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Focused sonographic examination of the heart, lungs and deep veins in an unselected population of acute admitted patients with respiratory symptoms: a protocol for a prospective, blinded, randomised controlled trial

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ABSTRACT

Introduction: Patients admitted to hospital with acute respiratory symptoms remain a diagnostic challenge for the emergency physician. The use of focused sonography may improve the initial diagnostics, as most of the diseases, commonly seen and misdiagnosed in patients with acute respiratory symptoms, can be diagnosed with sonography. The protocol describes a prospective, blinded, randomised controlled trial that aims to assess the diagnostic impact of a pragmatic implementation of focused sonography of the heart, lungs and deep veins as a diagnostic modality in acute admitted patients with respiratory symptoms.

Methods and analysis: The primary outcome of the study is the number of patients with a correct presumptive diagnosis within 4 h of admission to the emergency department. The patient is randomised to either an intervention or a control group. In the intervention group, the usual initial diagnostic work up is supplemented by focused sonographic examination of the heart, lungs and deep veins of the legs. In the control group, usual diagnostic work up is performed. The χ^2 test, alternatively the Fischer exact test will be used, to establish whether there is a difference in the distribution of the total number of patients with a correct/incorrect '4 h' presumptive diagnosis in the control group and in the intervention group.

Ethics and dissemination: This clinical trial is performed according to the Declaration of Helsinki and has been approved by the Regional Scientific Ethical Committee for Southern Denmark and the Danish Data Protection Agency. The results of the trial will be published according to the CONSORT statement with the extension for pragmatic trials. The results of the trial will be published in a peer-reviewed scientific journal regardless of the outcome.

ARTICLE SUMMARY

Article focus

- Focused sonography of the heart, lungs and deep veins.
- Initial diagnostics of acute admitted patients with respiratory symptoms.

Key messages

- The results of the study may help to determine whether sonography should be included as a fully integrated part of the primary evaluation in these patients.

Strengths and limitations of this study

- First randomised trial to compare the overall diagnostic performance between the conventional approach and an approach including focused sonography to evaluate and diagnose acute admitted patients with respiratory symptoms, admitted to an emergency department.
- Pragmatic design with inclusion of most patients with respiratory symptoms.
- Single-centre study that could affect external validity.
- Study not powered to investigate morbidity or mortality.

Trial registration number: This study is registered at http://clinicaltrials.gov, registration number NCT01486394.

INTRODUCTION

Patients admitted to hospital with acute respiratory symptoms remain a diagnostic challenge for the emergency physician. At the primary evaluation, the clinician has to

rely on the clinical examination when initiating treatment and further diagnostic work up. Beside the history taking and clinical examination, the initial diagnostics usually consist of blood samples, an ECG and a conventional chest x-ray (CXR).

Several studies have questioned the diagnostic accuracy of the clinical examination.[1–7] The conventional CXR also has its drawbacks and often a supine CXR is the only possible solution in the most critically ill patients. In addition, the diagnostic accuracy of the CXR in the diagnosis of acute respiratory diseases such as pulmonary oedema, pneumonia, pleural effusion and pneumothorax has been debated.[8–11]

The limitations of the initial investigations of acute admitted patients with respiratory symptoms may cause a significant proportion of the patients to receive a wrong diagnosis and thereby inappropriate treatment.[12] An incorrect diagnosis and initiation of an inappropriate treatment is associated with a higher mortality and an increased length of the hospital stay in elderly patients admitted with acute respiratory failure in an emergency department (ED).[12] Most of the patients misdiagnosed in the ED have very common diseases, such as heart failure, pulmonary oedema, community-acquired pneumonia, pulmonary embolism and obstructive pulmonary diseases.[12] A major challenge for the emergency physician is to achieve an as accurate presumptive diagnosis as possible and to differentiate between the most common causes for acute respiratory failure.

One method showing itself promising in improving the initial diagnostics is the use of focused sonography, as most of the diseases, commonly seen and misdiagnosed in patients with acute respiratory symptoms, can be diagnosed with sonography.[5 11 13–22] Although the sonographic findings are normal in patients with obstructive pulmonary disease, sonography seems to be useful in ruling out many coexisting diseases in these patients.[5 17] The cause of acute respiratory failure most often originate from the heart, lungs and deep veins of the legs[12 23] of which all three can be directly visualised using this approach. A combination of focused sonography of the heart, lungs and deep veins would therefore, theoretically, lead to a better differentiation between many of the causes of acute respiratory failure and thus must likely increase the diagnostic accuracy.

Patients admitted and triaged to the medical section of our ED with respiratory symptoms should have a presumptive diagnosis within 4 h of admission. The current standard is that the presumptive diagnosis is based on an evaluation performed by an ED physician in combination with initial diagnostics such as blood samples, ECG and CXR. We therefore aim to investigate whether the supplemental use of focused sonography of the heart, lungs and deep veins as a standard diagnostic tool increases the proportion of acute admitted patients with respiratory symptoms that are correctly diagnosed within 4 h of admission compared with our current initial investigations (eg, blood samples, ECG, CXR and an evaluation performed by an emergency physician).

