Impact of point-of-care ultrasound on the hospital length of stay for internal medicine inpatients with cardiopulmonary diagnosis at admission. – Study protocol of a randomized controlled trial: the IMFCU-1 (Internal Medicine Focused Clinical Ultrasound) study

Ximena Anaite Cid (anaite.cid@gmail.com)
University of Melbourne
David Canty
University of Melbourne
Alistair Royse
University of Melbourne
Andrea Maier
University of Melbourne
Douglas Johnson
University of Melbourne
Doa El-Ansary
Swinburne University of Technology
Sandy Clarke-Errey
University of Melbourne
Timothy Fazio
Royal Melbourne Hospital
Colin Royse
University of Melbourne

Study protocol

Keywords: randomized controlled trial, echocardiography, focused assessment sonography, lung ultrasound, internal medicine.

Posted Date: July 30th, 2019

DOI: https://doi.org/10.21203/rs.2.12182/v1

Version of Record: A version of this preprint was published on January 8th, 2020. See the published version at https://doi.org/10.1186/s13063-019-4003-2.

Abstract

Background Point-of-care ultrasound (POCUS) is emerging as a reliable and valid clinical tool that impacts diagnosis and clinical decision making, and timely intervention for optimal patient management. This makes its utility in patients admitted to internal medicine wards attractive. However, there is still an evidence gap in all the medical setting of how its use affects clinical variables such as length of stay, morbidity and mortality. Methods/design A prospective randomized controlled trial assessing the effect of a surface POCUS of the heart, lungs, and femoral and popliteal veins performed by an internal medicine physician during the first 24 hours of patient admission to the unit with a presumptive cardiopulmonary diagnosis. The University of Melbourne iHeartScan, iLungScan and 2-point venous compression protocols are followed to identify left and right ventricular function, significant valvular heart disease, pericardial and pleural effusion, consolidation, pulmonary edema, pneumothorax and proximal deep venous thrombosis. Patient management is not commanded by the protocol and is at the discretion of the treating team. A total of 250 patients will be recruited at one tertiary hospital. Participants are randomized to receive POCUS or no POCUS. The primary outcome measured will be hospital length of stay. Secondary outcomes include the change in diagnosis and management, 30-day hospital readmission and health care costs. Discussion This study will evaluate the clinical impact of multi-organ POCUS in internal medicine patients admitted with cardiopulmonary diagnosis on the hospital length of stay. Recruitment of participants has commenced in September of 2018 and is estimated to be completed by March 2020.

Introduction

Patients admitted to internal medicine wards with cardiorespiratory symptoms can be difficult to assess and treat as they are usually older, have multiple comorbidities and taking multiple medication. Traditionally, internal medicine physicians rely on the medical history and physical examination, collectively known as the clinical evaluation, to derive a differential diagnosis and formulate an initial management plan. However, it has been reported that clinical evaluation alone is frequently inaccurate in determining the correct diagnosis (1-4). The delay of making a precise diagnosis and starting an appropriate management could be detrimental for patient outcome. Further management is refined by investigations including medical imaging to confirm or rule out the differential diagnosis. However, unnecessary investigations can be associated with high cost and patient risk such as radiation exposure, contrast-induced nephropathy, and transfer of acutely ill patients to an investigation laboratory.

Ultrasonography has been used in medicine for at least 50 years, is a non-invasive and without ionizing radiation. Only in the last two decades have ultrasound machines evolved to produce portable, low-cost units that are readily available for use at the bedside, facilitating its clinical uptake. The terms “clinical ultrasound” and “point-of-care ultrasound” (POCUS) are used to describe a

