisposition stands as a prominent factor in the development of DCM. There is a multitude of genes linked to DCM, and alterations in these genes can adversely affect different aspects of myocardial function[56,57] as depicted in (Fig. 2, Table 2). A deep understanding of the genetic basis of DCM is essential for evaluating risk, early detection, and the potential development of therapeutic approaches.[12]

The mechanical stretching and straining experienced by cardiac myocytes initiate signaling pathways that contribute to these remodeling processes, ultimately resulting in structural changes, including myocyte hypertrophy and fibrosis, which can lead to an enlarged and weakened left ventricle.[80] Inflammation can contribute to the pathogenesis of DCM. Activation of the immune system and the release of pro-inflammatory cytokines have been observed in individuals with DCM.[12,81] Persistent inflammation can lead to myocyte injury and the development of fibrosis, further compromising cardiac function.[82,83] DCM is characterized by the presence of oxidative stress, which arises from an imbalance between antioxidants and reactive oxygen species (ROS). ROS can inflict harm upon cellular components, exacerbating myocardial dysfunction. Investigating the underlying mechanisms of oxidative stress and exploring potential antioxidant-based therapies are active areas of research in this field.[84]

In dilated cardiomyopathy DCM, the sustained activation of neurohormonal systems, such as the renin-angiotensin-aldosterone system and the sympathetic nervous system, initially serves as adaptive responses to cardiac dysfunction. However, over time, these responses can contribute to adverse cardiac remodeling and further progression of the disease.[85,86] As a result, pharmacological interventions targeting these systems play a central role in DCM treatment. The pathophysiological processes and molecular components in DCM are thoroughly reviewed in this part, with an emphasis on their interconnectivity and significance in the progression of cardiac dysfunction. It also explores recent advancements and emerging therapeutic strategies related to the pathophysiology of DCM.

The cardiomyocytes get larger in this form of cardiomyopathy, and the ventricular wall thickens. This thickening of the ventricular wall hinders blood flow. HCM was first discovered at St. George's Hospital in London in 1957.[87,88] At that time, eight patients had asymmetric left ventricular septal thickening (hypertrophy). HCM has since been internationally accepted and its prevalence in the general population is 0.2 percent.89, 90, 91

HCM is a heterogeneous disease of left ventricular hypertrophy and, in some cases, obstruction of the left ventricular outflow tract.[92,93] About 60 % of adults and adolescents with this illness have a family issue as the etiology.[94,95] Numerous genetic mutations in HCM, the fundamental building block of repeated contractile proteins in muscle cells, have been reported. Although autosomal and sex-related recessive modes have also been found, autosomal dominant inheritance is usually the mode of inheritance for these disorders.[50,96] Genetic abnormalities in the β-myosin heavy chain gene may

be found in 70–80 % of hereditary HCM cases, which are attributed to myosin binding protein C and troponin T.[94] This condition is significantly influenced by genetic factors, primarily due to mutations in specific genes such as MYBPC3 and MYH7 as shown in (Table 3).[97] These genetic mutations are the main contributors to the malfunction of cardiac muscle proteins, which disrupt the normal contractile function of the heart. Consequently, the cells that make up the heart, often referred to as cardiomyocytes, undergo hypertrophy, which causes them to become larger and thicker. This hypertrophic condition can give rise to various clinical symptoms, including the blocking of blood flow from the heart and the occurrence of arrhythmias.[98]

The molecular mechanisms that contribute to HCM involve intricate signaling pathways, for instance, the mitogen-activated protein kinase (MAPK) and calcineurin/NFAT pathways, which are activated in response to cellular stress.[98,114] Moreover, hemodynamic factors related to the inhibition of blood flow can lead to clinical manifestations like breathlessness, chest discomfort, and lightheadedness. Understanding the genetic and molecular factors at the core of HCM is pivotal for purposes such as diagnosis, assessing risk, and designing targeted therapies. Genetic testing and counseling play indispensable roles in the Management of HCM due to its strong hereditary component.[115,116]

Genetic issues can cause HCM, metabolic or neuromuscular conditions (5–10 %) illustrated in (Fig. 3), or rare non-hereditary causes like amyloidosis.[117,118] HCM is characterized by irregular amyloid protein accumulation in the heart, with age playing a significant role as it is more prevalent in neonatal and infant genetic metabolism or neuromuscular genetic diseases.[119] Reconstructing genetic history can identify disease patterns, with a family history of sudden death, mysterious heart failure, or arrhythmia as the main factors. Symptoms may indicate a systemic cause.[5,16]

Restrictive cardiomyopathy (RCM) is a less prevalent form of cardiomyopathy, presents a genetic basis that is currently in the process of being further elucidated, and is not as well-defined in comparison to other cardiomyopathies like DCM or HCM. Although RCM is frequently labeled as idiopathic or sporadic, there have been associations between the condition and specific genetic factors and mutations. RCM is ventricular stiffness, causing ventricular filling and diastolic volume reduction. Diastolic dysfunction on echocardiograms is suspected if the systolic output is normal.[120,121] It is the least prevalent cardiomyopathy, comprising 5 % of pediatric cardiomyopathy. There are several explanations for the RCM, but 50 percent of the reasons have not been identified.[122] Nonetheless, it is crucial to recognize the genetic diversity of RCM as it can manifest as both sporadic and familial cases, and the genetic foundations may differ among individuals and families. As our comprehension of the genetic factors behind RCM advances, genetic testing, and counseling become pivotal in assessing risk and managing the condition of affected individuals and their families.[123] Non-genetic elements and the intricate interplay between various genetic and environmental factors could also influence the onset of RCM.[124]

Many forms of Royal Canadian Mounted Police have more impact on some races than others. For example, RCM is caused by endocardial fibrosis and is most common in tropical and sub-Saharan African countries, such as Cameroon.[122,125] In other areas, RMCP is more widespread in amyloidosis, sarcoidosis, and hemochromatosis.[122] RCM can grow from a root cause. Endocardial fibrosis can be caused by conditions like hemochromatosis, glycogen storage disease, or Fabry disease, which causes excessive load in myocardial cells. Other forms of cardiomyopathy may result in restricted pathophysiology.[126,127] General etiologies or pathogenic causes include restrictive cardiomyopathy, intrusive amyloidosis disorder, sarcoidosis, primary hyperoxaluria, Gaucher disease storage disease, hemochromatosis, Fabry disease, systemic sclerosis, glycogen storage disease, type I and II mucopolysaccharidoses, Niemann-Pick disease, non-invasive idiopathic diabetic cardiomyopathy, pseudoxanthoma, sarcomeric protein disorder, Werner syndrome, myo-fibro myopathy, endocardial

carcinoid heart disease, endocardial fibrosis, drug-induced serotonin, methylated ergot, ergotamine, busulfan, anti-hydroxyquinoline, anti-tumor medications, and other forms of cardiomyopathies.[5,128]

Dilated cardiomyopathy, with a ratio of 1:250-500, is not normal in infants and adults. In childhood and adults, hypertrophic cardiomyopathy is uncommon, with a 1:250-500 ratio. In children and adults, restrictive cardiomyopathy is rare, and in children and adults, arrhythmogenic right ventricular cardiomyopathy is uncommon, with a ratio of 1:2,000-5,000. The level of presentation is 14 times that of infancy and puberty in the first year of life. Now, it is referred to as arrhythmic cardiomyopathy. HCM/DCM incidence data produced estimates.[129,130]

In most cases, when the enlargement of the heart becomes moderate or serious, symptoms usually appear. Significant symptoms include the abnormal rhythm of the heart, cough, chest pain, severe tiredness, dizziness, shortness of breath, bloating of the stomach, and swelling of the ankles, legs, and feet.[131,132]

Abnormal heart valves, amyloidosis, rare diseases that can affect heart function, anemia, arrhythmias, cardiomyopathy, cardiomyopathy, genetics, heart disease, diabetes, heart valve disease, hemochromatosis that can cause excessive iron in the body, high blood pressure, heart attack, hyperthyroidism, excessive work or diseases that damage the heart can cause mild cardiac hypertrophy, such as The cause of mild cardiac hypertrophy, however, is normally unknown.[133,134]

Medication may be required in some situations. Causes of transient cardiac hypertrophy can include heavy drinking or drug use due to alcohol abuse, which may cause mild cardiac hypertrophy. In reversing this situation, therapy will succeed.[135,136] Because of stress severe stress can cause acute stress-induced cardiomyopathy. About 75 % of people are affected by emotional or physical stress. Pregnancy the heart often gets larger in childbirth. This sort of cardiac hypertrophy may be called perinatal cardiomyopathy. Viral heart infection: Antiviral medicines may be required to treat a heart virus infection that causes heart hypertrophy.[137,138]

A series of clinical heart failure syndromes can result in an extension of the heart in the form of dilation or hypertrophy, disturbing nearly 5.8 million people in the United States. More than half of these cases account for heart failure with preserved ejection fraction (HFpEF). With male age and American African ethnicity, the incidence of heart failure increases. After diagnosis, about half of people diagnosed with heart failure die within five years.[139]

There are genetic and non-genetic components to the development of hypertrophy and heart remodeling[140,141] Dilated hypertrophy, fibrosis, and contractile dysfunction are the most critical pathophysiological changes leading to cardiac hypertrophy. Hypertrophic cardiomyopathy or dilated cardiomyopathy may result from systolic dysfunction and abnormal myocardial remodeling.[12] Important stimuli for MAP kinase and inflammatory cytokines signal transduction in cardiomyocytes are circulating neurohormones, mechanical stretching, and oxidative stress.[142,143] Transduction of signals leads to structural protein and protein changes that regulate excitatory contraction. Dilated cardiomyopathy mutations result in decreased sarcomere contractility and decreased sarcomere content. Hypertrophic mutations in cardiomyopathy lead to hyperdynamic contraction, poor relaxation, and increased energy expenditure in a molecular phenotype.[144,145]

Extensive hearts can lead to complications such as blood clots, heart failure, and sudden death. Blood clots can block blood flow, potentially causing stroke or heart attack. Heart failure can result from a failure in the heart's electrical system, leading to cardiac arrest and sudden death. Heart murmurs caused by faulty valve closure can be harmless but should be monitored.[146,147]

The precise and timely diagnosis of Cardiomyopathy is essential to initiate the right management and treatment approaches. The evaluation of DCM usually combines clinical assessment, non-invasive imaging methods, and targeted diagnostic tests.[148,149] The diagnostic procedure frequently commences with a comprehensive medical history and physical examination. The presence of symptoms like shortness of breath, fatigue, and edema can trigger further inquiry. Some or all of the following may be included in diagnostic tests. Cardiomegaly, indicated by an enlarged heart, requires a comprehensive diagnostic approach involving chest X-rays for initial size assessment and electrocardiograms (ECG or EKG) for evaluating electrical activity, but ECG alone may not determine the cause.[150,151] Echocardiography, particularly transthoracic echocardiography (TTE), provides detailed information on cardiac dimensions and function. Computed tomography (CT) and Cardiac Magnetic Resonance Imaging (MRI) scans offer high-resolution images to assess heart structure and scar tissue presence[152] (Fig. 4). The choice of diagnostic method depends on clinical presentation and suspected causes, with a combination of these modalities ensuring a comprehensive assessment for accurate diagnosis and management of cardiomegaly.[153,154]

These tests will disclose symptoms that suggest issues in the blood.[155] Blood tests measure biomarkers like BNP and troponins to detect cardiac stress or damage. Coronary angiography is used when coronary artery disease is suspected.[156] Some blood tests, including examining kidney, and liver function and thyroid as well as iron levels, may be performed. B-type natriuretic peptide (BNP), a protein made in the heart, can be measured with a single blood test.[157]

One common consequence of cardiomyopathy is heart failure, which can result in an increase in blood BNP levels screening or testing for genetics. Cardiomyopathy is a genetic condition that can run in families.[157,158] Genetic testing has become increasingly vital for the detection of mutations in genes associated with DCM. This approach aids in assessing the risk and may offer guidance for treatment strategies.[159]

Stress testing during workouts appears to be safe in well-chosen HCM patients.[160,161] A stress test requires a workout while connected to a heart and blood pressure monitor on a treadmill or exercise bike. An exercise stress test evaluates the heart's capacity to react properly during strenuous activity. The findings revealed the functioning of the heart during physical activity.[162]

A chest X-ray can demonstrate the condition of the heart and lungs. Further testing is usually required to determine the cause. (a = distance from the right heart border to the midline, b = distance from the left heart border to the midline, and c = maximum thoracic diameter) PA chest X-ray showing CTR (Fig. 5).[163]

This procedure uses sound waves to create a video picture of the heart so that physicians can examine the state of its chambers. It indicates any inflammation, congenital heart defects, heart attack damage, and heart twitch effectiveness (Fig. 6).

It is possible to use a CT scan or MRI scan to develop and develop the heart and chest (Fig. 7). Magnetic resonance imaging (MRI) of the heart having cardiomegaly. This MRI image provides a representation of Cardiomegaly, marked by an enlarged heart. It offers a comprehensive view of the heart's size, shape, and internal structures, allowing for a thorough assessment of the degree and root causes of cardiomegaly. Notably, the MRI highlights key aspects like cardiac chamber size, myocardial wall thickness, and overall heart dimensions.[164,165]

For the measurement of the heart's electrical activity and to diagnose abnormal heart rhythms, an electrocardiogram is used. With repolarization abnormality (LV "strain" pattern) in V5-6, left ventricular hypertrophy is marked. A 12-lead ECG is a valuable diagnostic tool as it can unveil

arrhythmias, conduction irregularities, and indicators of left ventricular hypertrophy (Fig. 8). Nonetheless, it may not consistently exhibit specific cardiomyopathy-related alterations in all cases.[166]

The effective Management of Cardiomegaly, characterized by an enlarged heart, necessitates a multifaceted approach aimed at improving cardiac health and addressing the underlying causes of the condition.[167] This comprehensive approach involves various treatment modalities and strategies tailored to the individual's specific clinical presentation and medical history.[168,169] A personalized along with intensive care and a multi-disciplinary approach are crucial to determine the most appropriate and optimal strategy for its treatment. A much strict consideration should be followed for the underlying causes and clinical presentation of the cardiomegaly.[170] as shown in (Table 1). It is worth notable that moderate cardiac hypertrophy is usually rectified on its own, although there are some therapeutic considerations available which include are as follows.

The recommended medication is dependent on a specific illness condition that causes the heart to expand. Medication might be necessary for the management of high blood pressure along with irregular a notable heart rhythm.[171,172] Diuretics can also cause a lowering of arterial pressure, whereas anticoagulants can easily lower the chances of blood clotting. Additionally, medications may be used to address other underlying conditions, including anemia and/or thyroid disease.[153,173] Heart failure patients needed to use the medication including beta-blockers and angiotensin-converting enzyme (ACE) inhibitors.[174]

If the medicine is ineffective for the treatment of mild heart hypertrophy or either symptoms worsen, the use of specialized medical equipment for the treatment may become necessary.[175] Heart rate monitors may be useful in treating people with DCM to control their heartbeat. An implantable cardioverter defibrillator (ICD) may be required to deliver electrical shocks to control the heart rhythm in people with severe arrhythmia.[176,177]

More severe cases of cardiac hypertrophy or patients who do not respond to other treatments are usually reserved for surgery. The following operation may be recommended for patients with cardiac hypertrophy, depending on many factors.[115,178]

Surgery for coronary artery bypass and heart transplantation.[179,180] Surgery, such as coronary artery bypass grafting and valve repair, may be required in specific cases. Implantable devices like pacemakers and ICDs address arrhythmias.181, 182, 183

People with cardiac hypertrophy can relieve symptoms through the following lifestyle and diet changes: quit smoking, maintain a healthy weight, regularly monitor blood pressure, exercise most of the week, limit alcohol and caffeine, and sleep 7 to 7 per night 9 h, increase the intake of fruits and vegetables, replace refined grains, such as white bread and whole grains of macaroni, cut out pro.[184,185] The following methods can reduce the risk of heart enlargement: discussing heart enlargement with a doctor, particularly in the case of symptoms or a family history of heart disease, managing heart enlargement-related diseases such as diabetes, high blood pressure, and obstructive sleep apnea by quitting smoking, maintaining a healthy weight, eating a balanced diet and keeping the body active.[186,187] Lifestyle changes, including diet, exercise, and quitting smoking, play a key role in its Management.[188,189]

Recent progress in the field of Cardiomegaly, with continual research going on, holds the probability of affecting the diagnosis and treatment of this state significantly. Research on Cardiomegaly suggests capable commands for further diagnosis. It is estimated that progressive imaging technologies would improve diagnostic accuracy and offer a complete understanding of heart

enlargement. Omics techniques, such as metabolomics, proteomics, and genomes, may assist in knowing the molecular facts of Cardiomegaly, and multi-omics integration can be beneficial to identify its other subtypes. The progress of telemedicine offers an opportunity to avail the effective use of these technologies, guaranteeing data security and enhancing patient outcomes. Understanding the fundamental causes of HCM has caused the development of personalized therapies, stressing the need for an etiological description of HCM patients. Additionally, there is a need to order patient-centered treatment, which calls for a deeper understanding of the psychological features of controlling an enlarged heart. It is vital to authenticate new biomarkers and therapeutics through research and clinical trials to regulate their clinical worth and safety. We must navigate these viewpoints and complications in a way that advances our knowledge and capability to treat Cardiomegaly.

Section snippets

Conclusion

A succinct overview of the many features of Cardiomegaly, such as its environmental and genetic roots, various therapeutic modalities, and diagnostic methods. Cardiomegaly is caused by inflammation of the myocardium brought on by chemicals or allergens, drugs, severe exercise, systemic endocrine or autoimmune problems, or infections (usually viral). Cardiomegaly may be caused by mutations in several genes, including those that code for desmosome and sarcomere structural elements. The discussion

Compliance with ethical standards

None.

This report describes a patient with a thoracic aortic aneurysm who presented with chest pain and dyspnea. Preoperative studies revealed a massive cardiomediastinal silhouette. Within hours after the operation, a profound reduction in cardiomegaly was observed. Herein, we describe the distinctive imaging and technical aspects of the surgical procedure.

Aneurysms of the aortic arch are typically associated with the ascending aorta and less commonly may extend to the descending thoracic aorta (DTA) or thoracoabdominal aorta. Most patients with aortic arch aneurysms are asymptomatic, and these aneurysms are typically discovered incidentally. Symptoms may be manifested—particularly in cases of large arch aneurysms—and include stroke, dysphagia (due to esophageal compression), dysphonia (resulting from recurrent laryngeal nerve compression), dyspnea (due to lung compression), and syncope resulting from rupture.

A 60-year-old woman with a history of smoking and hypertension presented with a 3-day history of chest pain and shortness of breath. Initial physical examination revealed blood pressure of 160/80 mm Hg, weight of 54.5 kg, and body mass index of 16.3 kg/m^2. On admission, laboratory results showed a hemoglobin level of 13 g/dL, creatinine level of 1.1 mg/dL, and white blood cell count of 9×10^9/L.