STUDY PURPOSE

The main purpose of the study is to evaluate whether the use of sonographic examination of the heart, lungs and deep veins of the legs can improve the total number of patients correctly diagnosed within the first 4 h of admission, in an unselected population of patients with respiratory symptoms who are acute admitted to the medical section in an ED compared with the conventional diagnostics without focused sonography (control group) using blinded audit as the gold standard.

TRIAL DESIGN AND METHODS

The study will be conducted as a blinded, prospective randomised controlled trial. The trial will use a parallel group design with a 1:1 allocation ratio. The framework chosen for the trial is a pragmatic and superiority design.

The trial aims to assess the diagnostic impact of the implementation of focused sonography of the heart, lungs and deep veins as a diagnostic modality in acute admitted patients with respiratory symptoms. The primary outcome of the study is the number of patients with a correct presumptive diagnosis within 4 h of admission to the ED. As secondary outcomes, the impact of sonography on inhospital and 30 day mortality, length of hospital stay and number of patients receiving appropriate treatment within 4 h of admission in the ED will be assessed.

The study will take place at the ED at Odense University Hospital, Denmark. In 2010, the ED had 8300 medical admissions. Due to organisational changes, this number is expected to rise significantly during the study period. All patients with respiratory symptoms as the primary complaint are admitted to the medical section of the ED. Patients suspected of having a heart disease (eg, acute myocardial infarction, pulmonary oedema, arrhythmia) are, however, admitted directly to our cardiology department.

The results of the study will be reported according to the CONSORT guidelines for pragmatic trials.[24] An overview of the patient flow in the clinical trial is shown in figure 1.

PARTICIPANTS

We will recruit 320 acutely admitted patients with respiratory symptoms through the ED at Odense University Hospital, Denmark. Patients will only be recruited if they are triaged to the medical section of our ED. Using the inclusion and exclusion criteria, the patients triaged to the medical section will be screened for participation in the study. The screening is performed by the primary investigator. Patients triaged to other sections of the ED

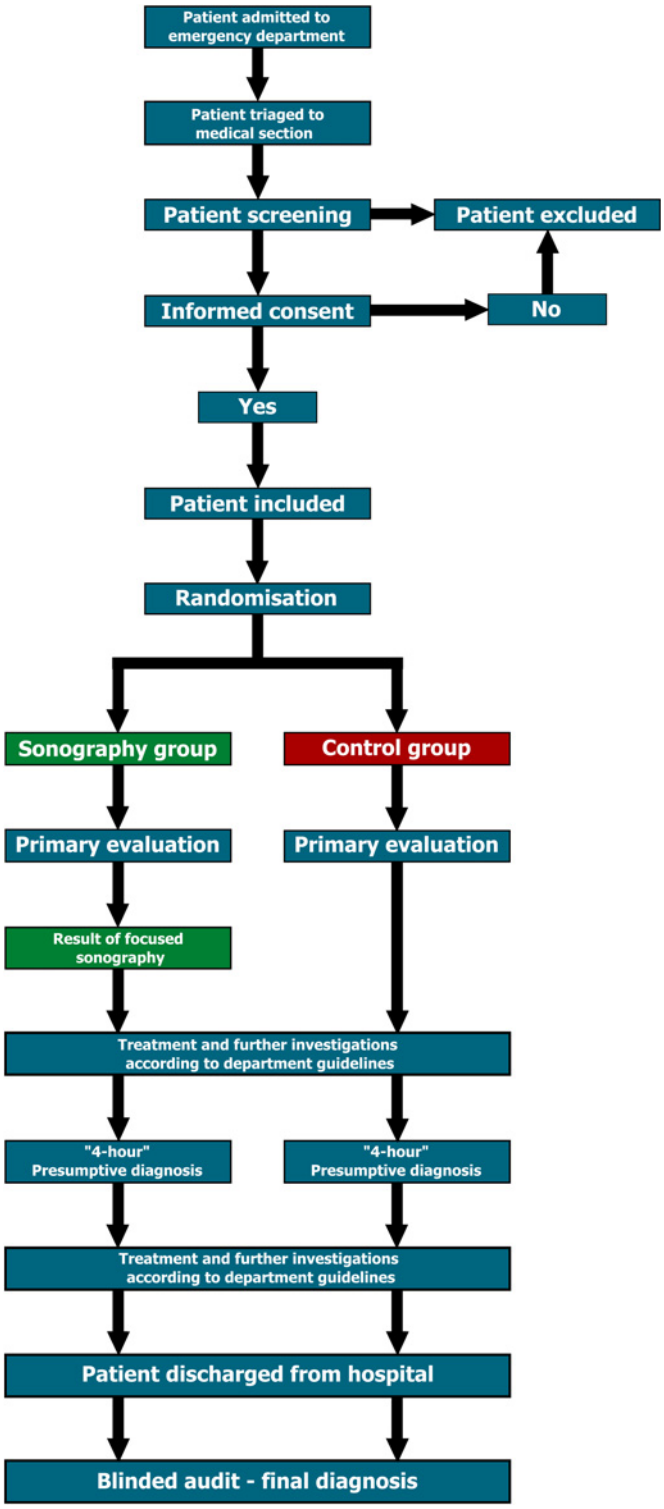

Figure 1 Patient flow in the clinical trial.