bedside ultrasound examination performed by the treating doctor; as an adjunct to clinical evaluation.(5) Its use has become very common in some medical specialties such as emergency medicine, anesthesia and critical care. Several prior studies have demonstrated validity and reliability (6-14). The organ scanned depends on the clinical question. By detecting omitted abnormalities in the physical examination (1, 2, 4) and improving the hemodynamic status evaluation(15, 16), heart POCUS has become an useful tool in the evaluation of undifferentiated shock, guiding resuscitation or as part of the preoperative evaluation in patients undergoing surgery.(17-21) Furthermore, lung ultrasound has proved to be superior than physical examination and chest X-ray diagnosing pneumonia, interstitial syndrome (including pulmonary edema) and pleural effusion(22, 23). In the emergency department and critical care setting it is now frequently used in the approach of patients with dyspnea, in which lung POCUS alone or in combination with heart POCUS has demonstrated to be very precise distinguishing the primary cause. (24-34).

Studies quantifying clinical impact of POCUS have shown that its use led to change diagnosis and modify management plans in 30% to 80% of the cases depending on the clinical scenario (17, 18, 35-38). Most of these studies have investigated imaging of one particular organ (17, 35, 39-42). However, a multi-organ approach may better align with the initial assessment of complex cases in internal medicine as they are frequently multi-organ in presentation (5, 43). This is especially true among cardiopulmonary patients in which a broad range of differential diagnoses can be proposed (44). In these patients a combined heart and lung POCUS can identify the cause of dyspnea in most of the cases or significantly narrow the range of diagnoses.(26, 33, 34) In addition to heart and lung POCUS, lower extremities veins POCUS can be used to accurately identify proximal deep venous thrombosis (DVT)(12, 45), which might cause pulmonary embolus and be the cause of shortness of breath or cardiovascular collapse. A multi-organ POCUS of heart, lungs and lower extremities veins has been already tested in a randomized trial with respiratory patients consulting to the emergency department, reporting superiority of POCUS to standard diagnostic tests alone for establishing a correct diagnosis within four hours.(27)

We expect that the addition of a heart, lung, femoral and popliteal vein POCUS in cardiopulmonary patients admitted to internal medicine wards will have a positive impact in the timely diagnosis formulation and impact on decision-making. Moreover, it is plausible that improving diagnosis and altering management plans, may lead to improvement in the workflow and reduction of the length of hospital stay.

Objectives And Hypothesis

The primary aim of the study is to determine whether a heart, lung, and lower extremities vein POCUS reduce the length of hospital stay of patients admitted to internal medicine wards with a cardiopulmonary diagnosis by greater than 24 hours.

The secondary aims are to evaluate the impact of POCUS on: 1) change in diagnosis and management plan, 2) 30-day hospital re-admission and 3) in-hospital health costs.

Trial Design

The IMFCU-1 trial is a single-center, prospective, randomized, parallel group, unblinded, superiority trial with 1:1 allocation ratio. The intervention is a bedside ultrasound examination, which makes blinding not feasible.

Methods

Ethics approval for the study was obtained from Melbourne Health Human Research Committee on 27th of June of 2018 (protocol reference 2018.200). The study has been conducted in accordance with the Declaration of Helsinki and registered with the Australian and New Zealand Clinical Trial Registry on 28th of August of 2018 (ACTRN12618001442291). Table 1 in additional file 1 shows all the items of the World Health Organization trial registration data set.

Methods are reported in accordance with the Guidance for protocols of clinical trials (SPIRIT). (46) SPIRIT check list in additional file 2.

Study setting

The trial is performed at the Royal Melbourne Hospital, a tertiary public university-affiliated teaching hospital, with 706 beds located in Victoria, Australia. Participants are recruited from the internal medicine wards, which are logistically divided in long and short stay units. Short stay has 32 beds and long stay around 68 beds. Approximately, 30% of the internal medicine patients are hospitalized due to a cardiopulmonary condition.