Preoperative chest radiography displayed a significant enlargement of the cardiomediastinal silhouette, consistent with an aortic aneurysm and pericardial effusion (Figure 1). Computed tomography angiography with intravenous administration of contrast material revealed the presence of a thoracic aortic aneurysm involving the distal ascending and aortic arch as well as the proximal DTA, measuring 6.2 cm in diameter (Figure 2).

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Figure 1. Preoperative chest radiograph. Massive cardiomegaly is revealed, with a maximum diameter of 22 cm.

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Figure 2. Composite image of preoperative computed tomography angiography with intravenous administration of contrast material revealing a 6-cm aortic arch aneurysm evaluated in (A) axial, (B) coronal, and (C) sagittal planes.

Preoperative echocardiography revealed normal left ventricular size and systolic function, with a left ventricular ejection fraction of 60% to 65%. The estimated right ventricular systolic pressure was 52 mm Hg, indicating moderate pulmonary hypertension. Notably, severe tricuspid regurgitation was observed. A 3.5-cm circumferential pericardial effusion was observed. No evidence of pericardial tamponade was seen. The patient was scheduled for urgent surgical procedure and underwent open repair under total cardiopulmonary bypass and systemic hypothermia to a temperature of 20 °C. Blood cardioplegia was perfused at 4 °C. This was supplemented with continuous retrograde cold blood, keeping the myocardial septal temperature below 15 °C. The ascending aorta, transverse aortic arch, and proximal DTA were resected and replaced with a 30-mm Gelweave (Terumo Aortic) woven Dacron graft repair with an added 18-mm Dacron graft selected for graft replacement of the aneurysm. The graft was sutured to the proximal DTA in an end-end fashion (zone 3 arch) by a running 3-0 Prolene suture with anastomosis of the left subclavian artery (LSA) in a beveled fashion. The innominate artery was bypassed with the 18-mm Dacron graft with a running 4-0 Prolene suture, and flow was restored. The left common carotid artery was bypassed with a 12-mm Dacron graft with a running 4-0 Prolene suture. The procedure was performed through a median sternotomy.

The patient was extubated within the first 8 hours after the operation. A chest radiograph on the first postoperative day (16 hours after surgical procedure) exhibited remarkable improvement, demonstrating a significant decrease in the cardiomediastinal silhouette by 40%. The postoperative echocardiogram revealed a significantly improved overall estimated ejection fraction, ranging from 75% to 80%, with only mild tricuspid regurgitation. A trivial pericardial effusion was observed (Figure 3).

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Figure 3. Combined echocardiography image. (A) Preoperative transthoracic echocardiogram showing a 3.5-cm pericardial effusion (arrow). (B) Postoperative echocardiogram demonstrating improvement of pericardial effusion.

After intensive care medical treatment, intravenous diuresis, and respiratory physical therapy, the patient was discharged home 9 days after the operation. Histopathologic analysis revealed a chronically dissected aortic wall with a fibrotic and organized dissection fork along with notable damage and loss of medial elastin fibers, as observed through elastin stain.

Postoperative computed tomography angiography performed 1 month after the intervention revealed a patent graft without stenosis or abnormalities. The patient remained asymptomatic during the 1-year follow-up, with no medical or surgical complications.

Comment

After the images were presented in our multidisciplinary meeting, most of the physicians agreed that this was the most significant modification in cardiomegaly size they had ever witnessed within a span of less than 24 hours. Multiple causes of cardiomegaly can be recognized, including coronary artery disease (the most common), hypertensive and valvular heart disease, aortic aneurysms, idiopathic cardiomyopathy, infiltrative diseases (such as amyloidosis), pulmonary conditions (such as primary pulmonary hypertension), and chronic obstructive pulmonary disease, among others.[1]

Whereas thoracic aortic arch aneurysms are less common than ascending or descending thoracic aneurysms, they represent a life-threatening condition because of the potential risk of rupture. Aortic arch aneurysms can be extremely complex and may be manifested with symptoms including compression of adjacent structures (hoarseness, due to the compression of the recurrent laryngeal nerve, or stridor, resulting from tracheal compression), chest pain, shortness of breath, and even syncope due to rupture.

Multiple surgical procedures have been described for aortic arch reconstruction, such as island reimplantation of the supra-aortic vessels and total arch repair with multiple Dacron graft side branches. Hybrid techniques include zone 0 debranching (with bypass from the ascending aorta to all 3 supra-aortic vessels); zone 1 debranching, involving bypass or transposition of the left common carotid and LSA; and zone 2 debranching (with bypass or transposition of the LSA). All of these techniques are followed by endovascular aneurysm exclusion.[2], [3], [4]

Complex, advanced endovascular total arch techniques have also been performed.[5] Minimally invasive techniques, including complete endovascular branched and multibranched reconstructions as well as a complete endovascular approach, are being presented and considered as alternatives to traditional open repair. However, open repair remains the standard for providing more durable reconstruction in treating aortic arch aneurysms.[5,6] When open repair of arch aneurysms is performed in high-volume centers and follows adequate patient selection with improvements in surgical techniques and perfusion strategy, results may be adequate, leading to excellent long-term outcomes.[7]

We investigated the contribution of a dilated right-sided heart to roentgenographic cardiomegaly in patients with heart failure (HF) and a normal ejection fraction (EF; diastolic HF) and those with HF and a decreased EF (systolic HF). We compared the cardiothoracic ratio (CTR) on upright chest roentgenograms and major- and minor-axis dimensions of the 4 cardiac chambers on echocardiograms in patients with HF and a normal EF (≥0.50, n = 35) and those with a decreased EF (<0.50, n = 37) and examined the correlation between the CTR and cardiac chamber dimensions. The CTR did not differ between patients with normal and decreased EF values (0.58 ± 0.07 vs 0.60 ± 0.06, p = 0.26). Left-side cardiac chamber dimensions were substantially smaller in patients with a normal EF than in those with a decreased EF (left ventricular minor-axis dimension, 4.4 ± 0.7 vs 5.8 ± 0.8 cm, p <0.001). In contrast, right-side cardiac chamber dimensions were generally similar between groups. The CTR correlated with major-axis dimensions of the right ventricle and right atrium (p <0.01 for the 2 comparisons), but not with the left-side cardiac chamber dimensions (all p values >0.05). In conclusion, the CTR predominantly reflects right- rather than left-sided heart size in patients with HF. Right-sided heart size is similar between patients with normal and decreased EF

values. Thus, despite the substantial difference in left ventricular size and EF, there is substantial overlap in the CTR between patients with diastolic and systolic HFs and the CTR is unable to discriminate between groups. Patients

We studied patients who were evaluated for the presence of HF at Wake Forest University Baptist Medical Center (Winston-Salem, North Carolina) between November 2001 and August 2002. HF was diagnosed as previously described.[1] Patients were excluded if they had hemodynamically significant valvular disease, prosthetic valve replacement, active myocardial ischemia or acute infarction, malignancy, and dialysis-dependent renal failure. Patients were eligible for the present study if they underwent

Results

The study population was obtained from 137 consecutive patients with a normal EF (≥0.50; diastolic HF) and 104 patients with a decreased EF (<0.50; systolic HF),4, 5, 6 in whom 102 patients with diastolic HF and 67 patients with systolic HF were excluded from the present study because of lack of contemporaneous (within 2 weeks) echocardiographic and upright chest roentgenographic studies. In consequence, the study population consisted of 35 patients with diastolic HF and 37 patients with

Discussion

The major findings of the present study are that (1) the CTR on chest roentgenogram reflects right- rather than left-sided heart size in patients with HF; (2) the left ventricle is substantially smaller in patients with diastolic HF than in those with systolic HF, but right-sided heart size is comparable between groups; and (3) there is substantial overlap in the CTR between patients with diastolic and systolic HF

Introduction

In forensic radiology, the cardiothoracic ratio (CTR) calculated from postmortem computed tomography (PMCT) images can be used to detect cardiomegaly. In this study, a new measurement method is studied that involves measurement in the anteroposterior (AP) and transverse directions, with a reference level based on the Thai population.

Objective

To screen for cardiomegaly using the CTR calculated from PMCT images.

Research method

A sample size of 116 deceased Thai individuals who underwent PMCT before autopsy was obtained. Individuals were divided into two groups: normal heart weight and overweight heart. Hearts heavier than the mean plus one standard deviation were categorized into the overweight group. The CTR was calculated in both the AP and transverse directions at six reference levels. Receiver operating characteristic curves (ROC) were calculated to determine the CTR cutoff point for the diagnosis of cardiomegaly.

Results

The CTR cutoff values for diagnosing cardiomegaly were as follows: 1) CTR >0.5 in the transverse direction at the mid-vertebra of T7 (sensitivity, 75.6%; specificity, 70.6%; area under the ROC curve 0.81), 2) CTR >0.49 in the transverse direction at the mid-vertebra of T8 (sensitivity 71%, specificity 81.4%, area under the ROC curve 0.80). The selection of the cutoff values depended on the location

of the heart. The area under the ROC curve in the AP direction was in the range 0.5-0.7, which is inferior compared to the transverse direction (0.7-0.9).

Conclusion

Calculating the CTR with a reference level on PMCT images can assist in the diagnosis of cardiomegaly.

Graphical abstract

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Introduction

The primary objective of a forensic autopsy is to determine the cause of death. Currently, forensic radiology, such as postmortem computed tomography (PMCT), plays a significant role in determining the cause of death[1], [2], [3]. Cardiovascular disease is the most common cause of death worldwide[4,5]. Cardiomegaly is a condition in which the heart is larger than normal, and is indicated by abnormally increased heart weight, or hypertrophy, or dilatation of the heart[6] and can lead to death.

The cardiothoracic ratio (CTR)[7], [8], [9] is a simple and widely used method for diagnosing cardiomegaly while individuals are still living. The CTR is calculated by dividing the maximum width of the heart by the maximum width of the thoracic cavity, and a CTR > 0.5 is indicative of cardiomegaly. This measurement is typically performed on plain film chest radiography but can also be determined using computed tomography (CT) images[10,11]. The CTR has been determined using PMCT images[[12], [13], [14], [15],25], mostly in studies conducted in Western countries, which predominantly involve Caucasians and there are differences in heart weights compared with the Thai population[16,19,22,23,26]. The aim of this study was to be calculate the CTR from measurements on PMCT images, from the Thai population. The measurements were performed in the anteroposterior (AP) and transverse directions, using vertebral level as a reference to reduce subjectivity. The measurement in the AP direction was performed because authors have predicted that when the heart develops cardiomegaly, it enlarges in all directions. This has not been studied previously and it may enhance the effectiveness of cardiomegaly detection. The objective of this study was to improve the accuracy of screening for cardiomegaly during postmortem examinations in the Thai population.

Section snippets

Materials and methods

This study was approved by the Research Ethics Committee of the Faculty of Medicine at Chulalongkorn University (IRB number 0269/66).

Results

A total of 950 deceased individuals were enrolled in this study. After applying the inclusion and exclusion criteria and random selection, the sample size was 116, divided into 54 (47%) with a normal heart weight and 62 (53%) with an overweight heart, and there were 104 males (89.7%) and 12 females (10.3%). The causes of death were cardiovascular disease (47 cases, 40.5%), trauma (26

cases, 22.4%), asphyxia (22 cases, 19%), undetermined causes (9 cases, 7.8%), electrocution (4 cases, 3.4%),

Discussion

From the results of the CTR study conducted in both the AP and transverse directions, at six reference levels, to determine the CTR cutoff values for diagnosing cardiomegaly, it was found that the CTR in the AP direction was not effective in identifying cardiomegaly because it had a low ability to distinguish between normal and overweight hearts. The CTR in the transverse direction is effective in distinguishing cardiomegaly. When considering the AUC, sensitivity, specificity, and number of

Conclusion

Calculating the CTR with a reference level from measurements on PMCT images can aid in the diagnosis of cardiomegaly [18]. The researchers suggest a CTR cut-off value of 0.5 for the transverse direction at the mid-vertebral level of T7 and a CTR cut-off value of 0.49 for the transverse direction at the mid-vertebral level of T8. In summary, this measurement method demonstrates good accuracy, ease of implementation, and reproducibility.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work the authors used ChatGPT-3.5 in order to correct grammar. After using this tool, the authors reviewed and edited the content as required and take full responsibility for the content of the publication.

Abstract

This report is from a 10-year cohort study of community-dwelling elderly men and women. Mean age at the time of entry into the study was 79 years. Annual chest x-ray studies were performed, and data are presented regarding prevalence, incidence, and prognosis of cardiomegaly. Cardiomegaly was defined as a transverse diameter of the cardiac silhouette ≥50% of the transverse diameter of the chest (increased cardiothoracic ratio). At the time of entry into the study 110 subjects (23%) had cardiomegaly. After 10 years, 51% of the subjects with cardiomegaly at baseline died compared with 33% of the subjects without cardiomegaly (mortality rate = 9.1 vs 4.8100 person-years respectively; p = 0.014). Cardiovascular disease incidence was also higher for those with preexisting cardiomegaly at baseline (rate 9.1 vs 6.1100 person-years; p = 0.0001). According to the Cox proportional hazards regression analysis, age, cardiomegaly, diabetes, and prior evidence of myocardial infarction were independent predictors for death in this cohort. Similarly, the best predictive variables for cardiovascular disease were age, diabetes, prior evidence of myocardial infarction, and cigarette smoking. Of the 359 subjects without cardiomegaly at baseline, 108 (30%) showed evidence of new cardiomegaly, and their risk of cardiovascular disease was 1.8 times that of subjects whose test results were negative for cardiomegaly throughout the study (p = 0.003). Thus cardiomegaly, as defined by an increased cardiothoracic ratio on x-ray films, irrespective of cause, is associated with a poor prognosis in very elderly men and women.

SESSION TITLE: Pulmonary Manifestations of Systemic Disease Case Report Posters 15

SESSION TYPE: Case Report Posters

PRESENTED ON: 10/09/2023 02:10 pm - 02:55 pm

INTRODUCTION: Congenital cardiovascular abnormalities can cause tracheobronchial compression in pediatric population; however, it is exceedingly uncommon for acquired cardiomegaly in

adulthood to cause pathologic compression of the airways. Our review of the literature indicates that this is the first reported case of severe cardiomegaly resulting in bronchial obstruction and subsequent lobar collapse.

CASE PRESENTATION: Our patient, a 44-year-old male with a history of ischemic cardiomyopathy and heart failure with left ventricular ejection fraction of 15%, presented with encephalopathy. He was febrile with temperature of 38.5C. Labs showed leukocytosis of 16,000/mcL. CT brain showed acute left thalamic, and right occipital infarcts. CT chest showed severe left ventricular (LV) dilation, compression of the left upper lobe (LUL) bronchus and near complete collapse of the LUL. Patient underwent bronchoscopy which demonstrated luminal narrowing of LUL bronchus and impacted mucoid secretions. Remaining airways were patent. LUL bronchoalveolar lavage cultures showed Staphylococcus Aureus. Patient's bronchial compression was deemed to be a result of severe dilation of the left side of the heart, which caused the collapse of the LUL of lung and the development of post-obstructive pneumonia. To improve left ventricular volume, IV diuretics were initiated. Cardiac afterload was reduced with antihypertensive medications. Pneumonia and bronchial obstruction were addressed with administration of antibiotics, bronchodilators, nebulized hypertonic saline, and chest physiotherapy. Although the patient showed a clinical response in terms of infection control and hemodynamic stability, he experienced a loss of all brainstem reflexes, and as a result, brain death was pronounced.

DISCUSSION: Airway compression can occur because of congenital abnormalities like vascular rings, dilated cardiomyopathy in children, and left atrial (LA) enlargement from mitral valve disease in adults. However, to our knowledge, no cases of bronchial compression caused by cardiomegaly secondary to ischemic cardiomyopathy have been documented in adults. Due to the close anatomic relationship between pulmonary and cardiovascular structures, severe heart failure can cause enlargement of the LV and LA that can be substantial enough to cause compression of the adjacent bronchi. Since cardiac and pulmonary pathology are inextricably interlinked in this case, a parallel approach should be taken to address both the root causes. This includes pulmonary clearance measures and administration of antibiotics, as well as optimizing volume status with diuresis to decrease left sided cardiac volumes.

CONCLUSIONS: Despite being uncommon, it is essential to acknowledge the possibility of severe cardiomegaly contributing to lobar collapse. While supportive therapy and antibiotics are used to treat pneumonia and facilitate airway clearance, it is crucial to optimize the underlying heart failure and reduce LV volume to relieve bronchial obstruction. Early recognition and directed treatment can improve patient-centric outcomes.

Abstract

This study examines an end-to-end technique which uses a Deep Convolutional Neural Network U-Net based architecture to detect Cardiomegaly disease. The learning phase is achieved by using Chest X-ray images extracted from the “ChestX-ray8” open source medical dataset. The Adaptive Histogram Equalization (AHE) method is deployed to enhance the contrast and brightness of the original images. These latter are compressed before undergoing a training stage to optimize computation time. By this method, we obtained a diagnostic accuracy greater than 93%, which outperforms published results for recognizing Cardiomegaly disease. In addition, with U-Net, precise localization of Cardiomegaly is possible, which is not the case in previous works.

1. Introduction

X-ray radiography is one of the simplest and most commonly available techniques that can be utilized for the detection and diagnosis of many diseases. Consequently, a large quantity of radiographic images and reports are generated and stored daily in hospital archives around the world. These archives constitute a considerable and valuable source of information, which remains minimally exploited because of the lack of means of automation of the image analysis process.

One of the solutions considered to solve this problem and give a value-added to these archives lies in the use of artificial intelligence, and in particular deep learning techniques, which have proved their effectiveness for objects detection [1] and image segmentation [2].

Among these techniques, Convolutional Neural Networks (CNN) have shown excellent performance in computer vision and machine learning. The medical field is one of the areas in which this technology has attracted a great deal of interest, which has manifested itself in numerous published articles. In particular, research has been conducted to develop CNN models capable of diagnosing thoracic diseases, including lung nodules at Computed Tomography (CT scan) [3], pleural effusion and cardiomegaly [4], pulmonary tuberculosis [5] and Pneumonia [6]. In all these works a high detection accuracy rate lying between 88% and 91% was reported. Nevertheless, much work remains to be performed for example in the field of the complexity of algorithms, learning methods and the use of more or less large databases, which are the main vectors for the development of efficient and inexpensive techniques for automating the medical analysis process from Chest X-rays (CXR).

This work focuses on Cardiomegaly disease, a medical term used to refer to cardiac hypertrophy. We have fixed three main objectives: the first is to achieve automatic detection of this disease in a CXR image, the second is to determine accurately its location in the image, and the third consists to improve the detection accuracy reported in other works.