(eg, trauma, abdominal surgery, obstetrics, gynaecology) will not be screened for participation in the project.

Immediate after screening patients receive oral and written information about the study, the information is given by the primary investigator. The written information used has been approved by the regional scientific ethical committee. If the patient is willing to participate in the study, written and oral informed consent will be obtained by the primary investigator.

Patient enrolment is carried out during all 24 h of the day.

Inclusion criteria

All five of the following must be present:

1. Patient is triaged to the medical section of the ED.
2. The sonographic examination can be performed before or within 1 h after the primary evaluation.
3. Patient age ≥18 years.
4. Informed consent is available.
5. The presence of one or more of the following symptoms or clinical findings at admission to the ED.
   - −Respiratory rate >20 breaths per minute.
   - −Saturation <95%.
   - −Oxygen therapy initiated.
   - −The patient has a principal complaint of dyspnoea.
   - −The patient has a principal complaint of coughing.
   - −The patient has a principal complaint of chest pain.

Exclusion criteria

One of the following:

1. The sonographic examination cannot be performed before or within 1 h after the primary evaluation.
2. Patient age <18 years.
3. Informed consent is not available.

RANDOMISATION

By the use of a random number generator, the randomisation lists will be established before initiating the study. The unique identification number and group assignment will be printed on a label and then fixed to a folded paper card. The card will be placed in a coloured envelope. This makes it impossible to see the group that the patient is assigned to through the sealed envelope.

Once the patient has been included in the study, the randomisation will be performed. An investigator will open the randomisation envelope containing the patient's unique identification number that also decides whether the patient is randomised to the sonography group or the control group.

BLINDING

In order to blind to the physicians performing the final diagnosis audit, the results of the randomisation and the results of the sonographic examinations are kept in a sealed envelope in the patient's paper journal. The physicians performing the audit have access to the patients' electronic journal. However, they are blinded to the paper journal and thereby the results of the randomisation and sonographic examinations. The emergency physicians are instructed not to record the results of the randomisation or the sonographic examinations in the electronic journal.

INTERVENTIONS

The patient is randomised to either an intervention or a control group. In the intervention group, the usual initial diagnostic work up (eg, evaluation by an ED physician, blood samples, ECG and CXR) is supplemented by focused sonographic examination of the heart, lungs and deep veins of the legs. In the control group, usual diagnostic work up is performed. In both groups, the patient is clinically assessed by the ED physician leading to registration of presumptive diagnosis, treatment initiated and any supplemental diagnostics ordered. The last performed evaluation within the first 4 h is used as the final '4-h' presumptive diagnosis.

SONOGRAPHY GROUP

For patients randomised to the intervention group, sonographic examination of the heart, lungs and deep veins will be performed before or within 1 h after the primary evaluation. The emergency physicians in our department do not have the competencies to perform focused sonography. Instead the sonographic examinations will be performed by a physician qualified for focused sonography (first author CBL). The results of the sonographic examinations are registered in a report sheet and delivered to the ED physician who is in charge of the patient's treatment and further investigations. Then the ED physician re-evaluates the suspected diagnosis along with treatment initiated and further diagnostics ordered. Furthermore, the ED physician grades the clinical information of the sonographic examination. The information is graded into one of the five following categories:

1. Inadequate information.
2. No new information.
3. No new information but presumptive diagnosis confirmed by sonography.
4. Added new information (but no change in treatment/further investigations).
5. Added decisive information (changes made in treatment/further investigations).

The diagnostic criteria for the sonographic examinations are listed in online appendix I. The sonographic examinations are performed according to the following protocols:

−*Focused echocardiography:* performed using the Focus Assessed Transthoracic Echocardiography protocol.[25] The lung views used in the original Focus Assessed Transthoracic Echocardiography protocol are performed as a part of the lung sonography.

−*Lung sonography:* performed using the principles described by Lichtenstein.[26]

−*Limited compression ultrasonography:* performed according to the American College of Emergency Medicine's imaging criteria compendium.[27]

Beside the sonographic examination, patient treatment and other diagnostic examinations performed during the patient's hospital admission are performed according to the ED guidelines.

Control group

The treatment and further investigations of the patients in the control group are performed according to the ED guidelines.

OUTCOME MEASURES

Primary

The primary outcome of the study is to establish whether the use of sonographic examination of the heart, lung and deep veins will increase the proportion of patients with a correct presumptive diagnosis within 4 h after hospital admission, using the final diagnosis obtained by audit as the gold standard. The methods used for the audit are described in online appendix II.