Eligibility criteria

Patients admitted to the internal medicine wards with a preliminary cardiopulmonary diagnosis are invited to participate in the study. Eligible participants are selected every workday morning by internal medicine physicians during their handover. After presenting the

new cases, physicians are asked to identify the cardiopulmonary cases. For the purpose of the study, a cardiopulmonary diagnosis has been defined as the medical suspicion that the main health problem of the patient is related with a heart or a lung condition. Under this definition are included the following symptoms: shortness of breath, chest pain, palpitations, cough, lower limb edema; and the suspicion or confirmed diagnosis of: heart failure, acute coronary syndrome, pulmonary embolism, pneumonia, decompensated chronic pulmonary obstructive disease, asthmatic crisis, cardiogenic syncope, interstitial pulmonary disease, cardiac valve disease, pleural and pericardial effusion.

Inclusion criteria:

- Age 18 years and older
- Less than 24 hours since admission to the internal medicine ward
- Cardiopulmonary diagnosis defined by an internal medicine specialist.

Exclusion criteria

- Previous echocardiography during the last 4 weeks prior to hospital admission
- Computed tomography chest during the current hospital admission
- Requiring infectious disease isolation (contact, drops or respiratory precaution)
- Unable to consent (by themselves or a third person who is nominated/identified as their next of kin).

Intervention

The intervention is a POCUS performed by an internal medicine physician with previous experience in POCUS and the certification of iHeartScan, iLungScan and Focused Cardiac Ultrasound courses from the Educational Ultrasound Group of the University of Melbourne. (XC).

POCUS is performed with an X-Porte portable ultrasonography machine (Sonosite, Bothwell, Andover, MA, USA) using a 1-5 MHz transthoracic and 6-13 MHz linear ultrasound probes. The ultrasound is performed at the patient bedside, taking an average of 20 minutes to be completed.

Assessment of the heart and lungs is performed based on the iHeartScan and iLungScan protocols, designed and validated by the Ultrasound Education Group of the University of Melbourne.(47-49) Heart structure and function are assessed using 2D images and color flow Doppler, spectral Doppler is not included in this study to facilitate timely completion of the ultrasound and to increase its reproducibility. Heart POCUS involves four anatomical windows to record eight views (Figure 1): parasternal long axis, right ventricle inflow, parasternal short axis at the level of aortic valve, parasternal short axis at the level of papillary muscle, apical four- chamber, apical five-chamber, subcostal four-chamber, and subcostal inferior vena cava.

Title Figure 1: Ultrasonography windows assessed in heart point-of-care ultrasound (POCUS).

Legend Figure 1: Four anatomical windows are used to assess eight views of the heart. 1) At the level of the fourth intercostal space lateral to the left border of the sternum, parasternal long axis (PLAX) and right ventricle inflow are recorded. 2) Second window is technically the same than the first, from PLAX the probe is rotated in clock direction ending in the parasternal short axis (PSAX). Two views are recorded at this point, one at the level of the aortic valve and other at the level of papillary muscle or mid left ventricle. 3) Apical window is found about the fifth intercostal space between the mid clavicular line ant the anterior axillary line. In this window the views assessed are apical four-chamber and apical five-chamber. 4) Subcostal window involves two views: subcostal four-chamber view of the heart and the inferior vena cava (IVC) view where the IVC can be identified ending in the right atrium.

The following variables are assessed and reported: volume and systolic function of the left and right ventricles, left atrial filling pressure based on the interatrial septum movement, significant regurgitation or stenosis of the valves, presence or not of pericardial effusion, diameter and collapsibility of the inferior vena cava. Definitions for each variable abnormality are summarized in Table 2. A final statement about the hemodynamic condition will be written as follows: normal, hypovolemia, vasodilated, primary systolic dysfunction, primary diastolic dysfunction, systolic and diastolic dysfunction, and/or right ventricle dysfunction as described by Royse et al. (15)and summarized in Table 3.

Table 2: Variables assessed and definitions of abnormality findings in heart point-of-care ultrasound.