For this purpose, we have developed a new CNN algorithm based on U-Net, in which the learning phase is performed using CXR images extracted from the open source medical database “ChestX-ray8” [7]. It should be noted that although the images used have good resolutions of (1024 × 1024) pixels, it has been found that the contrast for some extracted images is very low, which makes it difficult to make a correct diagnosis of the disease, and this fact impacts directly the accuracy of the detection. So we set up a pre-treatment step before using the “ChestX-ray8” images in order to improve their quality. This treatment is based on a well-known method called AHE (Adaptive Histogram Equalization) [8] that allows to increase the contrast and to spread out the most frequent intensity values in an image.

Using the “ChestX-ray8” database we have identified 1010 images dedicated to Cardiomegaly disease. Nevertheless, it is hard to work with such a great number of images in deep learning processes, especially if the images are kept at their original size. One of our main objectives being to propose a simple treatment model, we opted to undergo a phase of compression to the images. This compression was ensured without altering the quality nor the content of images by using HDF5, which allows to manipulate digital data quantities of several terabytes by preparing, categorizing and marking multidimensional arrays in a single file.

Another difficulty with the “ChestX-ray8” dataset is the absence of image masks, which leads to a poorly supervised learning problem. This is why we manually created masks for over a thousand images.

For the treatment phase, we used a particular architecture CNN namely U-Net, which uses a Fully Convolutional Network.

Model, giving better segmentation in medical imaging [9]. This proposed CNN model reaches a diagnosis accuracy greater than 93%, which is better than published results for recognizing Cardiomegaly disease. In addition, with U-Net, precise localization of Cardiomegaly is possible, which is not the case for the previous works.

The remainder of the paper can be summarized as follows. In the second section, we give a brief survey of recent works on the application of deep learning for medical image analysis. Then, in section three, we develop the different steps for the pre-treatment of images, starting by explaining the reasons for choosing the "ChestX-ray8" dataset, describing the different steps to extract Cardiomegaly images, and the operations of optimization and compression of images. In the fourth section we present in detail the different phases of the implementation of our U-Net based CNN algorithm. Finally, section five gives the results of implementation of this algorithm for Cardiomegaly disease detection from CXR images.

2. Related works

Previously published work has reported very high detection success rates; as in Ref. [10], where the authors employed a CNN based on ImageNet to identify different pathologies in CXR images and obtained a rate of 89%. In another work [11], the authors presented a new architecture named DualNet that processes simultaneously both frontal and lateral CXR images. In this case an accuracy of 91% has been reported, but the authors used a large set of MIMIC-CXR data (thousands of images). In Ref. [12], the authors achieved an accuracy of 92%, but this was reached using pre-configured and heavy models such as ResNet-101.

In another work, a team from Taishan Medical University [13], developed an automatic method, based on a CNN algorithm, to identify a patient's position and body region from digital radiographic images. For this aim, they have used only frequency curve classification and gray matching; however, in order to achieve the 90% prediction accuracy, more than 7000 images were necessary.

Otherwise, recent research [14] enabled to classify the 8 diseases present in the ChestX-ray8 database. Nevertheless, the method uses heavy and pre-trained models such as ResNet-101 and ImageNet and can't locate the disease inside the CXR. Another approach to use the concept of deep learning for detection pathologies from CXR was implemented by applying a preconfigured model, intended for generic visual recognition [15]. Nevertheless, the model is limited to detection and doesn't allow positioning of the disease in the CXR.

In this paper we are interested not only in detecting Cardiomegaly disease and to enhance detection precision with respect to previous works, but we aim as well to locate precisely the disease inside the CXR and to propose an algorithm using a small set of data for training. The U-Net based CNN algorithm we developed enabled us to obtain a high detection precision of between 93 and 94%, from a small dataset in the training phase. Up to now our method gives good results compared to cited works [10,11], that used heavy and preconfigured models (VGG16, VGG19 and ResNet). To the best of our knowledge, this is the first time such a procedure is reported, offering precise detection of Cardiomegaly disease, but also enabling to locate it inside the CXR images. The different stages of implementation of our model will be developed below.

3. Cardiomegaly disease

3.1. Pre-processing treatment

3.1.1. ChestX-ray8 dataset

“ChestX-ray8” is an open-source medical database consisting of 108,948 frontal views of CXR images of 32,717 unique patients, comprising classified images of 8 popular diseases. “ChestX-ray8” was launched by teams from the Department of Radiology and Imaging Sciences, National Library of Medicine, and National Institutes of Health, Bethesda A ELIMINER [7]. This dataset is available and shared for research purposes and for performance evaluation of different computer aided detection systems.

We extract first the Cardiomegaly images from the Excel files offered by “ChestX-ray8” dataset, using a basic Python script that separates files, based on their label, in separate folders. This allowed us to extract 1010 images corresponding to Cardiomegaly. Nevertheless, these 1024 × 1024 resolution images are given without any masks or annotations showing the position of disease. Thus, they have to be preprocessed before applying Deep Learning technique.

3.1.2. Optimization of image contrast

Image contrast enhancement is used widely in digital image processing; the main idea behind this technique is to show hidden details that can contain interesting information in the image.

One of the most popular techniques is HE (Histogram Equalization), which focuses on increasing the intensity of the image by enhancing the contrast. This is accomplished by applying all possible values of red, green and blue channels in each pixel. It shows good results in colorized images but it is very limited with grayscale ones. For these images it is more interesting to use the AHE method (Adaptive Histogram Equalization) [16] instead of HE, which takes each image and applies multiple histogram operations to differentiate between pixel levels of each image region. Nevertheless, in this work, we used a modified version of AHE called Low Contrast AHE Method (LC-AHE), introduced by a team at the Medical Image Display Research Group at the University of North Carolina [17]. This technique takes a small region of the image, called the contextual region, and modifies the brightness of each of its pixels according to the intensity levels of the neighboring pixels. This increases the cumulative distribution function (CDF), which improves the sharpness of the image in areas of low intensity pixels.

The LC-AHE process is based on five main steps [18]:

- 1.

Determine each grid and its points on the image (Starting from the top-left corner).

- 2.

Mapping calculation of points on each grid.

- 3.

Finding the four closest neighboring grid points of each pixel.

- 4.

Interpolating among these pixel values to obtain the mapping at the current pixel location. Map this intensity to the range [min:max] and put it in the output image.

- 5.

Mapping to each pixel location the intensity based on range of minimum and maximum values.

Fig. 1 compares the histograms and CDFs of a Cardiomegaly image in the following three cases: untreated image (a), image processed with the HE method (b) and image treated with LC-AHE (c).

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Fig. 1. Histogram and CDF of a Cardiomegaly image; (a) untreated image (b) HE treated image, (c) LC-AHE treated image.

Obviously image contrast in case “c” has been significantly improved as a result of sharpening. This is confirmed by the increase in the histogram of the image in a much wider range of gray levels and also by the improvement of the cumulative distribution function, going from case (a) to (c). The LC-AHE treatment is therefore more efficient than the conventional AHE treatment to improve quality of image.

3.1.3. Compression of the extracted images

The idea of working directly with the 1010 images with a resolution of 1024 × 1024 each was not practical. Indeed, the fact of loading each image separately, to apply a pretreatment to it and transmit it to the network to train, validate or test, is time-consuming compared to the possibility of reading all the existing images in a single file, which can be accessible via a single data group.

This Option is available by using HDF5 [19] as a unique open source technology suite for managing data collections of all sizes and complexity.

Another advantage of HDF5 is that it offers an API with multiple functions to be used to create, modify, or even delete objects throw multiple programming languages such as Python, JAVA or C++.

3.1.4. Creation of masks for cardiomegaly

The application of a supervised learning system that segments particular information from huge datasets is a great challenge, especially in the biomedical domain where, in general, there is a lack of annotated data. That is why we created manually custom masks localizing the disease in each image. This is done by delineating the pixels corresponding to the disease areas in each image and generating a new image of the same size as the original with these pixels.

In fact, Cardiomegaly is generally easy to detect by noticing only significant thickening of the ventricular cardiac walls [20]; hence, identifying the disease area does not necessarily require high medical skills. Fig. 2 represents four examples of created masks.

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Fig. 2. Examples of four manually created masks for Cardiomegaly localization.

4. Creation of custom CNN model

4.1. Convolutional neural networks concept

In this section, we will explore the Convolutional Neural Network (CNN) and its major components. CNN is known as a powerful visual model for building intelligent systems that takes an arbitrary input image and produces a correspondingly-sized output with the most relevant information. This architecture is achieved by connecting a set of features based on pixel-to-pixel multi-layer integrity and followed by one or more fully connected layers [21] as described in Fig. 3.

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Fig. 3. CNN mean components.

CNN architecture consists of several different types of sequential layers some of which are repeated. Below we describe the most common layers:

- ●

Input layer: represents the data entry of multiple images with standard dimension (Width x Height) with depth representation of RGB colors.

- ●

Feature-extraction (learning) sequence: at this level, the system looks for common characteristics and ranks them in ascending order of importance. As an example of these layers we have:

    - a.

Convolution layer: It consists of a set of filters that are convolved across the width and height dimensions of the image to preserve the relationship between pixels.

    - b.

Pooling layer: This layer is used to reduce the number of parameters when the dataset of images is too large. Spatial pooling can reduce the dimensionality of each map but retains the important information. Spatial pooling can be of different types: Max pooling which takes the largest element from the rectified feature map, average pooling that takes the average of all elements, or sum pooling which is based on the sum of all elements.

- ●

Classification (Fully-connected) layer: After several convolution and pooling layers, the system connects every neuron in one layer to every neuron in another layer as seen in Fig. 4.

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Fig. 4. Fully-connected layer.

Notice that usually we add an activation layer after the convolution layer, in order to increase the non-linearity of the network, the ReLu (Rectified Linear Unit) is an example of activation layer that is used as a common practice by researchers [22]. It is formally explained by the function f(x) = max(0,

x). Also, some effective techniques, such as batch normalization and dropout, are used to improve the performance of CNNs.

The combination between layers, batches, and normalizations leads to the birth of models with different characteristics in terms of performance, accuracy, and prediction speed that are ready for direct use like AlexNet, Microsoft COCO [23] and ImageNet [24], that provide thousands of object categories (cars, humans, cats, dogs … etc.) in different situations for a better recognition system.

The major advantage of these preconfigured models is that, although they are created to identify objects or classify certain images, they can be used also to identify new elements. This is done by making a re-learning of last layer by passing the new elements as new data inputs, while keeping the previous layers. This operation is called fine-tuning.

As an example of these models we introduce the ALEXNET model, as mentioned in the Fig. 5 which takes a 227 × 227 RGB image as input, and produces a distribution over the 1000 class labels [25].

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Fig. 5. ALEXNET CNN architecture.

The creation of these models requires a set of collection of organized images in three main sub-datasets that are commonly used in different stages of the creation of the model.

- ●

Training sub-dataset: This first category consists of pairs inputs: the image and the corresponding answer (can be: label, image or mask), which is commonly denoted as the target.

- ●

Validation sub-Dataset: this sub-dataset is important in order to observe the evolution of the learning process while tuning the model's parameters.

- ●

Test sub-Dataset: is an independent dataset with unlearned images used to provide an unbiased evaluation of target model fit on the first training dataset.

4.2. U-Net implementation as CNN algorithm

In May 18, 2018 the Computer Science Department of the University of Freiburg, Germany [26] suggested U-Net as new algorithm based on fully convolutional network developed for biomedical image.

The U-Net takes the position provided by the downsampling path and combine it with the contextual information in the upsampling path, to finally generate image with localization and context, which is necessary to predict a good segmentation map.

Fig. 6 gives the U-Net architecture. Generally it comprises two main parts:

- ●

Contracting/downsampling path: It is similar to an encoder that capture context through compact feature map, it is composed of 4 blocks with 3 × 3 Convolution Layer in each block. After each Convolution Layer there exists an Activation function (with batch normalization) with 2 × 2 Max Pooling. It should be noted that at each pooling, the system doubles the number of feature maps, starting with 64 feature maps for the first block, 128 for the second, and so on. The reason of this contracting path comes from the input image; the system extracts the corresponding context in order to segment the image and prepare it to upsampling path through a transformation called global feature.

- ●

Expanding/upsampling path: Represents the inverse operation of the previous one. It plays the role of decoder to guarantee the good location of the cropped mask. It is composed of 4 blocks, in each of them, a deconvolution layer is concatenated with the map of the cropped characteristics coming from the subsampling stage. Between these blocks, the data that has been lost during the maximum pooling of the outsourcing stage will be reconstructed.

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Fig. 6. U-Net downsampling/upsampling Architecture. This segmentation map is part of pixel image classification, which is made by giving label to each pixel, this labels correspond to specific class, the output of one or group of pixels is another image with good resolution and the same dimension as the original image.

Another advantage of this solution is that it doesn't use any dense layer so, images of different sizes can be used as input.

5. Test conditions and results

5.1. Test environment and model parameters

To test and validate the good functioning of our proposed method we chose a special working environment. We used Kaggle as platform for data analytics using high-level neural networks API written in Python, and offering preconfigure notebook with open source datasets and GPU/CPU options. In furtherance, we used TensorFlow for the development framework as open source deep learning framework designed to numerical computation.

Our dataset of 1010 images and corresponding 1010 masks were divided into training, validation and test sub-datasets. 20% of the images were used as test data and the remaining 80% was partitioned between training (70%) and validation (10%) sets. The images were then resized to 128 × 128 matrix. Then the images were made available to our U-Net model. This model has multiple layers, we have fixed the model to be 35 layer deep: it starts with two 2D Convolution Layers having 3 × 3 as kernel size and (16,16) as filters parameters (i.e. number of output filters), and ReLU as Activation Layer. After each 2D Convolution Layer we used Max pooling Layer with 2 × 2 as Pooling Size to reduce the size and complexity of the model. Note that we double the size of the filters after each block of (2 Conv2 and Max pooling) Layers until we reach 512, followed by a DropOut of 2%. After that we started decreasing the size of the filters on blocks until we reached the initial values of (16,16). As for the optimizer, we used ADAM (Adaptive Moment Optimization) because its works well in practice

and outperforms other adaptive techniques. Fig. 7 gives a basic illustration of the layers in U-Net algorithm.

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Fig. 7. U-Net order layers implementation.

Image from the original one by gathering pixels representing the region of the disease.

5.2. Results

For any deep-learning process, the following parameters must be defined before computations:

- ●

Epochs: which is the number of times for the learning process to walk through the entire dataset.

- ●

Batches: An epoch is usually too big to be processed at one time by the computer, so it is divided into several smaller sets or parts, called batches.

- ●

Batch size: number of training examples present in a single batch.

- ●

Iteration: number of batches needed to complete one epoch.

The main interest in the process of training a neural network is to improve its performance. Once the training process is triggered, the detection accuracy gradually increases and the error rate decreases. So, we established a mechanism called EarlyStopping [35], to help us define when to optimally stop training stage. This way, we avoid overloading the network during training.

5.2.1. Cardiomegaly detection

Our computations were launched by fixing the number of epochs at 30, that of iterations at 20 and by using a batch size of.

64. The Learning/Validation rates are represented in Fig. 8 versus number of Epochs. We note a significant increase in accuracy for the two processes until values around 90% from the fifth epoch. After the tenth epoch accuracy in the validation process increases to reach values between 93% and 94% from the fifteenth epoch.

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Fig. 8. Evolution of learning/validation process accuracy.

After customizing the U-Net algorithm and its 35 layers, the system was able to diagnose Cardiomegaly disease and its exact location in the CXR image. This was possible by creating new.

To make sure the obtained precision is the highest the system can achieve, we rerun the learning phase without EarlyStopping mechanism and by fixing the number of used epochs successively to 100, 120, 150 and 200. As we can see in Table 1, the learning accuracy decreases as the number of epochs used increases.

Table 1. Validation accuracy versus number of epochs.

Epochs	**Training/Validation accuracy (%)**
100	87.3
120	86.4
150	85.0
200	71.9

5.2.2. Cardiomegaly localization

After extracting Cardiomegaly images, creating a custom mask for each image and compressing the new dataset using HDF5, the U-Net model was able to localize the disease in test images (20% of full dataset). Fig. 9 represents four generated images showing Cardiomegaly localization.

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Fig. 9. Four examples of Cardiomegaly localization disease using U-Net. Original figures (up), generated images showing disease localization (down).

5.2.3. Discussion

Owing to our customized U-Net based CNN model a high accuracy of detection between 93 and 94% was possible, which is greater than previously published results for Chest Pathology Identification; namely [10], which used preconfigured and heavy models such as ResNet-101, to achieve an accuracy of 92%, or [11] that used a large MIMIC-CXR dataset (thousands of images) to reach an accuracy of 91% or even [13], where the accuracy was only 89%.

This method was tested on Cardiomegaly, but it can be used to detect and localize the seven other remaining diseases in the X-ray8 database. Nevertheless, this requires the integration of radiologists and physicians to set up the proper masks of each disease, and also to validate the obtained results.

6. Conclusion

In this work, we presented a complete process to automatically detect Cardiomegaly disease from X-Ray images. We relied on X-ray images that were obtained from the Chest Xray-8 dataset. The process is achieved in four steps starting with the extraction of Cardiomegaly images from Chest

Xray-8 dataset. In the second step we improved the quality of extracted images by applying the method of Adaptive Histogram Equalization (LC-AHE). In a third step, we compressed images to enhance the processing speed using HDF5. The fourth and final step was dedicated to data processing via a customized CNN model based on U-Net.

Accordingly, we obtained an accuracy between 93 and 94% for detecting Cardiomegaly, which is at the time of this article being written the highest percentage reported in the literature. We can say also that this work is the first one where deep learning methods were tested for the detection of thoracic pathologies using the U-Net algorithm, especially with a learning phase based on non-medical archive. In addition, with U-Net, precise localization of Cardiomegaly is possible, which is not the case for the previous works. Finally, the proposed model can be applied in a generic way to detect other thoracic pathologies.

Ethical statement

The authors whose names are listed in the end of the document certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Also The authors confirm that the manuscript has no actual or potential conflict of interest with any party, including but not limited to any financial, personal or other relationship with other people or organization within three years of beginning the submitted work that could inappropriately influence or be perceived to influence. We confirm that the paper has not been published previously, is not under consideration for publication elsewhere, and is not being simultaneously submitted elsewhere.

Keywords

Calcification

cardiomegaly

COVID-19

CT Scan

mortality

Dear Editor,

Recently, chest CT examination has been recommended as a reliable method for confirmed clinical diagnosis of COVID-19 [1]. In previous studies, COVID-19 patients with bilateral ground-glass opacities (GGO) with or without crazy-paving pattern or consolidation, lymphadenopathy and pleural effusion were presented [1] while in following study, we observed cardiomegaly in patients. Several etiologies as: coronary artery disease, hypertensive heart disease, pulmonary diseases as COPD, infectious myocarditis secondary to viral infection as HIV and specially arrhythmia are mentioned for cardiomegaly disease [2]. Among the studies which have been searched for the cardiovascular effects of new corona virus some illustrated that the cardiac arrhythmias beside of reactions to drugs employed in the treatment of the illness may be the consequence of direct effects of COVID-19 infection [3]. However, because of relation between arrhythmia and cardiomegaly and in this regard,

we presented a preliminary report on the cardiomegaly of CT findings and laboratory data of COVID-19 pneumonia.