In our ED, the primary evaluation should have been performed and all primary diagnostic examinations (eg, blood samples, ECG, CXR) should be available within 4 h after patient admission. Due to this, we have chosen the 4 h limit as the 'cut-off point' at which we compare the number of patients with a correct presumptive diagnosis in the two groups.

Secondary

As a part of the secondary end points, we will compare the two groups for differences in:

−Sensitivity, specificity, positive and negative predictive values and diagnostic accuracy of the primary evaluation by an ED physician and the '4-h' presumptive diagnosis.

−The proportion of patients with a correct presumptive diagnosis after the primary evaluation by an ED physician.

−The proportion of patients receiving an appropriate, inappropriate and no specific treatment within 4-h of admission.

−The proportion of patients where treatment with diuretics, bronchodilator therapy, steroids, antibiotics and antithrombotic medication are initiated within 4-h of admission.

−Total number and type of further investigations ordered at the primary evaluation by an ED physician (eg, thoracocenthesis, CT, echocardiography).

−Number of further investigations ordered by the ED physician that confirmed or could not confirm the suspected diagnosis.

−Time to diagnostic/therapeutic thoracocenthesis.

−30 day mortality from admission.

−Inhospital mortality.

−Length of hospital stay.

−Number of hospital-free days within 1 month after admission.

−Number of readmissions within 1 month after admission.

−Number of patients transferred to an intensive care unit.

These comparisons are exploratory by nature, and any positive findings will be interpreted conservatively.

For the intervention group, using the blinded audit as gold standard, we will determine:

−Sensitivity, specificity, positive and negative predictive values and diagnostic accuracy of the sonographic examinations.
−Time used to perform the sonographic examinations.
−Patient position during the sonographic examination.
−Image quality of the sonographic examinations (grading scale is described in online appendix I).
−Feasibility for the sonographic examinations (definition of feasibility is described in online appendix I).
−Clinical value of the sonographic examinations as graded by the emergency physicians performing the primary evaluation.
−Clinical value of the sonographic examinations determined by the number of presumptive diagnosis made at the primary evaluation that are changed after the result of the sonographic examinations is revealed for the emergency physician.
−Patient graded discomfort experienced during the sonographic examination (described in online appendix I).

SAMPLE SIZE DETERMINATION

Based on the preliminary non-published results of a descriptive pilot study (n=139) using the same inclusion criteria, approximately 65% of the eligible patients will have a correct presumptive diagnosis within 4 h after admission if sonography is not used. A clinically significant improvement in the presumptive diagnosis by the use of sonography would be an absolute improvement of at least 10%. Based on the preliminary results, the sonographic examination approximately increases the proportion of patients with a correct presumptive diagnosis to 80%. If 65% of the patients in the control group achieve a correct presumptive diagnosis and 80% in the intervention (sonography) group achieve a correct diagnosis, then a power of 80% at the 5% level is obtained with a sample size of 150 patients in each group. Allowing for a 6% dropout after randomisation, it is planned to enrol 160 patients in each group, that is, a total of 320 patients.

DATA ANALYSIS

Descriptive data

Descriptive statistics for both groups will be given including demographic characteristics; health characteristics; patient symptoms; measured variables in the ED; type of treatment initiated in the ED; total number and proportion of patients receiving appropriate, inappropriate and no specific treatment; other investigations ordered in the ED; need for referral for intensive care unit; time (eg, length of hospital stay, time to other imaging modality), mortality (eg, inhospital mortality, 30 day mortality), number of hospital-free days within 1 month after admission and number of readmissions within 30 days.

In the intervention group, the descriptive statistics will also include the clinical value of the sonography (as graded by the physician receiving the sonography rapport sheet), time (eg, time to sonography after primary evaluation, time to complete sonography), image quality, feasibility of the sonographic examinations, patient position while doing sonography and the patient graded experience of the sonographic examination.

Categorical data will be summarised using number and proportion of patients, while continuous data will be presented using the number of patients (n), mean, SD, median, minimum and maximum.

Primary end point

The χ^2 test, alternatively the Fischer exact test will be used, to establish whether there is a difference in the distribution of the total number of patients with a correct/incorrect '4 h' presumptive diagnosis in the control group and in the intervention group.

Secondary end points

To compare the intervention group with the control group, the following test will be used: for the comparison means, we will use the Student t test; for the comparison of medians, we will use the Mann−Whitney test and for the comparison of proportions, we will use the χ^2 or the Fisher exact test. All tests will be performed with a two-sided significance level of 5%.

Using the audit diagnosis as the gold standard, for both groups, we will assess the diagnostic performance of the primary evaluation, the '4-h' presumptive diagnosis and the sonographic examinations by calculating sensitivity, specificity, positive predictive values, negative predictive values and diagnostic accuracy and their 95% CI.