	Variable assessed	Definitions
LV volume	LV end of diastole diameter (LVEDD)	Normal LVEDD : 3 - 5.6 cm LV dilated > 5.6 cm Hypovolemia < 3 cm
LV systolic function	Overall subjective impression	Normal – Reduced -Increased
	Difference between diameters in diastole and systole (LVEDD-LVESD) in PLAX view	Normal 28 -44 mm Reduced < 28 mm Increased >44 mm
	Difference between areas in diastole and systole (LVEDA-LVESA) in PSAX view	Normal 50-65 mm^2 Reduced < 50 mm^2 Increased > 65 mm^2
RV size	Compared to LV size	Normal < 2/3 of LV size
	RV end of diastole diameter	Normal < 4 cm Increased > 4cm
RV systolic function	Overall subjective impression	Normal - Decreased
LA size	LA Diameter in PLAX or A4C views	Normal <3.5 cm
	LA area in A4C view	Normal < 20 cm^2 Increased >20 cm^2
LA filling pressure	Inter-atrium septum movement	Normal: systolic reversal of the inter-atrium septum High filling pressure: Fixed curvature of the inter-atrium septum to the right. Low filling pressure: Systolic buckling of the inter-atrium septum
Cardiac valves	Leaflets appearance and thickness Opening of the valve Presence of reverse jet	Significant Aortic stenosis: An opening <1.5 cm in PLAX or Heavy calcification with inability to see the valve opening
		Significant Aortic regurgitation: A jet that runs on the wall of the LV outflow track A jet that is wider than 25% of the diameter of LVOT A jet that extends down to the ventricle >2.5 cm
		Significant Mitral stenosis: Impaired opening of the mitral valve A hockey stick appearance of one or both of the mitral leaflets
		Significant Mitral regurgitation: Regurgitation jet covering more than 20% of the LA area in A4C or PLAX A turbulent jet that runs along the wall of the atrium Prominent flail mitral valve leaflet or rupture papillary muscle
		Significant Tricuspid regurgitation: Any edge-tracking jet

		Any central jet longer than 5 cm^2
Pericardial effusion	Presence of anechoic space between parietal and visceral pericardium	Significant pericardial effusion is defined as > 0.5 cm in any view
Inferior vena cava	Diameter of the inferior vena cava in the subcostal view during normal breathing	Maximum diameter in cm and percentage of collapsibility during normal inspiration are reported. Estimation of the right atrium pressure is informed as follows: IVC < 2.1 cm collapsing more than 50% à RAP: 3 mmHg IVC > 2.1 cm collapsing less than 50% à RAP: 15 mmHg Values between the two above à RAP:8 mmHg

Table 2. A4C: apical four chambers. LA: left atrium. LV: left ventricle. LVEDA: left ventricle end of diastole area. LVEDD: left ventricle end of diastole diameter. LVESA: left ventricle end of systole area. LVESD: left ventricle end of systole diameter. PLAX: parasternal long axis. PSAX: parasternal short axis. RAP: right atrium pressure. RVEDD: right ventricle end of diastole diameter.

Table 3: Hemodynamic state definitions

	Normal	Hypovolemia	Vasodilated	Primary systolic failure	Primary diastolic failure	Systolic & diastolic failure	RV failure *
LV volume	Normal	Decreased	Normal	Increased	Normal/decreased	Increased	RV increased
LV systolic function	Normal	Normal/Decreased	Increased	Decreased	Normal	Decreased	RV decreased
LA filling pressure	Normal	Decreased	Normal	Normal	Increased	Increased	Increased

Table 3. Hemodynamic state is defined based on left ventricle volume, left ventricle systolic function and left atrium filling pressure. LV: left ventricle. LA: left atrium. RV: right ventricle.

*RV failure can be a hemodynamic state by itself or in combination with LV failure.