The participants of the present study included 115 Patients with confirmed COVID-19 pneumonia (CT and RT-PCR Confirmed) undergoing a chest CT scan during their hospitalization in Baqiyatallah hospital between February 20, 2020 and March 9, 2020 in Tehran, Iran. Based on the CT finding, patients were divided into three groups: 1) with Cardiomegaly, 2) with Calcification, 3) without Cardiomegaly or Calcification.

The non-contrast chest CT scan was undertaken with the patient in the supine position, and scanning was performed at end inspiration and patients were instructed to hold breath to minimize motion artifacts. The main scanning parameters included tube voltage (120 kVp), automatic tube current modulation (30 - 70 mAs), pitch (0.99 - 1.22 mm), matrix (512 × 512), slice thickness (5 mm), and field of view (350 mm × 350 mm). Chest CT from cases was reviewed by two radiologists and physicists.

The clinical characteristics and laboratory results of all 115 COVID-19 patients of three groups are summarized Table 1. The results of the present study showed that 33 [28.9%] patients had cardiomegaly, 19 [16.52%] had calcification, 15 [78.94%] with Coronary arteries calcification, 2 [10.52%] with lung calcification and 1 [5.26%] with liver and 1 [5.26%] patient kidney calcification of CT abnormalities. The appearance of cardiomegaly is observed in all patients with coronary calcification.

Table 1. Clinical characteristics and laboratory findings of patients with COVID-19

Empty Cell	**Without cardiomegaly and calcification (n = 78)**	**With cardiomegaly) (n = 33)**	**With calcification (n = 19)**
Age	54 ± 1.68	64.25 ± 1.7	66.00 ± 2.74
Sex			
Female	22 (28.21%)	12 (36.36%)	7 (36.84%)
Male	56 (71.79%)	21 (63.64%)	12 (63.16%)
WBC(X10ˆ3/µl)	5.85 ± 1.78	6.27 ± 1.89	4.99 ± 1.31[b]
CRP (mg/L)	62.45 ± 30.27	79.07 ± 38.22	85.25 ± 34.88
ESR (mm/hour)	41.80 ± 3.09	47.29 ± 14.45	47.54 ± 19.58
Sodium (m Eq/L)	135.45 ± 2.70	133.32 ± 3.36[a]	131.5 ± 3.31[a] [(b)]
Potassium (mEq/L)	4.10 ± 0.42	4.11 ± 0.34	4.13 ± 0.35
Blood Urea Nitrogen (mg/dL)	13.58 ± 3.43	16.06 ± 4.57[a]	22.00 ± 1.78[a][(b)]

Empty Cell	**Without cardiomegaly and calcification (n = 78)**	**With cardiomegaly) (n = 33)**	**With calcification (n = 19)**
Creatinine (mg/dL)	1.11 ± 0.20	1.38 ± 0.38[a]	1.19 ± 0.39 [b]
Mortality (%)	8.86	12.13	36.84
Comorbidities (%)			
Diabetes	8.75	3.03	0
Hypertension	5.00	9.09	15.79
Cardio vascular disease (CABG, MI, Angioplasty or angiography)	3.85	6.06	5.26
Kidney disease	0	3.03	10.53
ANY [c]	72	48.49	30.02

Data are mean ± SD or (%).

a

Denotes significant difference of group 1 with group 2 or 3 ($P < 0.05$).

b

Denotes significant difference of group 2 with group 3 ($P < 0.05$).

c

ANY: Without Comorbidities, WBC: Wight Blood Cell, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, CABG: coronary artery bypass graft, MI: Myocardial Infarction.

The comparison of clinical characteristics of patients with cardiomegaly and coronary calcification showed significantly higher blood pressure. Maximum and minimum blood pressures of patients with cardiomegaly were 109 ± 13.18 and 68 ± 12.01 respectively. But, these parameters were 125 ± 5.66 and 78.84 ± 11.90 in patients affected with both cardiomegaly and coronary calcification. There are not significant differences between laboratory findings and heart rate of the two groups.

Based on the previous studies, cardiac complications are the secondary diseases of SARS-CoV and MERS-CoV (as an earlier coronavirus family). Moreover, cardiomegaly reported in patients with COVID 19 [4]. Thus, we decided to evaluate the prevalence of cardiac diseases, especially cardiomegaly in COVID-19 patients. Aline with our result, researches demonstrated that coronary artery calcification was detected on chest CT is a predictor of severity and mortality [4]. The results of the present study demonstrated that CRP, blood urea, nitrogen and creatinine levels significantly increased in patients with Cardiomegaly and Calcification compared to healthy groups (mild to severe trend). The data of the present study demonstrated that 48.49% of patients with cardiomegaly and

30.02% with cardiomegaly calcification did not report any comorbidities. It's worth noting that vascular calcification is a long-term process in which viral type has also been reported. But, it seems that patients who have not reported calcification were unaware of their disease.

The mechanism of novel corona-infected cardiovascular disease remained unknown. But, the investigators have indicated the high expression of ACE2 in the heart and lung. Moreover, ACE2 is expressed in other organs such as vascular endothelium and kidney explaining the multi-organ dysfunction and can be found in SARS-CoV-2 infection [3]. Moreover, the association between ACE2 and calcification may be considered as reason for the deleterious effects of cardiovascular disease in covid-19 patients [5].

In conclusion, preexisting cardiovascular disease may enhance vulnerability to COVID-19 and it can greatly affect the development and prognosis of pneumonia (Table 1: Mortality rate). Further, secondary damage of the virus on the cardiovascular system (short-term vs long-term cardiovascular effects) should not be forgotten. Therefore, therapists should pay attention to viral infection relating to cardiovascular diseases. The short time and longtime follow-ups of these patients are suggested.

Limitation

It is recommended to perform study in more centers and with larger sample size.

Abstract

Thymolipomas are rare anterior mediastinal tumors composed of mature adipose tissue and benign thymic tissue and they may rarely simulate cardiomegaly on chest radiograph. We report an adult male who presented with progressive dyspnea of 2 months' duration. Clinical examination was unremarkable. Chest radiograph showed enlarged cardiac silhouette. Computed tomography of chest revealed a giant anterior mediastinal noncontrast enhancing mass partially wrapping around the heart. A needle biopsy obtained lymphomatous material that was diagnosed as thymolipoma. The tumor was successfully removed en bloc through a median sternotomy. Histopathological examination confirmed thymolipoma. We emphasize the importance of considering mediastinal tumors as a differential diagnosis in patients with progressive dyspnea without any obvious cause and chest radiograph showing enlarged cardiac silhouette.

1. Introduction

Thymolipomas are rare anterior mediastinal tumors composed of mature adipose tissue and benign thymic tissue. The majority of these tumors are clinically quiescent; however, they may reach large dimensions and manifest themselves clinically by compression of adjacent structures. Thymolipomas are benign neoplasms for which complete surgical excision is curative. We report a 42-year-old man who presented with progressive dyspnea and was discovered to have an anterior mediastinal giant thymolipoma simulating cardiomegaly.

2. Case report

A 42-year-old male presented to the hospital with complaints of gradually progressive dyspnea of 2 months' duration. The patient had no history of cough, hemoptysis, loss of weight, loss of appetite, or other constitutional symptoms. Clinically, the patient was hemodynamically stable. The heart sounds were muffled with no gallop or murmur being heard. Routine blood investigations were within normal limits. A chest radiograph revealed an enlarged cardiac silhouette mimicking cardiomegaly (Fig. 1A). The outline of cardia was very difficult to delineate. The point against cardiomegaly and pericardial effusion was the left border of cardia extending above pulmonary

artery and aortic knuckle. 2D echocardiogram revealed normal chamber dimension with no evidence of segmental wall motion abnormality and normal Doppler hemodynamic data. It also showed a large anterior mediastinal extracardiac mass compressing the right ventricular outflow tract. A computed tomography (CT) scan of the thorax revealed a large mass measuring 22.5 cm × 15.4 cm × 11.5 cm fat attenuated (−80 to −120 HU) with minimally enhancing internal densities noted in the anterior mediastinum extending downwards into the left paracardiac region and partially wrapping around the heart obscuring the left border of the heart and touching the lateral chest wall on the left side (Fig. 1B). The mass was predominantly of fat density with multiple internal non-homogenous areas of soft-tissue density with no definite pattern. The mass was draping around the heart and great vessels with displacement of mediastinum to right and posteriorly. The patient underwent median sternotomy and a large lobulated fatty mass in the anterior mediastinum that was well encapsulated and was extending to surrounding recesses was noted and it was excised en bloc (Fig. 2). The mass weighed 1750 g. The histopathological examination of the specimen showed a lesion composed of an admixture of mature adipose tissue and microscopically normal thymus tissue with Hassal's corpuscles, features that are consistent with thymolipoma.

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Fig. 1. (A) Chest radiograph showing enlarged cardiac silhouette simulating cardiomegaly and (B) 64 slice CT scan thorax reconstruction image showing giant paracardiac noncontrast enhancing heterogenous mass.

1. Download: Download full-size image

Fig. 2. Excised lobulated mediastinal mass.

3. Discussion

The most common causes of enlarged cardiac silhouette on chest radiography in day to day clinical practice are cardiac chamber enlargement due to any cause or pericardial effusion. Rarely enlarged mediastinal structures or collection in the mediastinum [1] can simulate cardiomegaly on chest radiograph.

Thymolipomas are rare slow-growing mediastinal tumors constituting only 2–9% of all thymic neoplasms. Arising in the anterior mediastinum at the level of the thymus gland, these soft and pliable tumors droop inferiorly as they enlarge and are said to slump onto the diaphragm, accommodating themselves to the spaces between the lungs and the heart, diaphragm, or anterior mediastinum [2]. Their pendulous, elongated, teardrop shape leaves the anterior clear space unencumbered on the lateral chest film. They may simulate cardiomegaly on the frontal chest film. Because they are asymptomatic until marked mass effect occurs, thymolipomas often become large, sometimes weighing several kilograms at the time of excision. Thymolipomas are uncommon, accounting for approximately 5% of all thymic tumors. Most are discovered incidentally.

The most common location is the anterior mediastinum. Because of its large size and pliability, the mass usually drapes itself around the heart, conforming to its borders, and produces a large radiographic shadow easily mistaken for cardiomegaly. Noteworthy is the fact that although they adhere to surrounding structures, invasion per se has never been documented.

Most patients are asymptomatic, being identified on routine chest radiography. Symptoms, when present, are attributable to displacement of mediastinal structures. About 25% of patients complain of cough, dyspnea, and chest pain. The frequency of the symptoms increases as the tumor grows in size. The pathogenesis of thymolipoma is unclear and has been the subject of much speculation. Up to now, four theories have been proposed, but none has been solidly proved [3].

The radiologic features can mimic several conditions, including cardiomegaly, pleural tumors, pericardial effusion, pericardial tumors, basal atelectasis, and pulmonary sequestration. When small, thymolipomas usually are round or oval, are situated anterior to the heart base, and usually are indistinguishable from other benign anterior mediastinal masses. Due to its great pliability, a large thymolipoma drapes around the heart and simulates cardiomegaly. On a CT scan, the tumor appears almost entirely fatty with some areas of inhomogeneity of soft-tissue density, which represent thymic tissue [4]. Its sharp borders, its lack of compression of nearby vessels, and its location point to a benign lesion.

Microscopic features include the presence of normal adult adipose tissue with accumulation of lymphocytes and the characteristic scattered islands of Hassal's concentric corpuscles of thymic tissue. The amount of the latter is well in excess of that normally expected for the patient's age [5]. Surgery is the main modality of treatment and is well tolerated since the tumor can be removed easily because of its well-defined capsule and absence of invasion of surrounding structures.

Early diagnosis should be the major objective of the clinician to avoid late complications due to pressure effects. This will only be possible if a high degree of clinical suspicion and a pathophysiological perspective exist, because the patients are usually young, asymptomatic and once diagnosed it is curable. Therefore, we emphasize the importance of considering mediastinal tumors as a differential diagnosis in patients with progressive dyspnea without any obvious cause and chest radiograph showing enlarged cardiac silhouette.

4. Conclusion

Thymolipomas are rare anterior mediastinal tumors, the majority of which are clinically quiescent; however, they may reach large dimensions and manifest themselves clinically by compression of adjacent structures. It is important to consider mediastinal tumors in the differential diagnosis of patients presenting with progressive dyspnea without any apparent cardiac illness but chest cardiograph showing enlarged cardiac silhouette.

Abstract

The purpose of this study was to develop a computer-aided detection (CAD) device based on convolutional neural networks (CNNs) to detect cardiomegaly from plain radiographs in dogs. Right lateral chest radiographs (*n* = 1465) were retrospectively selected from archives. The radiographs were classified as having a normal cardiac silhouette (No-vertebral heart scale [VHS]-Cardiomegaly) or an enlarged cardiac silhouette (VHS-Cardiomegaly) based on the breed-specific VHS. The database was divided into a training set (1153 images) and a test set (315 images). The diagnostic accuracy of four different CNN models in the detection of cardiomegaly was calculated using the test set.

All tested models had an area under the curve >0.9, demonstrating high diagnostic accuracy. There was a statistically significant difference between Model C and the remainder models (Model A vs. Model C, *P* = 0.0298; Model B vs. Model C, *P* = 0.003; Model C vs. Model D, *P* = 0.0018), but there were no significant differences between other combinations of models (Model A vs. Model B, *P* = 0.395; Model A vs. Model D, *P* = 0.128; Model B vs. Model D, *P* = 0.373). Convolutional neural

networks could therefore assist veterinarians in detecting cardiomegaly in dogs from plain radiographs.

Abstract

In the last few decades, several epidemic diseases have been introduced. In some cases, doctors and medical physicians are facing difficulties in identifying these diseases correctly. A machine can perform some of these identification tasks more accurately than a human if it is trained correctly. With time, the number of medical data is increasing. A machine can analyze this medical data and extract knowledge from this data, which can help doctors and medical physicians. This study proposed a lightweight convolutional neural network (CNN) named ChestX-ray6 that automatically detects pneumonia, COVID19, cardiomegaly, lung opacity, and pleural from digital chest x-ray images. Here multiple databases have been combined, containing 9,514 chest x-ray images of normal and other five diseases. The lightweight ChestX-ray6 model achieved an accuracy of 80% for the detection of six diseases. The ChestX-ray6 model has been saved and used for binary classification of normal and pneumonia patients to reveal the model's generalization power. The pre-trained ChestX-ray6 model has achieved an accuracy and recall of 97.94% and 98% for binary classification, which outweighs the state-of-the-art (SOTA) models.

Keywords

Convolutional neural network (CNN)

ChestX-Ray6

COVID19

Cardiomegaly

DenseNet121

Lung opacity

MobileNetV2

VGG19

Pneumonia

Pleural

ResNet50

1. Introduction

In this era of computing, medical diagnosis can be highly associated with machine learning on an enormous scale. Automation of medical diagnosis is day by day improving to its desired level. X-ray images play a significant role here. X-ray image analysis-based machine learning tools can provide great assistance to radiologists. Machine can detect many fatal diseases by analyzing X-ray images. Pneumonia, COVID19 based pneumonia, lung opacity, pleural, cardiomegaly, and various heart diseases can be detected from X-ray image analysis. Image analysis using a computer can make the diagnosis system faster and cost-effective.

Pneumonia is one kind of lung disease that is caused by viruses, bacteria, or fungi. It is one of the top diseases that causes many deaths every year in developed, developing, and underdeveloped

countries. The fatality rate is higher among children. In 2016, 1.2 million children within five years age range were infected by pneumonia, and among them, 880,000 died (Jain, Gupta et al., 2020, Nahiduzzaman, Goni et al., 2021). When a patient is infected by pneumonia, it causes inflammation in the lung's air sacs, filling them. Because of that, the patient finds it difficult to breathe. If we detect pneumonia timely and start the treatment process, the mortality rate can be lessened. The radiologists use X-ray images to detect pneumonia by looking at the images. The process takes more time as it is checked manually. Also, there are not enough radiologists to speed up the detection process.

COVID19, a disease caused by the novel coronavirus, has created the pandemic of the century. It has reached every corner of the globe and causing thousands of deaths every single day. The whole world is suffering to provide adequate medication to the people. Even the number of newly infected people is so high that there are not enough facilities for testing. Also, infection to death is so short that we do not have enough time to provide not prominent but influential medication. One of the major symptoms of COVID19 is getting pneumonia. Thus, chest X-ray image analysis can improve the testing speed if we correctly detect COVID19 from the image analysis. Also, lung opacity, cardiomegaly, pleural, and many other disease detection can be aided by machine learning to develop an automated and better health care system.

In this paper, we have developed a lightweight deep learning-based model that can detect multiple diseases using chest X-ray analysis. We have used Convolutional Neural Network (CNN) for creating a model named ChestX-ray6. Also, we have used this model as a pre-trained model for binary classification of pneumonia and non-pneumonia and compared the results with other pneumonia detection models to show the generalization capability of the ChestX-Ray6 model. The critical contribution of this research are:

- •

Several datasets have been combined for more variations and created a multiclass environment.

- •

A lightweight CNN model named ChestX-Ray6 has been proposed to detect six types of diseases from chest X-ray images.

- •

Augmentation has been used to balance the datasets, and the model's performance improved.

- •

The models' performance has been compared with different transfer learning approaches, VGG19, ResNet50, DenseNet121, and MobileNetV2, at a new combined dataset in terms of classification criteria, parameters, and processing time.

- •

The pre-trained ChestX-Ray6 model has been used for binary classification of pneumonia disease with a relatively small dataset. The model surpassed the state-of-art accuracy, precision, and recall.

2. Literature review

Various neural network-based approaches have already been developed for detecting diseases from different types of medical images (Islam et al., 2022, Nahiduzzaman, Islam et al., 2021). Rajpurkar et

al. (2017) used deep learning on the ChestX-ray14 dataset and developed a model called CheXNet, which contained 121 layers. They provided a comparison of the results with practicing radiologists, while working with 14 other diseases alongside pneumonia. Guan et al. (2018) developed an AG-CNN model also using ChestX-ray 14 dataset for detecting thorax disease and achieved an average AUC of 0.871. Jain, Nagrath et al. (2020) developed 6 models for detecting pneumonia. Two of these models used 2 and 3 layer-based CNN and could detect pneumonia with 85.26% and 92.3% accuracy. The accuracy of the remaining four models — pre-trained VGG-16, VGG-19, ResNet-50, and Inception-V3 — was 87.28%, 88.46%, 77.56%, and 70.99%, respectively. They also suggested that those transfer learning-based pre-trained models can overcome the vanishing gradient problem. On the Mendeley X-ray image dataset, Chouhan et al. (2020) employed CapsNet, which made use of a group of neurons known as the capsule, to identify pneumonia. They combined convolutions with capsules to develop some models that outperformed the previously proposed models. Using models named Integration of convolutions with capsules (ICC), ensemble of convolutions with capsules (ECC), and EnCC, they achieved 95.33%, 95.90%, and 96.36% accuracy, respectively.