We will analyse data using the intention-to-treat principle. Data analysis will be conducted using STATA Release V.11.0 (StataCorp).

Data entry and security

Measured data are initially handwritten into a case report form. The case report forms will be transferred using double data entry into a computer database. In the database, each patient has a unique identification number securing patient identity. The database is stored on a hospital computer that is password protected and only can be accessed by the primary investigator and the physician who monitor data collection. The physicians performing the blinded audit do not have access to the database until after all audits have been completed and entered into the database. The computer and case report forms are stored in locked room at the research unit. All data are stored and managed according to the laws and regulations as stated by the Danish Data Protection Agency.[28]

TRIAL ORGANISATION AND MONITORING

The authors of this protocol comprise the investigative team of this clinical trial. The principal investigator will perform patient screening, enrolment and sonography

in the intervention group. The principal investigator manages data collection and flow, while one of the associate investigators (FR) monitors data collection, flow and integrity throughout the process.

Focused sonography carries no risk for the patient since its pain and radiation free; hence, a Data Monitoring Committee has not been appointed for the trial.

The patient allocations are concealed from the physicians performing the blinded audit (DPH, PHM and JRD). The auditors will only have access to the participant's electronic patient journal for the audit, but any information about allocation or result of the sonographic examinations is blinded for the auditors. No interim analysis or endpoint adjustments are planned.

DISCUSSION

This trial will be the first study to compare the overall diagnostic performance between the conventional approach to evaluate and diagnose acute admitted patients with respiratory symptoms, admitted to an ED, with a new approach that combines the conventional method with focused sonography of the heart, lungs and the deep veins in the legs. The results of the study may help to determine whether sonography should be included as a fully integrated part of the primary evaluation in these patients.

ETHICAL CONSIDERATIONS AND DISSEMINATION

Sonography is a non-invasive pain and radiation-free diagnostic imaging modality. The sonographic examinations performed in the study do not pose an additional risk for the patients in the intervention group. Beside the sonographic examinations, treatment and other investigations performed in the intervention group are done according to department/hospital guidelines.

This clinical trial is performed according to the Declaration of Helsinki and has been approved by the Regional Scientific Ethical Committee for Southern Denmark and the Danish Data Protection Agency.[29] The study was registered with http://clinicaltrials.gov, registration number NCT01486394.

PUBLICATION POLICY

The results of the trial will be published according to the CONSORT statement with the extension for pragmatic trials.[24] The results of the trial will be published in a peer-reviewed scientific journal regardless of the outcome.

PROJECTED TIMETABLE FOR TRIAL

October 2010: study approved by the Regional Scientific Ethical Committee for Southern Denmark.

November 2011: patient enrolment begins.

May 2012: patient enrolment completed.

August 2012: data entry completed.

October 2012: data analysis completed.

March 2013: article with study results submitted for publication.

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Contributors CBL conceived the idea for this clinical trial and is the primary investigator. All authors contributed to writing and reviewing the protocol, including the process of submitting the protocol for publication. CBL will perform all the sonographic examinations in the intervention group.

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Competing interests None.

Ethics approval Ethics approval was provided by the Committee on Biomedical Research Ethics for The Region of Southern Denmark.

Provenance and peer review Not commissioned; internally peer reviewed.

Data sharing statement No additional data available.

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Appendix I: Sonographic definitions and diagnostic criteria

Focused Echocardiography:

As previously stated the focused echocardiography is performed according to the FATE protocol (1~~25~~). The following criteria are used:

Pericardium:

Pericardial effusion: Presence of an echo-free zone separating the pericardium from the heart.

Left ventricle:

Dilated left ventricle: Left ventricle end diastolic diameter > 61 mm

Markedly hypertrophic left ventricle: Left ventricle wall > 1,2 cm

Left ventricle ejection fraction is estimated by "eye-balling" and sub classified into:

Moderate left ventricular systolic heart failure: 30% ≤ Ejection fraction < 45%

Severe left ventricular systolic heart failure: Ejection fraction < 30%

Hyperkinetic left ventricle: Ejection fraction > 65%

Right ventricle:

Markedly dilatation of the right ventricle: Left ventricle diameter < right ventricle diameter

Markedly hypertrophic right ventricle: Right ventricle wall > 0,8 cm

Right ventricle kinesis: Estimated by tricuspid annular plane systolic excursion (TAPSE), and sub classified into the following:

- TAPSE > 20 mm: Hyperkinetic
- TAPSE 16-20 mm: Normal
- TAPSE 13-15 mm: Mildly reduced
- TAPSE 10-12 mm: Moderately reduced
- TAPSE < 10 mm: Severely reduced

Aortic sclerosis / stenosis:

Defined as the visible presence of a hypomobile, greatly thickened / calcified aortic valve

Other obvious pathology:

Other findings of obvious pathology are registered. Examples are: a visible presence of a mass either localised in the lumen of vessel / cavity or fixed on a valve, visible papillary muscle rupture or severe pathology of the tricuspidal or mitral valve.