The lungs are scanned by division into three anatomical zones as previously reported by Ford et al.(49) (*Figure 2*). The anterior zone goes from the sternum edge to the mid-axillary line posteriorly; the upper posterior zone is defined by the mid-axillary line anteriorly, the spinous processes of the thoracic spine posteriorly, and the inferior tip of the scapular inferiorly: and the lower posterior zone defined by the mid-axillary line anteriorly, the spinous process of the thoracic spine posteriorly, and the inferior rip of the scapula superiorly. Abnormal findings are recorded as: collapse, consolidation, alveolar/interstitial syndrome, pneumothorax and/or pleural effusion. Definitions are described in Table 4. Normal lung pattern is defined as the presence of normal lung sliding, reverberation artefacts from the pleural, and absence of any of the pathologies described.

Title Figure 2: Anatomical zones scanned in lung point-of-care ultrasound (POCUS).

Legend Figure 2. Illustrations of the front (left) and back (right) of the chest showing the six anatomical zones scanned. RA: right anterior. LA: left anterior. LPU: left posterior upper. LPL: left posterior lower. RPU: right posterior upper. RPL: right posterior lower.

Table 4. Definitions of ultrasound lung abnormalities

Abnormal lung patterns	Definition / ultrasound findings
Alveolar/Interstitial syndrome	3 or more B-lines in a single rib space. B-lines were defined as hyperechoic, vertical artifacts arising from the pleural line and reaching the bottom of the screen without fading.
Collapse or atelectasis	Loss of lung volume, increased tissue density and hyperechoic static air bronchograms
Consolidation	Tissue-like pattern or "hepatization" with minimal volume loss and the presence of dynamic air bronchograms
Pneumothorax	Absence of lung sliding and lung pulse.
Pleural effusion	Anechoic space between the parietal and visceral pleura with movement with the respiratory cycle. Significant pleural effusion is defined as > 1 cm. An estimation of the volume of a pleural effusion in milliliters (ml) will be done multiplying by 200 the distance in centimeters (cm) in the vertical plane from the diaphragm to the inferior lung border at the junction of the collapsed lung and aerated lung.

Femoral and popliteal veins are assessed for intravascular thrombosis using the 2-point compression technique (12, 42) (*Figure 3*), in which the vein collapsibility is evaluated in two points for each lower extremity: the common femoral vein at the level of the groin and the popliteal vein in the popliteal fossa. A deep venous thrombosis is defined as inability to completely collapse the vein with the ultrasound probe. This technique has proved a sensitivity of 96.1 % and specificity of 96.6% diagnosing proximal deep venous thrombosis when it has been compared to standard vein ultrasound performed by radiologists.(12, 42)

Title Figure 3: Femoral and popliteal vein point-of-care ultrasound (POCUS).

Legend Figure 3: A) The illustration shows the two points of the lower extremities assessed for deep venous thrombosis: The common femoral vein at the groin level and popliteal vein at the popliteal fossa. B) and C) are ultrasound images showing the vein marked with yellow arrows before (B) and after (C) external compression has been applied. In this case, the vein is entirely collapsible, consistent with absence of a deep venous thrombosis.

Once the test has been performed, a structured report summarizing the main findings is written. The quality of this report is immediately assessed by a second POCUS expert reviewing the images recorded. There are three experts participating in this study as quality evaluators (CR, AR and DC), all of them with at least 10 years of experience in POCUS. The revised report is given to the treating team without any direction of management, who in turn are requested to fill out forms about their clinical assessment before and after receiving the POCUS report (Figure 4).

Title Figure 4: Steps involved in the intervention group

Legend Fig. 4: In the intervention group a point-of-care ultrasound (POCUS) of the heart, lungs, femoral and popliteal veins is performed bedside the patient. The report summarizing the main findings is assessed by a second expert in POCUS before it is given to the treating team. The treating team is requested to fill out forms about their clinical assessment and management plan before and after receiving the POCUS report. Difference between forms will be recorded as influence of POCUS.

The intervention will not be performed or will be stopped after being already started if the patient refers intolerable discomfort during the procedure or in any clinical condition that involves urgent management such as cardiorespiratory arrest, pain or respiratory distress. In these cases, if some of the variables were already assessed, a report with partial information will be given to the treating team.