To detect pneumonia, Mittal et al. (2020) employed two basic CNN and multi-layer perceptron deep learning models. They achieved 92.16% and 94.40% accuracy using MLP and CNN, respectively. Ayan and Ünver (2019) used transfer learning models: Xception and VGG-16 for training the X-ray images to detect pneumonia. They found that the VGG-16 approach outperforms the Xception model with 87% accuracy. Sharma et al. (2020) used different deep learning-based approaches for extracting features from X-ray images on the pneumonia dataset. They showed that, data augmentation could improve the performance of the model. Moreover, they also analyzed the impact of using dropout in the models and achieved the highest 90.68% test accuracy with augmentation & dropout, and without augmentation & dropout, the accuracy was 74.98%. Liang and Zheng (2020) developed a system that could recognize pneumonia by combining residual network and dilated convolution. They discovered that dilated convolution minimized information loss for the depth of the deep learning model and the residual network was able to help overcome overfitting. With these techniques, they were able to achieve an f1 score of 92.7%.

Several studies have been performed to detect COVID19 from CT and chest X-ray images (Islam & Nahiduzzaman, 2022). Heidari et al. (2020) used X-ray images to detect COVID19 based pneumonia and developed a convolutional neural network-based model that could detect COVID-19 with 98.8% accuracy. The overall accuracy of the model was 94.0%. Candemir et al. (2018) used X-ray images for the detection of cardiomegaly. Using CNN based ImageNet model, they were able to detect cardiomegaly with 88.24% accuracy. In addition, the CXR-based pre-trained model provided 89.86% accuracy. Maduskar et al. (2016) used segmentation and image localization-based techniques to extract features for supervised learning models and a tuberculosis dataset. They were successful in creating an automated method that could accurately identify pleural effusion. Khan, Sohail, Zahoora and Qureshi (2020) performed a survey on the most recent different architectures of CNN. In this survey, they focused to classify the CNN architectures into seven types of categories based on spatial exploitation, depth, width, attention, etc. Khan, Sohail, Zafar and Khan (2020) proposed two models, namely COVID-RENet-1 and COVID-RENet-2 architectures, for COVID19 specific pneumonia analysis. Furthermore, they employed regional and edge-based operations. Finally, they used a support vector machine algorithm for prediction and achieved an accuracy, precision, F-score, and sensitivity of 98.53%, 98%, 98%, and 99%, respectively. Khan, Sohail, Khan and Lee (2020) developed two-stage CNNs where in the first stage, they enhanced CT images using a two-level discrete wavelet transformation, and then they used a segmentation model for the identification of COVID19. They achieved an accuracy of 98.80% and a recall of 0.99. Khan, Sohail and Khan (2020) proposed a CB-

STM-RENet that was trained on three different datasets and compared their work with the existing works while they achieved accuracy and precision of 97% and 93% respectively.

3. Deep network architectures

In this section, we have described different types of deep CNN models which are used to identify multiple diseases using chest X-ray images. First, we have proposed a basic CNN model for predicting these multiple diseases. Then we have used the most advanced models which are ResNet50 (He et al., 2016), DenseNet121 (Huang et al., 2017), VGG19 (Simonyan & Zisserman, 2014), and MobileNetV2 (Sandler et al., 2018). All those models are different in architecture to achieve better performance. CNN was first used by LeCun et al. for recognition of handwritten zip codes in 1989 (LeCun et al., 1989). This network is one kind of deep neural network that is commonly used in the analysis of visual images (Valueva et al., 2020). CNN is also used in processing data, for instance, 1D sequences, 2D images such as medical image analysis and classification, and 3D videos (Jiang et al., 2018, Litjens et al., 2017, Sun et al., 2017). CNN was designed based on the architecture of the biological processes in which the type of connection between neurons is similar to the organization of the animal visual cortex (Fukushima and Miyake, 1982, Hubel and Wiesel, 1968, Matsugu et al., 2003). CNN is one kind of multilayer perceptron (MLP). But, CNN has two main peculiarities, one is local connectivity, and another is shared weights (Albawi et al., 2017). These two peculiarities have two main advantages: one ensures the affine invariance of the networks, and another diminishes the number of parameters. These types of networks are most commonly used to extract knowledge from image data (Xu et al., 2018). For this reason, we have used CNN for multiclass classification from X-ray images. Fig. 1 shows the basic architecture of CNN. It contains an input, an output layer, and between these two layers, multiple hidden layers have resided. The first few stages of hidden layers are consist of a convolutional layer (CL) which convolve with multiplication or dot product.

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Fig. 1. Basic architecture of CNN.

3.1. Convolution layer

The image passes through the CLs in the form of a matrix. CLs are used to extract knowledge or learn features from the input matrix of the image (Bailer et al., 2018). A group of filters, kernels, or feature detectors of various dimensions such as 3 × 3, 5 × 5, etc., are moved on the whole input image. The process means that the filters convolve with the matrix of the image and map a specific matrix which is known as a feature map (Jain, Nagrath et al., 2020). After each convolutional operation, the image dimensions are reduced, making the image easier to process.

3.2. Activation layer

The activation layer is very effective because it helps the CNN to estimate nearly any nonlinear function (Goyal et al., 2019). There are several activation functions, for instance, ReLU, sigmoid, tangent, etc. Most often, ReLU is used as an activation function because it is efficient, faster, remove vanishing gradient problem and gain better performance than any other activation function (Jain, Nagrath et al., 2020, Krizhevsky et al., 2017).

Another activation function is used in the final fully connected layer known as softmax. The process of the softmax includes the probabilistic distribution of the input image to each category where the CNN was learned (Saraiva et al., 2019).

3.3. Pooling layer

The pooling layer is placed between the two successive convolutional layers. Pooling layers reduce the spatial size of the image. Two types of pooling layers are used: one is max-pooling which selects the maximum value, and another is average-pooling which selects the average value from the entire neuron of each cluster at the preceding layer (Ciregan et al., 2012, Mittal, 2020, Yamaguchi et al., 1990). In our model, we used max-pooling with a 2 × 2 filter because it can extract the principal features from the image (Jain, Nagrath et al., 2020). It is used more frequently in real-life application (Krizhevsky et al., 2017, Scherer et al., 2010).

3.4. Fully connected layer

In the fully connected layer, every neuron in one layer is connected to every other neuron in the successive layer. The output of the preceding layer acts as an input of the first fully connected layer. Before feeding these outputs into the fully connected layer, the output of the last layer is flattening the matrix into a vector. Finally, this vector is fed into the fully connected layer. For multi-class classification, the final layer of the CNN uses a softmax as an activation function, which is responsible for making the classification (Hashmi et al., 2020).

3.5. Dropout layer

Almost every parameter is held by a fully connected layer which results in overfitting. There are several methods to reduce overfitting. One of the methods for removing overfitting complexity is dropout (Srivastava et al., 2014). Overfitting is decreased with dropout by randomly avoiding training all neurons of each layer during the training process and hence significantly increase the speed of training (Kovács et al., 2017). Conventionally, a fully connected layer uses dropout. Still, it can be used after the max-pooling layer, followed by the convolution layer.

4. Materials

4.1. Dataset

Most scientists have recently focused on medical images for binary classification using deep learning and transfer learning. In our study, we have focused on the multiclass category using CNN. Here we have merged several medical image datasets to form multiclass. We have collected images of normal and pneumonia patients from the Kaggle chest X-ray pneumonia database with resolutions varying from 400p to 2000p (Mooney, 2018). This chest X-ray images was collected from Guangzhou Women and Children's Medical Centre, Guangzhou (Jain, Nagrath et al., 2020). Joseph Paul Cohen et al. provided the images of COVID19 patients from which we have collected the samples of COVID19 (Cohen et al., 2020). Images of cardiomegaly, pleural, lung opacity, and no finding patient have been gathered from Neo X-ray database (Ingus, 2019). We have merged images of no-finding patients into images of the normal patient, and then there is a total of 6 classes: normal, pneumonia, COVID19, cardiomegaly, lung opacity, and pleural. Fig. 2 illustrates samples for normal, pneumonia, COVID19, cardiomegaly, lung opacity, and pleural chest X-ray images.

From 9,514 chest X-ray images, the number of normal, pneumonia, COVID19, cardiomegaly, lung opacity, and pleural patients are 2,128, 3,190, 196, 1,000, 1,500, and 1,500.

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Fig. 2. Data samples from the dataset, (A) Normal, (B) Pneumonia, (C) COVID19, (D) Cardiomegaly, (E) Lung Opacity, (F) Pleural.

4.2. Data splitting

The main concept of the deep learning algorithms is that first, we need to learn the model using some of the sample data, for instance, medical image data, and using test data for calculating the model performance (Koza et al., 1996). Using validation data, we can make our model validate, i.e., how accurate the model is. Using this validation set, the model will tune its parameters based on the results (Tyrell et al., 2002).

Finally, the model's accuracy is calculated by using new unseen samples data known as test data. Using this testing set, the final evaluation of the model has been made. So it is necessary to split the whole medical image data into training, testing, and validation sets. We have used 12% data for testing and 12% data for validating our models. Table 1 shows the details of the training, testing, and validation sets. The dataset contains 7,368 images, 1,144 images for testing, and 1,002 validation sets.

Table 1. Datasets splitting into training, testing, and validation sets.

Type	Training set	Testing set	Validation set
Normal	1,650	254	224
Pneumonia	2,471	382	337
COVID19	148	28	20
Cardiomegaly	775	120	105
Lung opacity	1,162	180	158
Pleural	1,162	180	158
Total	7,368	1,144	1,002

5. Proposed methodology

In this article, we have tried to give an optimum solution for predicting multiclass disease from chest X-ray images. First, we have split the total 9,514 images into training, testing, and validation set that we have described in Section 4.2. From Fig. 2, it is clear that the training data is so imbalanced. We have balanced the training data using augmentation, which will describe afterward in this section. Then we have preprocessed our data and built our lightweight ChestX-Ray6 model. After that, we trained our model and calculated our model accuracy using different types of performance measures equations. Fig. 3 shows the block diagram of our proposed methodology for multiclass classification.

For binary classification, we have followed the concept of transfer learning models. Transfer learning models concentrate on extracting knowledge while solving one problem and using this knowledge to solve another problem (West et al., 2007). In this article, we only test our pre-trained ChestX-ray6 model using various test data from the different datasets and finally classify two classes of normal and pneumonia. Fig. 4 demonstrates the proposed architecture for binary classification.

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Fig. 3. Proposed methodology for multiclass classification.

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Fig. 4. Proposed methodology for binary classification.

5.1. Data balancing

Data balancing is one of the crucial parts of training the model. Because if the dataset is imbalanced, for instance, if the number of images of one class is two or three times more significant than another class, then the performance measures might not be feasible or optimum (Fernández et al., 2008). So it plays a considerable part in balancing the training data. The training data is highly imbalanced because of the number of chest X-ray images for normal, pneumonia, COVID19, cardiomegaly, lung opacity, and the pleural patient is 1,723, 2,583, 158, 810, 1,215, and 1,215 respectively. Hence, we must balance our training data. There are several techniques for balancing the data. In this article, we have balanced training our data using data augmentation. After augmentation, we have 21,000 chest X-ray images and each class has 3,500 ray images.

Again, if we trained our model using a larger dataset, then our model would give better performance because suitable training of CNN claims big data (Rahman et al., 2020). With the help of image augmentation, we made the smaller image datasets large. Besides that, during training, the model data augmentation is used to reduce the overfitting problem and behaves like a regularizer (Albawi et al., 2017, Shorten and Khoshgoftaar, 2019).

In this article, we have used five augmentation methods to create new training sets as demonstrated in Fig. 5. We have used 45° of rotation. We have translated the image in a horizontal direction (width shift) by 20% and in a vertical direction (height shift) by 20% as demonstrated in Fig. 5C, D, respectively. In total, 20% of image shearing and zooming are done as shown in Fig. 5E, F, respectively.

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Fig. 5. (A) Original image, (B) Image after rotation, (C) Image after width shift, (D) Image after height shift, (E) Image after shearing, (F) Image after zooming.

5.2. Data preparation

Data preprocessing is an essential part of CNN because the classification results depend on how well we preprocess our image data. First, we resized the image into a dimension of 150 × 150 pixels for our training process. Then we performed histogram equalization and normalized the resized image, as demonstrated in Fig. 3.

In image processing, histogram equalization is used to adjust or improve the contrast of the image (Hum et al., 2014). This method dramatically impacts the images, which have backgrounds and foregrounds that are both dark or bright. Hence, this method significantly affects images of X-rays, satellites, etc. For that reason, we performed histogram equalization on the chest X-ray images. Then we performed normalization on these processed images.

In image processing, the range of pixel intensity values has changed in the normalization process (Gonzalez & Woods, 2008). In computer vision, every image is represented as a group of pixels, where the pixel value 0 means the color of the pixel is white, and the pixel value 255 indicates the color of the pixel is black. Depending on the magnitude of the pixel value, the color of the images varies from white to dark or dark to white (Chunduri, 2018). So we need a vast number of pixel values to represent our image, which is more complex. To reduce this complexity, we normalized our images by dividing the pixel value by 255, and finally, we reduced the scale from 0–255 to 0–1. Consequently, after normalization, we could represent our image using pixel values ranging from 0 to 1.

5.3. ChestX-Ray6 model

Designing a CNN model is the most critical part of the research. When designing a model, we need to keep in mind that we should build a model that gives the best classification accuracy and reduces both layers and processing time. Moreover, it should also correctly diagnose the disease to help the medical physicians provide the proper treatment for the patient. We have used the convolution layer to extract the relevant features from the chest X-ray images that significantly impacted the diseases and passed those features through the fully connected layer to correctly diagnose the condition. Fig. 6 reveals our proposed lightweight CNN model named ChestX-Ray6 for classifying six classes of disease.

Since we proposed a lightweight CNN model, as a result, six convolutional layers and two dense layers have been used. ReLU has been used as an activation function after every two convolutional layers. A 2 × 2 max pool has been used after each convolutional block. For more reduction in complexity, three dropouts have been used: one dropout has been used after the final convolutional layer and two after each dense layer. The result has been determined by applying the filters to all image tuples; hence, we have inserted the 'SAME' padding in the first two convolution layers. Due to this, border elements have been investigated because they frequently include critical properties for this particular dataset. Padding has been omitted from the border elements during the design process. The padding designated as 'VALID' in the remaining convolutional layers has been used and does not consider the boundary components. Finally, a flattening layer has been used to flatten the matrix into a vector. Then this output is fed into the fully connected layer. A dropout with a 0.5 probability has been used in the first two fully connected layers. This dropout speeds up the processing time of the model and also reduces its overfitting. A softmax activation function has been used to make a prediction in the final fully connected layer. Finally, the cost has been calculated using the sparse categorical cross-entropy cost function depending on the prediction. In addition, the cost function has been determined using back-propagation and features map to make the CNN optimized.

In this study, the Adam optimizer has been used because it is very efficient for CNN. Moreover, it also gives better results while training on huge datasets and reduces the computational cost (Kingma & Ba, 2014). The learning rate has been set to 0.001. We have trained the ChestX-Ray6 model using a batch size of 128 and the total number of epochs is 100.

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Fig. 6. Proposed lightweight ChestX-Ray6 model for multiclass classification.

In our ChestX-Ray6 model, the image shape after the first two convolution layers is 150 × 150x32. Afterward, the image shape is 75 × 75x32 after applying the first max-pooling layer. Table 2 shows the rest of the output image shapes and a summary of our ChestX-Ray6 model.

Table 2. Summary of ChestX-Ray6 model.

Layer(type)	Output shape	Number of parameters
Conv1_1(Conv2D)	(None, 150, 150, 32)	832
Conv1_2(Conv2D)	(None, 150, 150, 32)	25 632
pool1(MaxPooling2D)	(None, 75, 75, 32)	0
Conv2_1(Conv2D)	(None, 73, 73, 64)	18 496
Conv2_2(Conv2D)	(None, 71, 71, 32)	36 928
pool2(MaxPooling2D)	(None, 35, 35, 64)	0
Conv3_1(Conv2D)	(None, 33, 33, 128)	73 856
Conv3_2(Conv2D)	(None, 31, 31, 128)	147 584
pool3(MaxPooling2D)	(None, 15, 15, 128)	0
dropout1(Dropout)	(None, 15, 15, 128)	0
flatten(Flatten)	(None, 28800)	0
fc1(Dense)	(None, 1024)	29 492 224
dropout2(Dropout)	(None, 1024)	0
fc2(Dense)	(None, 512)	524 800

Layer(type)	Output shape	Number of parameters
dropout3(Dropout)	(None, 512)	0
fc3(Dense)	(None, 6)	3 078

5.4. Performance matrix for classification

The following performance matrices have been used to compare the results in this study: accuracy, precision, recall, f1-score, and the area under the curve. After our ChestX-Ray6 model had finished training, we calculated its performance for the testing dataset (AUC). One model can achieve high accuracy when the model has high precision and trueness (Menditto et al., 2007) and the accuracy is given by Eq. (1). Precision can be defined as the fraction of related samples among the recovered samples, and the precision is provided by Eq. (2) (Olson & Delen, 2008). Whereas recall could be defined as the fraction of the total number of related samples which are exactly recovered, and the recall is given by Eq. (3) (Olson & Delen, 2008). The F-measure could be defined as the measure of a harmonic mean, and this measure is given by Eq. (4) (Powers, 2020).(1)Accuracy=TP+TNTP+TN+FP+FN(2)Precision=TPTP+FP(3)Recall=TPTP+FN(4)F=2∗precision∗recallprecision+recall

In the above equation, for binary classification, true positive (TP) means that pneumonia patient is detected as pneumonia, true negative (TN) means that a normal patient is detected as normal, false positive (FP) means that a normal patient is incorrectly detected as pneumonia. A false-negative (FN) means that the pneumonia patient was incorrectly detected as a normal patient. For multiclass classification, TP means that pneumonia, COVID19, cardiomegaly, lung opacity, and pleural patients are correctly detected as pneumonia, COVID19, cardiomegaly, lung opacity, and pleural, respectively. TN means that a normal patient is detected as normal, FP implies that a normal patient is incorrectly detected as pneumonia or any other four diseases, and FN means that pneumonia or any other four conditions is incorrectly detected as a normal patient.

6. Experimental results and performance analysis

In this section, the experiments and results of different performance measures are presented. We used the Pycharm Community Edition (2020.2.3 × 64) software and Keras with TensorFlow as the backend. We utilized a computer with an Intel(R) Core(TM) i7-6700 CPU @3.40 GHz processor and 32 GB RAM, a NVIDIA GeForce GTX 1650 SUPER 4 GB GPU on a 64-bit Windows 10 Pro operating system for performing the training and testing of our model.