Inferior vena cava:

Interpretation of inferior vena cava (IVC) measurements (230):

- IVC diameter < 1,2 cm with spontaneous collapse: Intravascular volume depletion
- IVC diameter > 1,7 cm with no inspiratory collapse: Markedly increased right atrium pressure

Lung ultrasound (LUS):

The definitions and diagnostic criteria for the LUS findings are based on the EFSUMB course book (331). Two exceptions are made. One is a sub classification of interstitial syndrome (IS) into a pattern suggestive of pulmonary oedema, and a pattern which is not characteristic of pulmonary oedema, but may be seen in a variety of other diseases such as adult respiratory distress syndrome and interstitial lung disease. The other is definition of a posterior IS (PIS). Focal IS (FIS), PIS and IS are considered as a continuum, when a patient meets the diagnostic criteria of IS and also posterior IS, then the patient is diagnosed as having IS.

FIS:

Presence of unilateral multiple (≥3) close (< 8 mm) B-lines in a focal area of the lung. Since FIS a sign of localized pulmonary oedema, it can not be considered diagnostic for a specific disease. It is, however, still a sign of focal lung disease such as pneumonia; hence focal interstitial lung syndrome is still considered a pathological finding.

PIS:

The definition of IS are based upon LUS findings of the anterior and lateral areas of the chest. Patients with extensive interstitial lung disease is expected to be diagnosed as “Non pulmonary oedema IS”, but many patients with interstitial lung disease have the most prominent pathological findings in the posterior and basal part of the lungs, and do not necessarily have any changes in the lateral or anterior parts of the lungs. These patients would not necessarily fit into the IS definition. When scanning the lung, the posterior part of the thorax are roughly divided into three areas an

upper, middle and lower area. In this study PIS is defined as the presence of multiple (≥3) close (< 8 mm) B-lines in at least 2 areas on each side. PIS are then sub classified into:

- Nonspecific PIS: Interstitial syndrome with a pattern where there are no spared areas in the dependent regions of the lungs and the pleural line always appears normal.
- Interstitial lung disease PIS: A pattern where there may be spared areas in the dependent regions of the lungs and where the pleural line appears fragmented, irregular and hyperechoic.

Nonspecific PIS is considered non diagnostic, whereas interstitial lung disease PIS is considered as a sign of underlying interstitial lung disease.

Interstitial syndrome (IS):

The probe is positioned on four chest areas per side: two anterior and two lateral. IS are defined as the presence of multiple (≥3) close (< 8 mm) B-lines in at least 2 areas on each side. As mentioned above IS are sub classified into:

- Pulmonary oedema IS: IS with a pattern where there are no spared areas in the dependent regions of the lungs and the pleural line appears normal.
- Non pulmonary oedema IS: IS with a pattern where there are spared areas in the dependent regions of the lungs and where the pleural line may appear fragmented, irregular and hyperechoic.

Pneumonia:

The diagnostic criteria for pneumonia are lung consolidation with all of the following sonomorphologic characteristics:

- Liver like
- Air bronchogram present
- Blurred and serrated margin

Pulmonary embolism:

The diagnostic criteria for pulmonary embolism are lung consolidation with all of the following sonomorphologic characteristics:

- Echopoor
- Well demarcated

- Pleural based
- Triangular or rounded shape
- No visible air bronchogram

The sonographic findings of pulmonary embolism are registered according to the following 3 diagnostic categories (4~~19~~):

- LE confirmed: Two or more characteristic triangular or rounded pleura-based lesions
- LE probable: One typical lesion with a corresponding low-grade pleural effusion
- LE possible: Nonspecific subpleural lesions < 5 mm in size or a single pleural effusion alone

Tumor:

The diagnostic criteria for a tumor / pulmonary carcinoma are subdivided into two categories:

Possible tumor: A lung consolidation with all of the following sonomorphologic characteristics:

- Hypoechoic, inhomogeneous
- Rounded, polycyclic
- Sharp, serrated margins
- Ramifications and fringes

Confirmed malignant tumor

- Infiltration of the adjacent structure (e.g. chest wall, diaphragm)

Compression atelectasis:

The diagnostic criteria for compression atelectasis are lung consolidation with all of the following sonomorphologic characteristics:

- Liver-like with no air or fluid bronchograms
- Triangular
- Blurred margins to ventilated lung parenchyma
- Consolidation is “floating” in the effusion
- Presence of a voluminous pleural effusion

Obstructive atelectasis:

The diagnostic criteria for obstructive atelectasis are lung consolidation with all of the following sonomorphologic characteristics:

- Pleural effusion absent or small
- Liver-like
- No or few air bronchograms
- Fluid bronchograms

Uncharacteristic lung consolidation:

If a lung consolidation is present and the sonomorphologic characteristics does not meet any of the above mentioned diagnostic criteria, the finding is then described as being an uncharacteristic lung consolidation.