The control group follows the standard care pathway, which does not include POCUS. Diagnosis and management will be based on clinical evaluation and other investigations. Ultrasound examinations are not precluded such as those performed by cardiology or radiology staffs, but POCUS of the heart, lungs or lower extremities veins are not allowed during the time that the participant remains admitted to an internal medicine ward.

There are no restrictions in medication use or further standard investigations in any of the two groups.

Results

Outcomes

Primary outcome

The primary outcome is the difference in the median of length of hospital stay between the intervention group and the control group. Length of stay is defined as number of hours from admission to the internal medicine ward to hospital discharge.

Secondary outcomes:

Impact on diagnosis and management will be reported as follows: 1) Number and proportion of patients in whom a new diagnosis was found with POCUS. 2)Number and proportion of patients in whom the main cardiorespiratory diagnosis was changed after POCUS. 3) Number and proportion of patients who had a management modification. Management includes adding or removing medications to treat cardiorespiratory conditions (e.g. diuretics), requesting further investigations and consulting to another specialist.

Readmission to the hospital will be presented as proportion of patients readmitted to the hospital during the next 30 days after hospital discharge in both groups.

Health care costs involves total costs spent in each patient during their hospital stay presented in Australian dollars. The data will be organized in several categories (bed stay, imaging tests, pathology investigations). Average of cost of each category will be compared between groups.

Participant timeline

Screening for eligibility, enrolment, allocation and intervention is performed on the same day (Figure 5). No follow-up of participants is done after hospital discharge. Data about length of stay, 30-day readmission and costs will be obtained from the hospital electronic databases after finishing the recruitment.

Figure 5. Title: Schedule of enrolment, intervention, and assessments.

Sample size

A sample size of 122 participants in each group has been estimated, which is being rounded up to a total of 250 participants to allow withdrawals. This estimation has been calculated using the statistical software G Power Version 3, based on a t-test of log transformed length of stay in hours from internal medicine wards of the Royal Melbourne Hospital (median of 103 hours), a clinically important effect on length of stay defined as 24 hours, power of 80% and alpha of 0.05.

Recruitment

One of the investigators (XC) attends every internal medicine handover from Monday to Friday assuring that all the new cardiopulmonary patients from the previous night shift are screened for eligibility. Once the internal medicine physicians have identified the potential participants, the order in which these patients will be approached is done following a randomized sequence created by computer software. In this way, selection bias is significantly reduced. Participants received verbally information and a written document about what it means to participate in this study and how the study is conducted. Once they have agreed to participate, they are asked to sign an informed consent form. In case participants cannot give their consent due to cognitive impairment, a person responsible or a person already stablished as their medical treatment decision maker will be asked to sign the consent on their behalf.

The recruitment rate for the past 8 months has been 15 participants per month. Therefore, we expect to complete the recruitment in 8 months. A proposed of Consolidated Standard of Reporting Trials (CONSORT) flow-chart is shown in Figure 6.

Title Figure 6: Proposed of Consolidated Standard of Reporting Trials (CONSORT) flow-chart for IMFCU-1 study.

Allocation

Participants are randomly assigned to the intervention or control group with a 1:1 ratio. The allocation sequence is based on permuted blocks of random size, generated by computer software. Blocks sizes are 4, 6 or 8. Sealed, numbered, double-layered, opaque envelopes are used for concealment. The concealment was performed by a non-investigator. Enrolment and allocation will be done by the same investigator after participant has signed the informed consent form. The only person who has access to the allocation sequence is the main investigator, who is not involved in the recruitment process.

Blinding

Due to the nature of the intervention blinding is not possible. It was considered unethical to perform POCUS and conceal the results in the control group.

Withdrawal from the study

If participants withdraw from the study, their data will not be available for analysis. To date this has not occurred, and we anticipate a very low withdrawal number.