6.1. Performance of the proposed model multiclass classification

We have trained our lightweight ChestX-Ray6 model using 21,000 training data and validated our model using a 1,002 validation set where the number of normal, pneumonia, COVID19, cardiomegaly, lung opacity, and pleural patient images are 224, 337, 20, 105, 158, and 158, respectively. Finally, we have tested our model using the 1,144 test dataset where the number of normal pneumonia, COVID19, cardiomegaly, lung opacity, and pleural patient images are 254, 382, 28, 120, 180, and 180, respectively, for classifying these six classes. We trained our model for 100 epochs, and the batch size is 128. The best training and validation accuracy of our model is 98.56% and 77.34%, respectively. The minimum training and validation losses of our model are 0.09 and 0.58, respectively.

Furthermore, the robustness of our model has been examined by calculating the accuracy, precision, recall, f1-score, and AUC of our model. We have used a confusion matrix for calculating the above measurement, which is demonstrated in Fig. 7. We have also calculated the true positive, true negative, false positive, and false negative using this confusion matrix, which helped us to find our model's efficiency. For medical data, recall should be maximized because the patient with the disease must be correctly identified. The average precision, recall, and f1-score of our model without augmentation are 66%, 67%, and 66%, respectively, which are shown in Table 3.

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Fig. 7. Confusion matrix for multiclass classification.

Without augmentation, the area under the curve (AUC) of our model is 92.04% and the overall accuracy of our ChestX-Ray6 model is 75%. The performance of our model has been enhanced using the augmentation technique. Our model's average precision, recall, and f1-score with augmentation are 72%, 76%, and 73%, respectively. From Table 4 it is observed that the overall performance of the ChestX-Ray6 model is better than the transfer learning model. The accuracy of VGG19, ResNet50, DenseNet121, and MobileNetV2 are 0.73, 0.69, 0.77, and 0.74 respectively. We have achieved better accuracy using our model, which is 0.80.

Table 3. Values of performance measures of ChestX-Ray6 model without augmentation.

Type	Precision	Recall	F1-score
Normal	74%	98%	84%
Pneumonia	96%	95%	95%
COVID19	57%	61%	59%
Cardiomegaly	62%	57%	60%
Lung opacity	53%	37%	44%
Pleural	57%	52%	54%
Average	66%	67%	66%

The receiver-operating characteristics (ROC) and precision–recall (PR) curves of our model and different transfer learning algorithms for different classes are demonstrated in Fig. 8, Fig. 9, respectively.

Table 4. Values of performance measures of different models with augmentation.

Type	Precision					Recall				
Empty Cell	**ChestX-Ray6**	**VGG**	**ResNet**	**DenseNet**	**MobileNet**	**ChestX-Ray6**	**VGG**	**ResNet**	**DenseNet**	**Mobile**
Normal	**0.89**	0.73	0.64	0.69	0.76	**0.99**	0.95	0.95	0.94	0.95
Pneumonia	**0.98**	0.97	0.95	0.94	0.98	**0.97**	0.96	0.91	0.91	0.95
COVID19	0.63	0.79	0.58	**0.8**	0.74	**0.96**	0.54	0.5	0.71	0.61
Cardiomegaly	**0.68**	0.62	0.56	0.52	0.59	**0.63**	0.59	0.45	0.6	0.5
Lung Opacity	**0.54**	0.47	0.45	0.48	0.45	0.50	0.39	**0.51**	0.41	0.39
Pleural	0.56	0.5	0.5	**0.58**	0.52	**0.51**	0.43	0.22	0.36	0.49
Average	**0.72**	0.68	0.61	0.67	0.67	**0.76**	0.64	0.59	0.65	0.65

The AUC of VGG19, ResNet50, DenseNet121, and MobileNetV2 are 90.58%, 89.88%, 90.46%, and 90.62% respectively. The AUC of our model is 94.99%. From Fig. 10, we have concluded that the overall classification performance of our model is better than other transfer learning models.

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Fig. 8. (A) ROC, and (B) PR curve of ChestX-Ray6 model.

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Fig. 9. ROC of (A) VGG19, (B) ResNet50, (C) DenseNet121, and (D) MobileNetV2.

A lightweight model has been developed here, for that reason, we have measured the layers and processing time to validate the model's high-speed capability and compared them with the other transfer learning models. The convolutional layers for ChestX-Ra6, VGG19, ResNet50, DenseNet-121, and MobileNetV2 are 6, 16, 50, 121, and 53, respectively, and the training times are 6150.62, 8215.94, 7018.10, 7571.84, and 6457.20 s, respectively. These results could be changed with a different computer's configuration. The testing time of the ChestX-Ray6 model is 2.72 s, which is quite low compared to other transfer learning models. From the Table 5, it can be concluded that the convolutional layers and processing time of the proposed model are quite less than the other four transfer learning models, which reveals the robustness of the proposed model. From the above discussion, it is understood that the proposed lightweight ChestX-Ray6 performs well in the case of classification criteria and also performs well in terms of architectural complexity and processing time for the detection of six classes from the chest X-ray images. Though the model performed well in the

combined dataset, the performance may vary if applied to other datasets. This criterion is not considered in this study.

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Fig. 10. Graphical comparison for multi-class classification with different approaches.

Table 5. Convolutional layers and processing time comparison for ChestX-Ray6 with different transfer learning approaches.

Model	Layers	Train time (s)	Test time (s)
VGG19	16	8215.94	8.17
ResNet50	50	7018.10	5.29
DenseNet121	121	7571.84	9.59
MobileNetV2	53	6457.20	4.03
ChestX-Ray6	6	6150.62	2.72

6.2. Visualization analysis

In this section, we have used Grad-CAM (Gradient-weighted Class Activation Mapping) to get a heat map of where pneumonia is most likely to manifest itself (Selvaraju et al., 2017). This technique employs the gradient of a target notion to produce “visual explanations” for CNN models. We have generated a crude localization map using Grad-CAM, showing us where we need to focus on our prediction-conception image. While classifying the six classes, the gradients of the final convolutional layer emphasize the chest X-ray accurately recognized by the filters and represented in the feature maps. The Grad-CAM visualization of the different classes has been shown in Fig. 11. From the visualization, it is observed that the lightweight ChestX-Ray6 model correctly detects the affected region of various lung-related diseases.

We demonstrated how our proposed model extracted the most discriminant features from the chest X-ray images and visualized them using principal component analysis (PCA). The dimension of the extracted features from the images is too high, and we need to reduce the dimension using PCA for visualization since it is used to convert the higher-dimensional data into a much smaller dimension (Fontes & Soneson, 2011). Our proposed model’s visual discrimination feature space is shown in Fig. 12 through a PCA-based comparison. ChextX-ray6, VGG19, ResNet50, DenseNet121, and MobileNetV2 for the test dataset are shown in Fig. 12 as two-dimensional plots with the first principal component, second principal component and their relative variance. It is observed that the proposed lightweight ChestX-Ray6 model captured more prominent information than the other transfer learning models.

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Fig. 11. Gradient-weighted class activation mapping of some diseases using ChestX-Ray6, (A) Original images indicated infected regions by radiologists, (B) Heat map, (C) Grad-CAM.

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Fig. 12. PCA based visualization of (A) the proposed lightweight ChextX-ray6 model, (B) VGG19, (C) ResNet50, (D) DenseNet121, and (E) MobileNetV2 for test data.

6.3. Performance of the proposed model for binary classification

In this study, we trained and tested our lightweight ChestX-Ray6 model using a merged dataset with six classes: normal, pneumonia, COVID19, cardiomegaly, lung opacity, and pleural. In this section, we did not train our model but only tested our pre-trained ChestX-Ray6 model using a binary class normal and pneumonia dataset. We have tested our model using multiple folds of the test dataset to calculate our model efficiency and compared the result of our model with other research work to ensure that our ChestX-Ray6 model correctly predicted the diseases better than the other models.

We have tested our model using multiple folds of test data, including 624 (normal: 234, pneumonia: 390), 875 (normal: 234, pneumonia: 641), 303 (normal: 151, pneumonia: 152), and 449 (normal: 170, pneumonia: 279) images of normal and pneumonia patients for comparison with other works.

Fig. 13 shows the four ROC curves (also known as AUROC (area under the receiver operating characteristics)) of our pre-trained ChestX-Ray6 model for multiple fold test data. This acts as a significant evaluation metric to estimate the performance of any classification model.

Fig. 14 shows the confusion matrix of our pre-trained model for these four-fold test data. From the confusion matrix, we have calculated the precision, recall, f1-score, AUC, and accuracy of our model to test our pre-trained model's robustness for binary classification. The accuracy of 624, 875, 303, and 449 chest X-ray images are 97.91%, 97.94%, 97.02%, and 97.77% respectively. Table 6 shows the overall values of performance measures for multiple-fold test data.

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Fig. 13. ROC curves for binary classification, (A) 624 test images, (B) 875 test images, (C) 303 test images, (D) 449 test images.

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Fig. 14. Confusion matrix for binary classification (A) 624 test images, (B) 875 test images, (C) 303 test images, (D) 449 test images.

Table 6. Values of performance measures of ChestX-Ray6 model for binary classification.

Test images	Type	Recall	F1-score	AUC	Accuracy
624	Normal	98%	97%	–	–
	Pneumonia	98%	98%	–	–
	Average	98%	98%	99.76%	97.91%
875	Normal	98%	96%	–	–
	Pneumonia	98%	99%	–	–
	Average	98%	97%	99.81%	97.94%
303	Normal	97%	97%	–	–
	Pneumonia	998%	97%	–	–
	Average	97%	97%	99.90%	97.02%
449	Normal	98%	97%	–	–
	Pneumonia	98%	98%	–	–
	Average	98%	98%	99.92%	97.77%

6.4. Performance comparison with related works

In this section, we have compared our model performance with other existing methods for the same dataset. The lightweight ChestX-Ray6 has been saved and is further used as a transfer learning model. The pre-trained model has been tested on different datasets to detect pneumonia patients, and the result has been compared with the existing work. The details of the existing techniques were described in Section 2. Jain, Nagrath et al. (2020) used two CNN models and some of the transfer learning algorithms (VGG16, VGG19, ResNet50, and Inception-v3) were used to detect the two classes, normal and pneumonia. They used the Kaggle chest X-ray dataset to train their various models and tested them using 624 (normal: 234, pneumonia: 390) images. The best recall and accuracy of their model were 98% and 92.32%, respectively. Chouhan et al. (2020) used Guangzhou Women and Children's Medical Center dataset for training their ensemble model achieved an accuracy of 96.39%, recall of 99.62%, and an AUC of 99.34%. Ayan and Ünver (2019) achieved good accuracy while using VGG16 over the Xception network. They used the same fold images for testing their model, and the recall and accuracy of their model were 88%, and 87% respectively. Liang and Zheng (2020) used CNN to detect the pneumonia patient. They trained their model using the same dataset and achieved an accuracy of 90.5%, recall of 96.7%, and an AUC of 95.3%. We have tested our pre-trained ChestX-Ray6 model using the same test images and achieved more optimistic results than the existing methods. The precision, recall, f1-score, AUC, and accuracy of our model are 98%, 98%, 98%, 99.76%, and 92.92% respectively which are shown in Table 7.

Mittal et al. (2020) trained their integration of convolutions with capsules (ICC) and an ensemble of convolutions with capsules (ECC) using the Mendeley dataset. They tested their models using 875 (normal:234, pneumonia: 641) test images and achieved the best accuracy with the E4CC model. We have calculated the precision, recall, and f1-score from their confusion matrix. They reached an accuracy of 96.36%, a recall of 98.28%. We have tested our pre-trained ChestX-Ray6 model using the same 875 test images and achieved a better result than the E4CC model. We have achieved an accuracy of 97.94%, a recall of 98.28%, and an AUC of 99.81%.

Table 7. Performance comparison of ChestX-Ray6 model for binary classification with existing models.

No of test images	Model	Precision	Recall	F1-score	AUC	Accuracy
624	Jain, Nagrath et al. (2020)	–	98%	94%	–	92.31%
	Chouhan et al. (2020)	93.28%	**99.62**%	–	99.34%	96.39%
	Ayan and Ünver (2019)	87%	88%	87%	–	87%
	Liang and Zheng (2020)	89.10%	96.7%	92.7%	95.3%	90.5%
	Proposed Method	**98**%	98%	**98**%	**99.76**%	**97.92**%
875	Mittal et al. (2020)	96.77%	98.28%	97.54%	–	96.36%
	Proposed Model	**98.43**%	98.28%	**98.59**%	**99.81**%	**97.94**%
449	Sharma et al. (2020)	–	–	–	–	90.68%
	Proposed Model	**98**%	**98**%	**98**%	**99.92**%	**97.77**%

Sharma et al. (2020) trained their CNN model using the Kaggle chest X-ray dataset. They tested their model using 449 (normal:170, pneumonia:279) test images and achieved an accuracy of 90.68%. We have tested our pre-trained model using the same 449 test images and achieved a higher accuracy of 97.77% than their model. The recall and AUC of our model are 98% and 99.92%, respectively. From the above discussion, it is concluded that the pre-trained ChestX-Ray6 model outperformed six state-of-the-art models for binary classification and validated the robustness of the proposed model.

6.5. Discussion

This section discusses the lightweight ChestX-Ray6 model's convenience of use to diagnose diseases from a merged dataset.

In this study, a lightweight CNN model has been proposed to classify multiple diseases from chest X-ray images and its performances have been compared with other transfer learning models. The performance is shown in the Table 4. Though the model is simple in architecture, it has only six convolutional layers and two dense layers. Still, the model classification performance is better than

the other four models. One of the main concerns of this study is designing a model that provides higher classification accuracy and reduces the number of layers and processing time for large amounts of data. For that reason, here, a lightweight ChestX-Ray6 model has been designed to measure whether it performed well for these criteria in the case of a multiclass environment. Table 5 shows that the convolutional layers and processing time are also less than the other transfer learning models. So, it is concluded that the ChestX-Ray6 model achieved optimistic classification performance results and also reduced layers and processing time.

Another concern of this study is to check the generalization power of the proposed ChestX-Ray6 model. For that reason, the model has been used as a pre-trained model and then measured the classification performance in the case of binary classification. It is observed from the comparison section that the pre-trained model has outperformed various well-known state-of-the-art models. The proposed model achieved a high classification performance for both multiclass and binary classification. Moreover, reduced processing time has made our model a strong candidate for use in real-time applications. These are the main contributions of this study.

7. Conclusion and future work

This work presents a novel lightweight CNN ChestX-Ray6 model for detecting multiple diseases from digital chest X-ray images. We have combined six classes to develop a complex multiclass environment for lung diseases. Hence, the model has more discriminant features to differentiate the classes. Further, classes are balanced using augmentation and preprocessed using various preprocessing techniques such as image normalization and histogram equalization. We trained our model using 21,000 chest X-ray images and saved our model for calculating the performance of our model for binary classification. The classification accuracy for six classes is 80%. Here we have used our ChestX-Ray6 model as a transfer learning model. Hence we tested our pre-trained ChestX-Ray6 model for binary classification of normal and pneumonia patients and achieved an accuracy of 97.94% with precision, recall, and f1-score of 98%, which shows better performance than the previous works. We have also compared different transfer learning algorithms with our ChestX-Ray6 model in other performance criteria. Here, our ChestX-Ray6 model has achieved an excellent performance for both multiclass and binary classification, which can help medical physicians diagnose these types of diseases correctly. We intend to use big data in the future and expand the multiclass to more classes.

Enlarged cardiac silhouette on chest x-ray (CXR) in the absence of cardiopulmonary disease is often dismissed as “pseudocardiomegaly.” We aimed to assess the impact of epicardial adipose tissue (EAT) on radiographic heart size and to determine the clinical significance of cardiomegaly caused by EAT. In total 112 patients (52 ± 13 years old, 53% women, body mass index 32 ± 8 kg/m^2) with structurally normal hearts by transthoracic echocardiography underwent cardiac computed tomography (CCT). EAT volume was measured by CCT and cardiothoracic ratio (CTR) and cardiac transverse and lateral horizontal transverse diameters were measured on posteroanterior and lateral view CXR. EAT volume (mean 122 ± 49 ml) correlated directly with age, body mass index, hypertension, hyperlipidemia ($p < 0.05$ for all comparisons), transverse diameter ($r = 0.50$, $p < 0.001$), CTR ($r = 0.45$, $p < 0.001$), and lateral horizontal transverse diameter ($r = 0.38$, $p < 0.001$). EAT volume was larger in those with increased (n = 22) compared to those with normal (n = 90) CTR (154 ± 54 vs 115 ± 54 ml, $p = 0.0005$). Patients with cardiomegaly were also older (58 ± 13 vs 50 ± 12 years old, $p = 0.009$) and more often had diabetes (32% vs 9%, $p = 0.03$), hypertension (86% vs 46%, $p = 0.001$), hyperlipidemia (68% vs 44%, $p = 0.04$), or obstructive coronary artery disease by CCT (32% vs 11%, $p = 0.04$). Coronary artery calcium score was also higher in those with cardiomegaly (median 56 [first tertile 0, third

tertile 298] vs 0 [0, 55], p = 0.006). In conclusion, cardiomegaly on CXR can be caused by excessive EAT. This is associated with several coronary risk factors and with coronary calcification and stenosis. Cardiomegaly in this setting may be regarded as another noninvasive marker of coronary atherosclerosis. Section snippets

Methods

The study population consisted of 112 adults from 356 consecutive admissions to the Geisinger Medical Center Chest Pain Decision Unit who underwent technically adequate posteroanterior and lateral view CXR, transthoracic echocardiography, and CCT during the same short stay (23-hour observation). They also fulfilled the following criteria: had normal cardiac size and function and no pericardial effusion by transthoracic echocardiography, had no pulmonary disease by CXR or CCT, and had

Results

The age ranged of the 112 patients was 26 to 79 years (mean 52 ± 13) and 59 were women (53%). Average body weight, height, and body mass index were 93 ± 21 kg, 170 ± 10 cm, and 32 ± 8 kg/m^2, respectively. Diabetes mellitus, hypertension, and hypercholesterolemia were present in 15 (13%), 60 (54%), and 55 (49%), respectively, and 22 (20%) were smokers.

CTR ranged from 36% to 70% (mean 50 ± 7) and exceeded the upper normal limit in 22 patients (20%). Corresponding numbers for transverse and

Discussion

This study provides objective evidence for the impact of EAT volume on CXR measurements of cardiac size. Thus, presence of large EAT volumes resulted in cardiomegaly on CXR in 20% of adults without cardiopulmonary disease or chest wall deformities. The findings further emphasize that cardiomegaly caused by EAT is directly related to several coronary artery risk factors and to computed tomographic evidence of coronary atherosclerosis manifested as hard (calcified) or soft plaques.