Pneumothorax:

Confirmed pneumothorax: Area with absence of lung sliding and B-lines, with the presence of a lung point in an adjacent area.

Suspected pneumothorax: Absence of lung sliding, B-lines, lung pulse and lung point.

Pleural effusion:

The diagnosis of pleural effusion is based on the presence of one or more of the following findings:

- Echo-free zone separating the visceral and parietal pleura
- Echo-free zone displaying a change of form during breathing

Complicated pleural effusion / possible empyema:

A septated or loculated pleural effusion.

Other LUS findings:

Other incidental findings by LUS are diagnosed according to the sonomorphologic characteristics described in the EFSUMB course book (3~~31~~)

Limited compression ultrasonography:

The diagnostic criteria for deep vein thrombosis are based on the American College of Emergency Medicine's imaging criteria compendium (5~~27~~):

- Complete compression of the vein is not attained with sufficient pressure to cause arterial deformation

Feasibility of the sonographic examinations

Focused echocardiography:

Defined as the percentage of patients in which it is possible to:

- determine whether there is pericardial effusion present or not
- determine left ventricle ejection fraction
- determine whether marked dilatation of the right ventricle is present or not

Lung ultrasound:

Defined as the percentage of patients in which it is possible to perform focused sonographic examination of the anterior, lateral and posterior surface of the chest according to the principles defined by D. Lichtenstein (6~~26~~).

Limited compression ultrasonography:

Defined as the percentage of patients in which, using sonography, it is possible to visualise the common femoral, the superficial femoral and the popliteal veins in both legs.

Image quality of the sonographic examinations

The image quality will be graded on a scale from one to five. Each number on the scale is defined as:

- 1. Poor image quality: it is not possible to recognise any anatomical structures.
- 2. Impaired image quality: Some anatomical structures can be visualised, but it is still not possible to diagnose or exclude any pathology.
- 3. Suboptimal image quality: Some anatomical structures can be visualised, and it is possible to diagnose or exclude rough pathology.
- 4. Acceptable image quality: All relevant anatomical structures and any potential pathology can be visualised, but still the resolution of the image are not perfect.
- 5. Excellent image quality: All relevant anatomical structures and any potential pathology can be visualised and the resolution of the picture are near perfect.

Patient graded discomfort experienced during the sonographic examination

After completion of the sonographic examinations the patient grades the level of discomfort experienced during the three sonographic examinations. Each sonographic examination are given a

grade by the patient. The patient grades the level of discomfort on a scale from one to ten, where one represents no discomfort and ten represents the worst possible level of discomfort that the patient can imagine.

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Appendix II: Blinded audit and audit diagnostic criteria.

Final diagnosis

The final diagnosis in both groups is established by partly by blinded audit and partly by the result of diagnostic imaging. Two physicians, independent of each other, perform audit of the patients' entire stay at the hospital. The physicians use the diagnostic criteria listed below. For each patient the physician performing the audit fills out a registration form containing the diagnostic criteria below and performs registration of which criteria / diagnosis are meet and which are not meet. When the two physicians, independent of each other, agree on a diagnosis, then this diagnosis is considered to be the final diagnosis of the hospital stay. When there is a disagreement of the final diagnosis, then a third physician will make a consensus agreement about the final diagnosis.

Blinded audit diagnostic criteria

The following criteria are used:

COPD with exacerbation:

All of the following criteria must be present:

- Patient diagnosed with COPD according to GOLD guidelines (1~~32~~)
- Symptoms compatible with COPD exacerbation, with a worsening in one or more of the following: dyspnoea, sputum production or cough.

Asthma with exacerbation:

All of the following criteria must be present:

- Patient diagnosed with asthma according to GINA guidelines (2~~33~~)
- Symptoms compatible with asthma exacerbation with a progressive worsening in one or more of the following: dyspnoea, wheezing or cough at night.
- Clinical examination with signs compatible with asthma exacerbation (prolonged expiration, wheezing, PEF lower than personal best)

Interstitial lung disease:

The patient has, either previously or during the hospital stay, been seen by a specialist in pulmonary medicine and diagnosed as having an interstitial lung disease according to the ERS guidelines (3~~34~~).

Pneumonia:

The diagnostic criteria are based on the BTS definition of community acquired pneumonia (4~~35~~). The exception being that the BTS criteria which states that "No other explanation for the illness, which is treated as CAP with antibiotics" is omitted. Pneumonia is defined as the presence of all of the following:

- Symptoms of an acute lower respiratory tract illness (cough and at least one other lower respiratory tract symptom).
- New focal chest signs on examination.
- At least one systemic feature (either a symptom complex of sweating, fevers, shivers, aches and pains and/or temperature of 38°C or more)
- New radiographic shadowing for which there is no other explanation (eg, not pulmonary oedema or infarction).