Data collection methods

Demographic data and baseline information will be gathered prospectively by one of the investigators from the medical notes. Baseline data is detailed in Table 5.

Table 5. Patient basal data to be collected

Demographic data	Age (years) Gender (female) Height (cm) Weight (kg) Body mass index (BMI)
Prior medical conditions	Hypertension Congestive cardiac failure Angina Myocardial infarction Coronary intervention Known significant valve disease Valve replacement Cardiac arrhythmia Pulmonary hypertension Chronic obstructive pulmonary disease Interstitial lung disease Asthma Smoking Diabetes Known renal failure Stroke Human immunodeficiency virus (HIV) Venous thromboembolism Cancer (type, active/remission, metastasis) Chronic liver disease Hypothyroidism Hyperthyroidism Cognitive impairment/dementia
Chronic medication	Antihypertensive Beta blockers Antiplatelet

	Anticoagulant Systemic steroids Diuretics Chemotherapy Other
Cardio-pulmonary symptoms	Dyspnea/shortness of breath Chest pain Palpitations Cough Fever suspected to be respiratory or cardiac Lower limb edema Altered state of consciousness Other
Vital signs	Blood pressure (mmHg) Heart rate (beats per minute) Temperature (Celsius degree) Respiratory rate (breaths per minute) O2 saturation (percentage)

Primary outcome:

Hospital length of stay is obtained from the hospital operating system and is not influenced by any of the investigators. A list with full name, patient number, and the date of admission, but blinded to allocation will be sent to the hospital Business Intelligence Unit to generate the length of stay data.

If patients are transferred from physical internal medicine wards to the 'Hospital in the home' (HITH) programme, an acute general care programme in the patients homes, the length of stay will be added to the length of stay on internal medicine wards.

Secondary outcomes

New diagnosis and change in management will be evaluated using forms about clinical assessment completed by the treating physician before and after the findings of POCUS are revealed to them. Both forms are exactly the same. The difference between them will be interpreted as the effect of the intervention. (Figure 4)

The information requested in these forms includes (Additional file 3):

1. The hemodynamic state of the patients from the following options: normal, hypovolemia, primary diastolic failure, primary systolic failure, systolic and diastolic failure, vasodilation, and right ventricle failure.
2. Describing physical examination findings specifying left ventricular function, significant valve regurgitation or valve stenosis, pericardial effusion, suspicion of pulmonary embolism, abnormalities of the lungs and evidence of deep venous thrombosis.
3. Recording the most likely diagnosis.
4. Detailing further investigations. In this section they will have a list of pathology tests, imaging tests and consultations to other medical specialties. They will be asked to mark all the further investigations that they are requesting.
5. Describing the type of treatment prescribed from five options: (1) heart failure treatment (defined by one of the following treatment: diuretics, vasodilators and/or fluid restriction), (2) COPD/asthma treatment (defined as the use of bronchodilators and/or systemic steroids), (3) antibiotics, (4) anticoagulation in therapeutic dose, and (5) “other” in case it is a different treatment from the four above. More than one option can be chosen.

The seniority of doctors who will complete the forms is restricted to internal medicine specialists and specialist trainees.

Readmission to the hospital data will be gathered from hospital operating system in the same form that has been explained for the primary outcome. Planned readmissions will be excluded, analysing only unplanned readmissions in the following 30 days after hospital discharge.

Information about economic health will be gathered directly from the Business Intelligence Unit. This unit centralizes all the information related to health costs and analyses it for administrative purpose.

Once the trial has finished recruiting, we will send them the blinded list of patients specifying the admission and discharge date. Hospital costs include total costs and categories such as bed stay, imaging tests and pathology tests.

Statistical Methods

The primary outcome, length of stay in hours, will be analysed using Student´s t-test on the log scale, in anticipation of skewness in raw length of stay. Log transforming will normalize a skewed data, making outliers unlikely. However, a cut-off of 30 days will be

applied to length of stay to avoid the effect of extremely long hospital stays. Statistical analysis will be done using the software G power, version 3.