Abstract

Although the etiologies of both trapped lung and cardiomegaly are well-established, co-presentation of the two conditions, and possible interactions between them, are much rarer. Here we describe the case of 78 year-old male found to have both cardiomegaly and trapped lung, with a cause of death of congestive heart failure and subsequent cardiac arrest. This case prompted consideration of possible interactions between the two conditions. Issues related to decision-making for imaging and clinical interventions are also discussed.

1. Introduction

A trapped lung, or fibrothorax, is a shrunken lung surrounded by a cortex of fibrotic visceral pleura. This fibrotic peel prevents inflation of the lung, and is typically caused by a chronic inflammatory process leading to uncontrolled fibrin deposition. Although it is a known sequela of recurrent pleural effusion, other disease processes, such as malignant or metastatic visceral pleural disease, can also lead to trapped lung [10], [14], [18], [1]. Cardiomegaly is defined as an increase in heart size caused by ventricular hypertrophy or chamber dilation such that the ratio of heart diameter to maximum thorax diameter, measured transversely, is greater than 0.5 [24]; [25].

Although neither trapped lung nor cardiomegaly is considered unusual, simultaneous presentation of both conditions, or a causal connection between them, is virtually unmentioned in the literature. Furthermore, both conditions can be difficult to diagnose with a plain chest radiograph, which is the most common imaging ordered for patients with dyspnea. Failure to recognize and identify trapped lung can lead to unnecessary interventions such as repeated thoracenteses, or can delay more appropriate interventions such as surgical decortication.

2. Case report

During routine dissection of a 78 year-old male cadaver we found a trapped left lung and enlarged heart almost completely occupying the left pleural cavity (Fig. 1). The subject's past medical history included congestive heart failure (CHF), chronic pleural effusion with prior thoracenteses, atrial fibrillation, non-sustained ventricular tachycardia, stage III kidney disease, hypertension, chronic anemia, cardiac pacemaker placement, and hydrocephalus with ventriculoperitoneal shunt placement. Cause of death was given as cardiac arrest and CHF.

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Fig. 1. Anterior view of lungs and pericardial sac after removal of the anterior chest wall. Note the tip of superior lobe of left lung protruding over the left contour of the heart (arrow).

One week prior to death, our subject was admitted to the hospital with complaints of shortness of breath and diffuse edema, and was given primary diagnoses of anasarca and CHF exacerbation. At that time his vital signs were normal, and he required 2 L of oxygen by nasal cannula to maintain an oxygen saturation of 95%. Multiple chest radiographs taken during that hospital stay (Fig. 2) showed “persistent subtotal opacification of the left hemithorax,” and “massive left pleural effusion with minimal aeration of the left lung [and] at least mild cardiomegaly.” The subject then underwent thoracentesis to remove the fluid in his left hemithorax, and a repeat radiograph showed “persistent opacification” of the left hemithorax, and noted that “cardiac and mediastinal contours are difficult to evaluate due to adjacent opacification.”

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Fig. 2. Chest radiograph taken during the week before death. Note opacification in left pleural cavity which limits visualization of the heart contours and the trapped lung.

At the time of our dissection, the subject's right lung appeared normal in dimensions and gross appearance. The left lung was deformed, and markedly diminished compared with the right lung, particularly in the lower lobe (Fig. 3). The thickness of the cortex around the lung varied from 0.5 to 1.5 mm. Subject presented with cardiomegaly, with a cardiothoracic ratio of 0.54. The right ventricular wall, interventricular septum and left ventricular wall measured 240%, 255%, and 326% of values for healthy adults, respectively (Fig. 4), indicating substantial biventricular hypertrophy [15], [11]. Comparing ventricular wall thickness values can be challenging because norms are based on end-diastolic measurements, and significant regional variations exist in the thickness of any individual ventricle [5]. Wall thickness has been shown to be greatest during systole; however, the maximum differences in ventricular thickness measured at diastole and systole have been reported to average less than 62% [23]. Given this fact, the measurements in the present

subject would appear to represent substantial hypertrophy regardless of the cardiac phase at the time of death.

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Fig. 3. Anterior view of the chest after removal of the heart, showing deformed and fibrotic left lung. Note diminutive left lower lobe (arrow).

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Fig. 4. Heart opened to show hypertrophy of ventricular walls and interventricular septum.

3. Discussion

3.1. Etiology and clinical course of trapped lung and cardiomegaly

Trapped lung causes a hydropneumothorax, with both fluid and air present in the pleural cavity. Signs and symptoms of trapped lung include shortness of breath, an absence of breath sounds on the affected side and, in some cases, hypoxemia [8], [1]. Diagnosis is made by clinical exam, chest xray and computed tomography (CT). Analysis of the pleural fluid is done to differentiate malignant from inflammatory or infectious processes. Although ultrasound guidance can greatly enhance the accuracy of thoracentesis for pleural effusion, it is not considered a reliable imaging modality to identify a trapped lung [7]; [18].

Chronic pleural effusion is a known cause of trapped lung. In the early stages of pleural effusion, before the development of the fibrotic cortex, lung expansion is limited only by the pleural fluid build-up separating visceral from parietal pleura. Thus, when the fluid is removed by thoracentesis, the lung is able to fully re-expand. Over time, however, the thickening fibrotic coat on the visceral pleura prevents the re-expansion of the lung, even after fluid has been drained [1]. The time frame for development of trapped lung is unknown, and in many cases, individuals with trapped lung are asymptomatic and the condition remains undiagnosed [14]. In cases where a patient is symptomatic, decortication, i.e. surgical removal of the fibrotic cortex, is the standard of care if the patient is considered a good surgical candidate ([14], [1].

Chronic pleural effusion is caused most commonly by cancer, followed by left heart failure and pneumonia. There have, however, been a small number of reported cases of pleural effusion caused by isolated right ventricular failure [16], [17]. The underlying mechanism of pleural effusion caused by left ventricular failure results from increased pulmonary capillary pressure creating an increased pressure gradient, leading to movement of fluid from the capillaries into the pulmonary interstitial space, then across the visceral pleural membrane into the pleural space [9], [16].

Cardiomegaly results either from chamber dilation or, as seen in the present subject, hypertrophy of one or both ventricles [22], [25]. Ventricular hypertrophy has been shown to be a sequela of chronic, uncontrolled hypertension, although recent research has shown mutations in the gene coding for sarcomeric proteins to also be an important cause of hypertrophic cardiomyopathy [6], [21], [22]. Arterial hypertension causes increased afterload, and the left ventricular hypertrophic response. This hypertrophy ultimately leads to reduced compliance of the left ventricle and subsequent decreased end diastolic volumes, and thus to CHF [22] [3]. Right ventricular hypertrophy, which was

also seen in the present subject, results from a chronic increase in afterload due to pulmonary hypertension, often caused by prior left heart failure [19].

We have found only one reference to the co-presentation of cardiomegaly and trapped lung in the literature. Our literature search methodology included database searches of PubMed and Web of Science, and identical search results were obtained for all keywords for both databases. Using the keywords of cardiomegaly, trapped lung, fibrothorax, and heart failure, in various combinations, yielded one article by Ref. [4]. In this article, the authors reported on a case of cardiomegaly and right sided heart failure, associated with fibrothorax, in a 57 year-old woman, who had reportedly been asymptomatic since the likely onset of right lung collapse 39 years prior. The patient was treated with surgical decortication, and had transient improvement in pulmonary function tests, although she died of heart failure three years later.

3.2. Evidence of a reciprocal effect between trapped lung and cardiomegaly

Was the presence of both a trapped lung and enlarged heart in the present subject a coincidence, or was there some sort of causation? Although no direct causal connection has been established between the two conditions, analogies can be found in the literature.

For example, right ventricular ejection fraction has been shown to decrease after pneumonectomy or major pulmonary resection due to lung cancer. This lower ejection fraction is the result of an increase in afterload due to the missing pulmonary vascular bed of the missing or resected lung. Increased afterload is known to cause right ventricular hypertrophy and ultimately right heart failure [13]. It is possible that the small and non-functioning left trapped lung in the present subject led to a similarly increased afterload and thus compensatory right ventricular hypertrophy.

Conversely, the increased size of the subject's heart may have contributed to the collapse of his left lung. It has been shown that increased heart size will cause compression of the left lung, and cardiomegaly is significantly correlated with decreased left lower lobe ventilation, particularly in the supine position [20], [2]. Neves et al. [12] studied the effect of increased heart weight in 17 patients undergoing coronary artery bypass grafting. Post-surgical edema and other mechanisms caused an average 32% increase in post-surgical heart weight. Using CT scans they were able to measure pre- and post-surgical volumes and masses of both the heart and lungs, and measure the pressure of individual cardiac segments on adjacent lung segments. One day after surgery, they found increases of 75% and 45% in the pressure of the heart on the left and right lower lobes, respectively; and significantly decreased gas volumes in those lobes. They hypothesize that this pressure of heart on lung plays an important role in the post-surgical atelectasis commonly seen after open heart surgery. The present subject showed grossly decreased size in his left lower lobe (Fig. 3) that is consistent with the above-described mechanism.

3.3. Clinical considerations

Our subject had three chest radiographs in the final week before his death, in order to monitor his pleural effusion before and after thoracentesis. Visualization of a trapped lung would require CT scanning [14]. Yet given the subject's clinical presentation and end-stage progression of his CHF it is highly unlikely that further interventions for trapped lung, if it had been identified, would have been recommended, as surgical decortication is a very invasive procedure that requires good cardiopulmonary reserve.

Our subject may have benefitted, however, from earlier identification of his trapped lung in prior years as he was being treated for pleural effusion. Early identification may have offered additional

treatment options, and also would have prevented the cost, discomfort and risks of repeat thoracentesis. Thoracentesis is not recommended in the case of trapped lung, as the pleural cavity will immediately refill due to the negative pleural pressure [14]. Greater awareness, and a higher overall index of suspicion among clinicians for the presence of trapped lung and its sequelae, would lead to more routine use of CT scans in similar cases, and likely overall improved, and potentially more efficient, patient care.

4. Financial disclosure and conflict of interest

We affirm that we have no financial affiliation (including research funding) or involvement with any commercial organization that has a direct financial interest in any matter included in this manuscript. Nor do we have any other personal or professional conflict of interest related to this manuscript.

Abstract

Purpose

We aimed to demonstrate the consequences of rotation on neonatal chest radiographs and how it affects diagnosis. In addition, we demonstrate methods for determining the presence and direction of rotation.

Background

Patient rotation is common in chest X-rays of neonates. Rotation is present in over half of chest X-rays from the ICU, contributed to by unwillingness of technologists to reposition new-borns for fear of dislodging lines and tubes.

There are six main effects of rotation on supine paediatric chest X-rays: 1) unilateral hyperlucency of the side that the patient is rotated towards; 2) the side 'up' appears larger; 3) apparent deviation of the cardiomediastinal shadow in the direction that the chest is rotated towards; 4) apparent cardiomegaly; 5) distorted cardio-mediastinal configuration; and 6) reversed position of the tips of the umbilical artery and vein catheters with rotation to the left. These effects can cause diagnostic errors due to misinterpretation, including air-trapping, atelectasis, cardiomegaly, and pleural effusions, or disease may be masked. We demonstrate the methods of evaluating rotation with examples, including a 3D model of the bony thorax as a guide. In addition, multiple examples of the effects of rotation are provided including examples where disease was misinterpreted, underestimated or masked.

Conclusion

Rotation is often unavoidable in neonatal chest X-rays, especially in the ICU. It is therefore important for physicians to recognise rotation and its effects, and to be aware that it can mimic or mask disease.

Background

Interpretation of paediatric chest X-rays can be influenced by the technical quality, and this requires consideration by those reporting on these examinations [1]. Patient rotation is common on paediatric radiographs, particularly of small children and neonates and can directly impact management. Small children and neonates are not able to follow instructions and are often crying and moving during the procedure. In the neonatal ICU setting patients often have multiple supporting lines and tubes

The six main effects of rotation on chest radiographs (Fig. 2)

- 1.

The side rotated towards (or in supine imaging, the side that is ‘down’) becomes more lucent (or darker) than the side up. This can be explained by X-ray attenuation, as the side rotated towards has decreased tissue distance compared to the side rotated away from (or in supine imaging, the side that is ‘up’) and therefore the X-ray transmission is increased on the side rotated towards, producing a hyperlucent hemithorax [5]. This is counterintuitive for those who use the side down for CT

Evaluating rotation

The European guidelines on quality criteria for diagnostic radiographic images in paediatrics were published in 1996 [8]. Although these guidelines state that no rotation should be present on chest X-rays, they do not elaborate on any methods evaluating rotation. There is currently no universally accepted methods for assessing rotation, but it is generally accepted that paediatric chest radiographs are assessed differently to adult chest X-rays.

In contrast to adult chest radiograph assessment,

Diagnostic errors that may arise from rotation

Hyperlucency of one lung may be due to the presence of a foreign body or air-trapping due to another cause, such as compression of the airway by a mass; chest wall abnormalities, such as Poland Syndrome; or decreased pulmonary blood volume including due to pulmonary artery hypoplasia [5], [13]. Hyperlucency can also be caused by rotation towards one side [Fig. 5].

Hyperdensity of a hemithorax may be caused by an effusion (especially on a supine radiograph); a confluent air-space process due to

Rotation and the position of the umbilical artery and umbilical vein catheters on chest radiographs

Umbilical arteries enter the internal iliac arteries in the pelvis, and the umbilical artery catheter can therefore be differentiated from the umbilical vein catheter on abdominal radiographs by its inferior direction after entering the body, before advancing superiorly [15] [Fig. 9 a]. Using this feature is not a solution for catheter identification when there is only a chest radiograph available in the NICU setting. Lateral or cross-table lateral X-rays can differentiate the umbilical vein

Conclusion

Rotation on neonatal chest X-rays is common and often unavoidable. There is no universally accepted method to measure the degree of rotation, and different methods can be used. All these methods involve measurement of the bony chest or ribs on each side of the thorax. Hyperlucency of the side rotated towards, is one of the expected outcomes. Diagnostic errors, including misidentification of umbilical artery and vein catheter position, can arise if a physician does not correctly identify the

Future research directions

The contribution of this review can lead to more extensive studies that focus on the quality assessment of technical aspects, especially rotation, of paediatric chest x-rays at general and paediatric hospitals. This review highlights the need for further research to establish an easy and reliable method to assess rotation in paediatric chest X-rays and for universal guidelines to be specified.

Described herein are certain clinical and morphologic findings in 9 patients who at necropsy had hearts weighing >1000 g, a weight approximately 3 times normal. With the exception of 2 patients

with hypertrophic cardiomyopathy, the common finding in the remaining 7 patients was obesity. None had valvular heart disease, the previously described major cause of massive cardiomegaly. Thus, obesity needs to be added to the causes of massive cardiomegaly, a cause not previously recognized. Electrocardiograms in 4 patients disclosed high total 12-lead QRS voltage on the electrocardiogram in only one despite the massive cardiomegaly. Section snippets

Methods

The clinical records were searched in each of the 9 patients and pertinent data recorded. The total 12-lead QRS voltage was determined in the 4 patients with available electrocardiograms (Figure 1).

All hearts were weighed by one of us (WCR) after opening the heart from 2 to 5 days after fixation in 10% formaldehyde by transverse cuts of the ventricular walls each about 1 cm in thickness and parallel to the posterior atrioventricular sulcus (Figure 2) or by left and right parasagittal cuts (

Results

Pertinent clinical and morphologic findings in each of the 9 patients are presented in Table 1. All were male aged 15 to 67 years (mean 44). None either clinically or at necropsy had evidence of coronary artery disease. Eight of the 9 patients had systemic hypertension and 5 had diabetes mellitus. The body weight, known in 5 patients, ranged from 242 to 434 pounds (mean 306), and their body mass indexes ranged from 32 to 65 kg/m^2 (mean 44). Two patients were known to have atrial fibrillation

Discussion

Described herein are findings in 9 obese men whose hearts at autopsy weighed >1000 g (All were weighed by the same method by the same person [WCR].). The unusual feature is that none had evidence either clinically or morphologically of valvular heart disease, the usual cause of massive cardiomegaly. The valvular disease most commonly is pure aortic regurgitation (no element of stenosis) with or without associated mitral regurgitation or ventricular septal defect.[2] All 8 adults also had systemic

AIM

To evaluate the performance of a machine learning based algorithm tool for chest radiographs (CXRs), applied to a consecutive cohort of historical clinical cases, in comparison to expert chest radiologists.

MATERIALS AND METHODS

The study comprised 1,960 consecutive CXR from primary care referrals and the emergency department (992 and 968 cases respectively), obtained in 2015 at a UK hospital. Two chest radiologists, each with >20 years of experience independently read all studies in consensus to serve as a reference standard. A chest artificial intelligence (AI) algorithm, Lunit INSIGHT CXR, was run on the CXRs, and results were correlated with those by the expert readers. The area under the receiver operating characteristic curve (AUROC) was calculated for the normal and 10 common findings: atelectasis, fibrosis, calcification, consolidation, lung nodules, cardiomegaly, mediastinal widening, pleural effusion, pneumothorax, and pneumoperitoneum.

RESULTS

The ground truth annotation identified 398 primary care and 578 emergency department datasets containing pathologies. The AI algorithm showed AUROC of 0.881–0.999 in the emergency

department dataset and 0.881–0.998 in the primary care dataset. The AUROC for each of the findings between the primary care and emergency department datasets did not differ, except for pleural effusion (0.954 versus 0.988, $p<0.001$).

CONCLUSIONS

The AI algorithm can accurately and consistently differentiate normal from major thoracic abnormalities in both acute and non-acute settings, and can serve as a triage tool.

Introduction

Chest radiographs (CXRs) are the most commonly requested radiological investigation in clinical medicine, causing a significant burden on the radiology services in the National Health Service.[1] The combination of manpower shortages, the increased demand on (complex) radiological procedures, and the "need for speed" in reports being issued to enable timely patient management have all combined to create a perfect storm in radiology reporting practice.[2]

Machine learning based (otherwise known as artificial intelligence, AI) software tools are being developed to target specific, common areas, where these types of software can help speed up reporting practices, allow greater overall diagnostic accuracy and certainty, and provide speedier direct feedback to referring clinicians. CXR assessments by a number of AI tools are at various stages of development and being tested in both research and clinical application. Several of these studies, which were all retrospective in nature, have focussed on tuberculosis detection or exclusion.,[3], [4], [5], [6] one study was on COVID-19 detection,[7] and a few had wider applications including malignancy and pneumonia.[8], [9], [10], [11], [12], [13] Only one of these studies was performed in the UK[11]; however, this field is rapidly evolving. New systems are being tested and coming into the clinical domain on a regular basis.