Parapneumonic effusion:

All of the following must be present:

- Pleural effusion diagnosed by either radiological examination (chest X-ray, CT of the chest, sonography by radiologist) or by thoracocentesis
- Co-existing infection in the lung on the same side as the effusion (e.g. diagnostic criteria for pneumonia met)
- Diagnostic criteria for empyema not met

Empyema:

The presence of purulent / turbid / cloudy pleural fluid or a positive Gram stain / culture of pleural fluid.

Pulmonary embolism:

Pulmonary embolism diagnosed by:

- CT of the chest

- MR of the chest
- Angiography
- Ventilation perfusion scan (examination with a high risk of pulmonary embolism)

Pneumothorax:

Pneumothorax diagnosed by a radiological examination (chest X-ray, CT of the chest)

Heart failure:

Diagnosed when either the criteria for systolic or non-systolic heart failure are meet.

Systolic heart failure: The criteria used are based on Task Force for Diagnosis and Treatment of Acute and Chronic Heart Failure 2008 of European Society of Cardiology guidelines (5~~36~~). All of the following criteria must be present:

- Symptoms typical of heart failure (breathlessness at rest or on exercise, fatigue, tiredness, ankle swelling)
- Signs typical of heart failure (tachycardia, tachypnoea, pulmonary rales, pleural effusion, raised jugular venous pressure, peripheral oedema, hepatomegaly)
- Objective evidence of a functional abnormality of the heart at rest, defined as echocardiography with reduced left ventricle ejection fraction (< 45%)
- Diagnostic echocardiography performed by a cardiologist

Non-systolic heart failure: The criteria are based on recommendations by European Society of Cardiology Study Group on Diastolic Heart (6~~37~~). All of the following criteria must be present:

- Signs or symptoms of congestive heart failure: Exertional dyspnoea, eventually objective evidence by reduced peak exercise oxygen consumption, orthopnea, gallop sounds, lung crepitations, pulmonary oedema.
- Normal or mildly reduced left ventricular systolic function
- Evidence of abnormal left ventricular relaxation, filling, diastolic distensibility and diastolic stiffness (Slow isovolumic left ventricular relaxation and / or slow early left ventricular filling and/or reduced left ventricular diastolic distensibility and/or increased left ventricular chamber or muscle stiffness)
- Diagnostic echocardiography performed by a cardiologist

Pulmonary oedema:

2 or more of the following criteria must be present:

- Signs of pulmonary oedema defined as the presence of increased respiratory rate, hypoxemia and auscultation with bilateral lung crepitations.
- Radiological examination with signs of pulmonary oedema (Chest X-ray, CT of the chest)
- Elevated B-type natriuretic peptide (BNP) or elevated N-terminal fragment BNP (NT-pro-BNP).

Acute myocardial infarction:

Diagnosed according to the consensus document of The Joint European Society of Cardiology/American College of Cardiology Committee for the Redefinition of Myocardial Infarction (7~~38~~).

Criteria for acute, evolving or recent MI: Either one of the following criteria satisfies the diagnosis for an acute, evolving or recent MI:

(1) Typical rise and gradual fall (troponin) or more rapid rise and fall (CK-MB) of biochemical markers of myocardial necrosis with at least one of the following:

- ischemic symptoms
- development of pathologic Q waves on the ECG
- ECG changes indicative of ischemia (ST segment elevation or depression)
- Coronary artery intervention (e.g., coronary angioplasty).

(2) Pathologic findings of an acute MI.

Criteria for established MI: Any one of the following criteria satisfies the diagnosis for established MI:

(1) Development of new pathologic Q waves on serial ECGs. The patient may or may not remember previous symptoms. Biochemical markers of myocardial necrosis may have normalized, depending on the length of time that has passed since the infarct developed.

(2) Pathologic findings of a healed or healing MI.

Pericardial effusion:

Diagnosis confirmed by echocardiography performed by a cardiologist.

Deep vein thrombosis:

Diagnoses confirmed by one of the following:

- Sonography performed by a radiologist
- Intravenous venography (conventional or computed tomography)

Anemia:

Diagnosed according to the WHO diagnostic criteria (8~~39~~). The anaemia's are subdivided into light, moderate and severe, according to the following:

Men:

- Light anemia: 6 mmol/l < Hb < 8.1 mmol/l
- Moderate anemia: 4 mmol/l < Hb < 6.1 mmol/l
- Severe anemia: Hb < 4.1 mmol/l

Women:

- Light anemia: 6 mmol/l < Hb < 7.5 mmol/l
- Moderate anemia: 4 mmol/l < Hb < 6.1 mmol/l
- Severe anemia: Hb < 4.1 mmol/l

Malignancy:

Diagnosis confirmed by either histology or cytology. The extent of the disease estimated by radiological examination (computed tomography, magnetic resonance imaging, positron emission tomography, chest X-ray etc).

No diagnostic criteria meet:

If the patient does not fulfil any of the above mentioned criteria, final diagnosis is made by the auditor. The auditor reaches the final diagnosis by clinical judgement based upon the patient's previous medical history and all information from the hospital.

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