One of the major shortfalls of previously conducted studies is that they are often conducted with a curated dataset, which is not reflective of real clinical practice. The curated datasets frequently contain artificially high rates of pathological findings compared to the real world, and more often have selection bias issues through selective addition of cases, which may lead to inappropriately positive outcome reports. Currently, no studies using consecutive data exist for the UK primary care and emergency department (ED) population. Furthermore, there has been no UK study that focused on the AI standalone performance for detecting and classifying pathologies from a CXR.

The present study was intended to validate one particular AI tool (INSIGHT CXR, version 3.1.2.0, Lunit, Seoul, Republic of Korea) in comparison with two expert chest radiologists, by applying this software to a consecutive historical clinical cohort of CXRs obtained at a large UK teaching hospital.

Materials and methods

This was a retrospective validation study to assess the performance of AI in detecting and classifying major thoracic abnormalities from a CXR.

Study population

A consecutive series of CXRs were obtained using standard radiography systems. There were two sources of origin, primary care and ED, with all referrals starting from 1 January 2015 at a large teaching hospital. The images consisted of 1,046 CXRs obtained after referral by primary care (GP films) and a further 1,072 CXRs obtained at the request of the ED (ED films). The CXRs were posterior–anterior (PA) and anterior–posterior (AP) projection images. No other selection criteria were applied.

Ethics approval was not required, and a waiver of informed consent was provided as this was a historical cohort and there no perceived risks to the patients nor potential for changes in management.

In the initial group of 2,118 CXR studies, there were 27 patients in the GP group and 40 patients in the ED group, who had repeat examinations within the study time. These patients were removed from the analysis.

CXRs that were deemed of too poor quality (*n*=91; 4% of the initial cohort) by either the initial reporting radiology or the annotating radiologists, were also removed from the analysis. This resulted in 992 GP films (554 female, mean age 60 years, range: 13–96 years) and 968 ED films (474 female, mean age 64 years, range: 13–102 years), which amounted to a total of 1,960 radiographs included in this study.

Ground truth creation

All radiographs were reviewed and annotated by two independent expert chest radiologists both with >20 years of experience. They reached a consensus on the following parameters: normal or presence of lung nodule, consolidation, pneumothorax, pleural effusion, cardiomegaly, fibrosis, pneumoperitoneum, mediastinal widening, calcification, and atelectasis. In addition, free-text descriptions for "other findings" were allowed.

The expert readers were blinded to the original report and the annotations of the other radiologist, and also did not have access to the subsequent AI tool assessment. Following the independent assessment, the two radiologists reached a consensus diagnosis for cases of initial disagreement.

For the sub-analysis, the findings were split into critical, urgent, and non-urgent groups, based on their clinical criticality. The split can be found in Table 5.

Table 5. Area under the receiver operating characteristic curve (AUROC) comparisons between emergency department (ED) and primary care findings (GP) datasets.

Finding	**ED AUROC (95% CI)**	**GP AUROC (95% CI)**	***p*-Value**
Atelectasis	0.914 (0.884, 0.943)	0.891 (0.851, 0.931)	0.377
Calcification	0.92 (0.877, 0.963)	0.922 (0.882, 0.961)	0.953
Cardiomegaly	0.943 (0.922, 0.964)	0.97 (0.942, 0.998)	0.133
Consolidation	0.903 (0.881, 0.925)	0.881 (0.845, 0.918)	0.316
Fibrosis	0.948 (0.913, 0.984)	0.92 (0.882, 0.957)	0.277
Mediastinal widening	0.909 (0.764, 1)	0.998 (0.995, 1)	0.230
Nodule	0.881 (0.814, 0.949)	0.905 (0.84, 0.97)	0.617
Pleural effusion	0.954 (0.937, 0.971)	0.988 (0.982, 0.995)	<0.001

Finding	ED AUROC (95% CI)	GP AUROC (95% CI)	*p*-Value
Pneumoperitoneum	0.999 (0.998, 1)	[a]	
Pneumothorax	0.954 (0.868, 1)	[a]	

CI, confidence interval.

a

Insufficient case numbers to conduct the AUROC calculation.

Assessed software tool

The applied AI software tool was Lunit INSIGHT CXR (version 3.1.2.0), which is a commercially and clinically available AI computer-assisted diagnosis (CAD) product. The AI algorithm has been trained on 168,056 CXRs, which has been annotated by > 20 board certified radiologists. A total of 3 million CXR images have been used in total to pre-train the algorithm, using semi-supervised learning.

The algorithm has adopted ResNet34-based convolutional neural network as a basis of its architecture. The loss function used is binary cross entropy. The algorithm also adopts the AutoAugment and Attend and Compare modules to improve its performance.

The algorithm can use Digital Imaging and Communication in Medicine (DICOM) CXR images, both AP and PA projections, as an input, without the need for further data pre-processing. The output by the algorithm includes the probability map and the abnormality score, on a scale of 0–100, to determine the presence of lesions. A predefined cut-off value of 15.0 was used for all findings, to determine the presence of a lesion.

A dedicated server was installed within the research environment to allow processing of all the data independently from the expert radiologists and the AI algorithm vendor.

Statistical analysis

The areas under the receiver operating characteristic curve (AUROCs) of AI performance on both GP and ED were calculated and compared using DeLong's test. The sensitivity and specificity for each group were calculated and comparisons were made using generalised estimated equations. The accuracy by criticality was reviewed for each group. The significance level was set to $p<0.05$ for all tests. The analyses were done using R software, version 4.0.4.

Results

Following quality evaluation, 1,960 of the 1,962 included studies (99.9%) were successfully processed by the AI engine. The patient demographics and the number of pathologies found after the ground truth annotation can be found in Table 1, Table 2, Table 3. It is shown that GP dataset contains significantly fewer pathologies compared to the ED dataset.

Table 1. Demographics of chest radiographs included into this study.

Empty Cell	**GP**	**ED**
Projection		

Empty Cell	**GP**	**ED**
AP images	607	396
PA images	385	572
Gender		
Female	554	474
Male	438	494
Age range		
10–20	14	21
20–30	54	59
30–40	69	72
40–50	121	103
50–60	209	121
60–70	227	153
70–80	202	197
80–90	85	184
90–100	11	56
>100	0	2

GP, general practitioner; ED, emergency department; PA, posterior–anterior; AP, anterior–posterior.

Table 2. Emergency department findings: presence of pathology as determined by two expert chest radiologists.

Findings	**Count**	**Total CXRs**	**Proportion**
Atelectasis	76	968	0.0785
Calcification	34	968	0.0351
Cardiomegaly	92	968	0.0950

Findings	Count	Total CXRs	Proportion
Consolidation	210	968	0.2169
Fibrosis	45	968	0.0465
Mediastinal widening	5	968	0.0052
Nodule	34	968	0.0351
Pleural effusion	74	968	0.0764
Pneumoperitoneum	2	968	0.0021
Pneumothorax	6	968	0.0062
Total	578		

CXRs, chest radiographs.

Table 3. Primary care findings: presence of pathology as determined by two expert chest radiologists.

Findings	Count	Total CXRs	Proportion
Atelectasis	80	992	0.0806
Calcification	39	992	0.0393
Cardiomegaly	60	992	0.0605
Consolidation	90	992	0.0907
Fibrosis	49	992	0.0494
Mediastinal widening	6	992	0.006
Nodule	30	992	0.0302
Pleural effusion	43	992	0.0433
Pneumoperitoneum	0	992	0
Pneumothorax	1	992	0.001
Total	398		

CXRs, chest radiographs.

Fig 1 shows some examples of AI findings confirmed by expert readers. As the AI tool is sensitive, it is expected that false-positive findings also occur, and examples are provided in Fig 2.

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Figure 1. Examples of true-positive cases with original and AI detected abnormalities (heat map and probability). (a) Free subdiaphragmatic air. (b) Left pleural effusion. (c) Left lower lobe atelectasis. (d) Pulmonary nodule right middle lung zone.

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Figure 2. Examples of false-positive cases by AI tool when compared to annotations of expert readers. (a) False consolidation, which coincides with double contour from *bowel* loop. (b) False-positive lung nodule due to ECG clip. (c) False-positive effusion due to hyperinflated lungs. (d) False-positive pneumoperitoneum due to bowel double contour.

ED dataset and GP dataset

Sensitivity and specificity

Table 4 demonstrates the sensitivity and specificity of the 10 pathological findings when applying the predefined threshold of 15.0.

Table 4. Performance (sensitivity and specificity) of the AI software tool for emergency department (ED) and primary care findings (GP).

Finding	**ED sensitivity (95% CI)**	**GP sensitivity (95% CI)**	***p*-Value**	**ED specificity (95% CI)**	**GP specificity (95% CI)**	**P-value**
Atelectasis	0.816 (0.71, 0.895)	0.550 (0.435, 0.662)	<0.001	0.887 (0.864, 0.907)	0.961 (0.946, 0.972)	<0.001
Calcification	0.765 (0.588, 0.893)	0.692 (0.524, 0.83)	0.489	0.887 (0.864, 0.906)	0.919 (0.9, 0.936)	0.016
Cardiomegaly	0.88 (0.796, 0.939	0.850 (0.734, 0.929)	0.587	0.884 (0.86, 0.904)	0.962 (0.948, 0.974)	<0.001

Finding	ED sensitivity (95% CI)	GP sensitivity (95% CI)	*p*-Value	ED specificity (95% CI)	GP specificity (95% CI)	P-value
Consolidation	0.886 (0.835, 0.925)	0.922 (0.846, 0.968)	0.341	0.792 (0.761, 0.82)	0.674 (0.642, 0.705)	<0.001
Fibrosis	0.933 (0.817, 0.986)	0.714 (0.567, 0.834)	0.006	0.895 (0.873, 0.914)	0.924 (0.905, 0.94)	0.031
Mediastinal widening	0.8 (0.284, 0.995)	1 (0.541, 1)	0.251	0.97 (0.957, 0.98)	0.993 (0.985, 0.997)	<0.001
Nodule	0.794 (0.621, 0.913)	0.833 (0.653, 0.944)	0.688	0.848 (0.823, 0.87)	0.886 (0.864, 0.905)	0.016
Pleural effusion	0.784 (0.673, 0.871)	0.837 (0.693, 0.932)	0.483	0.942 (0.924, 0.956)	0.986 (0.977, 0.993)	<0.001
Pneumoperitoneum	1 (0.158, 1)	[a]		0.975 (0.963, 0.984)	0.996 (0.990, 0.999)	<0.001
Pneumothorax	0.833 (0.359, 0.996)	1 (0.025, 1)	0.659	0.978 (0.967, 0.986)	0.992 (0.984, 0.997)	0.012

CI, confidence interval.

a

No pneumoperitoneum case exists for the GP dataset.

For the ED dataset, the lowest sensitivity was shown for calcification (0.765, 95% CI: 0.588, 0.893) and the highest sensitivity was shown for pneumoperitoneum (1, 95% CI: 0.158, 1). The lowest specificity was shown for consolidation (0.792, 95% CI: 0.761, 0.82) and the highest specificity was shown for pneumothorax (0.978, 95% CI: 0.967, 0.986).

For the GP dataset, the lowest sensitivity was shown for atelectasis (0.550, 95% CI: 0.435, 0.662) and the highest sensitivity was shown for mediastinal widening (1.00, 95% CI: 0.541, 1). The lowest specificity was shown for consolidation (0.674 95% CI: 0.642, 0.705) and the highest specificity was shown for pneumoperitoneum (0.996, 95% CI: 0.990, 0.999).

Overall, significant differences in sensitivities were seen for atelectasis (0.816 versus 0.550, $p<0.001$) and fibrosis (0.933 versus 0.714, $p<0.0058$) in ED and GP datasets, respectively. Significant differences in specificities were seen for all findings (Table 3).

AUROCs

As seen in Table 5, the AI engine showed AUROCs of 0.881–0.999 and 0.881–0.998 in the ED and GP dataset, respectively. The AUROCs between the two groups showed no significant difference, in terms of performance across the findings except for pleural effusion (0.954 versus 0.988; $p<0.001$).

Criticality

The findings were split by their criticality and their accuracy was calculated (Table 6). The engine showed consistent and high accuracies, with the highest accuracy seen in the critical group (0.9852, 95% CI: 0.9809, 0.9887) followed by non-urgent group (0.902, 95% CI: 0.8942, 0.9095) and urgent group (0.895, 95% CI: 0.8888, 0.901). These differences were statistically significant ($p<0.001$).

Table 6. Total dataset accuracy by criticality.

Criticality	Finding	Count	Total	Proportion	Accuracy	Accuracy 95% CI
Critical	-	9	3,920	0.0023	0.9852	(0.9809, 0.9887)
	Pneumoperitoneum	2	1,960	0.001	0.9857	(0.9794, 0.9905)
	Pneumothorax	7	1,960	0.0036	0.9847	(0.9782, 0.9896)
Urgent	-	644	9,800	0.0657	0.895	(0.8888, 0.901)
	Cardiomegaly	152	1,960	0.0776	0.9199	(0.907, 0.9315)
	Consolidation	300	1,960	0.1531	0.7536	(0.7339, 0.7725)
	Mediastinal widening	11	1,960	0.0056	0.9811	(0.9741, 0.9867)
	Nodule	64	1,960	0.0327	0.8653	(0.8494, 0.8801)
	Pleural effusion	117	1,960	0.0597	0.9551	(0.945, 0.9638)
Non-urgent	-	323	5,880	0.0549	0.902	(0.8942, 0.9095)
	Atelectasis	156	1,960	0.0796	0.9046	(0.8907, 0.9172)
	Calcification	73	1,960	0.0372	0.8964	(0.8821, 0.9096)
	Fibrosis	94	1,960	0.048	0.9051	(0.8913, 0.9177)

Accuracy defined as correctly identified cases/total number of cases.

When assessing critical abnormalities, the software performed equally well in both GP and ED groups. There were only a few patients with pneumothorax, pneumoperitoneum, or widened mediastinum, but sensitivity was consistently greater >80% for these findings with specificity >95%.

Discussion

The use of AI software tools to support reporting of CXRs is a compelling potential application to enable timely feedback of imaging findings to referring clinicians. As shown in this study, the software is able to correlate to expert reader's findings in a high number of CXRs, which should enable more rapid identification of key findings.

The study has shown that the AI performance is maintained, even when a consecutive series of CXRs is used. This is an important observation, as it more closely reflects on normal clinical practice. In contrast, curated datasets, which include more pathologies, will lead to artificially high accuracy, which is a reason for failures of clinical implementation in the past. This research shows that the AI is able to retain its performance in the real-world setting, even when artefacts (e.g., electrocardiography leads) and pathologies that are not covered by the AI algorithm's output (e.g., bullae), are present. This work compares well in diagnostic accuracy compared to several other studies (particularly in an emergency medicine setting).[14], [15], [16] This should facilitate introduction and confidence for implementation in the day-to-day active clinical setting.

Furthermore, this research shows that AI performance remained high between two vastly different datasets. As expected, many more critical findings were present in the ED dataset than GP dataset. Clearly, pneumoperitoneum should be a rare finding in GP CXRs, so this was along the line of expectations. This also makes the sensitivity and specificity not reliable for this particular diagnosis. The software was able to pick up the pathologies requiring referral in each setting well and showed similar performance across these two datasets, thus exhibiting its potential for general application in a routine radiology department setting.

A single predefined abnormality score threshold was used, rather than a tailored operating point for each lesion. The AI product does offer an adjustable threshold for detecting and classifying lesions; however, this was not considered for this exercise in order to see how the AI performs at a predefined threshold to avoid greater complexity of the application in clinical use. In this research, for the predefined threshold, higher specificities were seen in the GP dataset when compared to the ED dataset, for all findings except for consolidation. This suggests that perhaps a higher cut-off threshold could be used in an ED setting to improve the specificity, as patients are more likely to have complex CXRs on presentation. Using the predefined threshold further strengthens the independent nature of the validation exercise. Additional analysis in the future could include tailored thresholds for each finding, which may further increase the accuracy of the AI-derived CXR interpretation.

As demonstrated in this study, it is not suggested that this AI tool will replace radiologists, rather it has the potential to help triage more urgent findings for more rapid reporting, and may provide the clinician with an immediate provisional diagnosis, and thus help reduce the number of patients who are discharged inappropriately prior to a final radiologist report being issued. Both these new opportunities will facilitate workflow improvement as well as increase the clinical acumen of clinicians and radiologists benefitting direct patient management.

Using expert readers as ground truth for exploration of machine learning tools for CXRs is a standard approach[16,17]; however, it goes without saying that experts are also human observers and not necessarily fail proof. In fact, multiple experts often have divergent annotations and interobserver and intra-observer disagreement is commonplace.[18,19] A post-hoc analysis of cases where the AI

detected findings that were not independently reported by the two experts demonstrated that in fact, AI has detected findings correctly while the experts had failed to annotate these (examples are provided in Fig 3). To avoid bias, the original ground truth data were not corrected, but it is likely that the false-positive rate may be slightly overestimated in this study.

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Figure 3. Examples of false-positive findings, which were shown as real findings not annotated by experts. (a) Cardiomegaly. (b) Left lower-lobe atelectasis.

This study has some limitations. First, it was a retrospective cohort of patients referred for CXRs; however, this was a consecutive series with a wide range of pathologies, and both primary care and ED patients were included. Furthermore, the number of CXRs studied was 1,960, which is substantially larger than previous published studies.

Second, the expert readers offered a consensus report, which served as the reference standard. Only two readers were used for this task, albeit that they were both extremely experienced (both >20 years) in this field. One could argue for the involvement of more radiologists, but the sheer number of studies that required assessment prevented us from doing so in the current climate of high pressure on radiology services.

Third, the AI tool was not studied in patients already admitted to hospital and was limited to 10 common pathologies. The reasoning behind this was that the tool will likely have the greatest impact on direct patient management decisions of those patients presenting for the first time to either their primary care physician or the ED. In these settings, the 10 most common pathologies covered the most important, and potentially life-threatening findings on CXRs. Whether lines or tubes were in the correct location was not of interest in this patient cohort.

Other AI software tools have been undergoing development. Some have particularly focused on tuberculosis diagnosis, which is most relevant in countries where this disease is endemic. In the UK, tuberculosis has a very low prevalence, and therefore those tools are less applicable in this setting. Others have assessed wider diagnostic AI applications, but those studies have almost all been exclusively retrospective, some with small patient numbers and only one was performed in the UK.

In conclusion, the present study was a validation study in a historical, consecutive cohort of 1,960 patients referred from primary care and the ED. The study has shown high correlation between expert readers and the AI software tool, which is very promising for future clinical application. A prospective management study is due to start, which will further define the exact role this AI tool may have in direct patient care.

Conflict of interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Edwin J.R. van Beek reports financial support and statistical analysis were provided by Lunit. John Murchison reports financial support was provided by Lunit. Min Jeong Kim reports employment by Lunit. Jong Seok Ahn reports employment by Lunit. Edwin J.R. van Beek reports a relationship with Aidence that includes: board membership and consulting or advisory. Edwin J.R. van Beek reports a relationship with AstraZeneca Pharmaceuticals LP that includes:

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