For patients who die in hospital be treated as hospital discharge for the primary analysis as the unpublished mortality rate of patients admitted to internal medicine wards of the Royal Melbourne Hospital is low (2.7%). However, a sensitivity analysis will be conducted to explore the impact of this approach.

Missing data about the primary outcome is not expected as it is anticipated that length of stay will be available for every patient in the study. If for some reason this information is missing, those patients will not be included in the primary statistical analysis.

For the primary outcome, significance is defined as $p<0.05$. Secondary outcomes will be analysed using parametric or non-parametric tests according to the type of data, whether the data are skewed, and whether repeated measures are used. For secondary endpoints significance will be defined as $p<0.01$ to reduce risk of Type 1 error.

Data Management

All data will be entered electronically using numerical codes. Paper records will be stored in files in a locked filing cabinet, in a locked room in the Department of Surgery of the University of Melbourne. Electronic data is stored on password protected databases, available only to researchers involved in the study. The primary outcome and health cost data are generated from the hospital electronic systems and not under the influence of investigators. Other data will undergo double data entry range checks for data value errors.

Due to the small trial size, there is neither Data Monitoring Committee (DMC) established nor stopping rules applied. There is no planned interim analysis.

The final results of this study are intended to be disseminated through publications in peer-reviewed medical journals. After publishing, data about demographic, primary and secondary outcomes will be shared to other researchers who request it to the principal investigator with a project proposal and with acceptance of release of data by the Melbourne Health Human Research Ethics Committee.

Discussion

This study will show whether the addition of a multi-organ POCUS in internal medicine patients reduces the length of stay at the hospital. Length of stay was selected as the main outcome as it was considered objective, reliable data and clinically relevant to

both the patient and the health care system. Demonstrating an impact in length of stay will encourage physicians around the world to incorporate this technique in their routinely practice.

The novelty of this study is that it is the first randomized trial assessing the impact on length of stay of a multi-organ focused ultrasound in internal medicine. Last year, Mozzini et al. (50) have described a positive impact of repetitive lung ultrasounds on the length of hospital stay in heart failure patients admitted to the internal medicine ward. Based on their results, we are optimistic about finding a positive effect this time assessing a multi-organ focused ultrasound which not only evaluate lung but also heart and deep venous thrombosis.

The limitations of the study are that the outcomes are short-term and related to the hospital admission. This study will provide clinical data that can serve to assess feasibility and sample size for a trial investigating morbidity and mortality outcomes. A randomized pilot study investigating focused cardiac ultrasound in patients undergoing fractured neck of femur surgery showed a group separation of 30-day mortality and morbidity outcomes of 39% favouring the use of cardiac ultrasound (51) and a lower 12 month mortality (52). The sample size of this study, however, is too small to investigate morbidity and mortality outcomes for the cardiopulmonary admissions to internal medicine wards. Further, the use of ultrasound in not a medical intervention but rather an investigation. The behaviour change consequent on the information is the actual mechanism whereby improved outcomes can occur. If the treating medical staffs choose to ignore the findings, or not act appropriately upon them, then the value of the ultrasound examination is diminished. This problem is most likely to occur at the start of the study where scepticism regarding the POCUS study exists and reduce over time as the additional knowledge form a feedback loop on the clinician's diagnostic approach.

Trial Status

Recruiting. Protocol version 2, dated 23rd August 2018. Recruitment has begun on the 3rd of September 2018 and it is estimated to be completed by March 2020.

Abbreviations

A4C: apical four chambers. COPD: chronic obstructive pulmonary disease. CT: computed tomography. DVT: deep venous thrombosis. HIH: Hospital in home. HIV: human immunodeficiency virus. LA: left atrium. LV: left ventricle. LOS: length of stay. LVEDA: left ventricle end of diastole area. LVEDD: left ventricle end of diastole diameter. LVESA: left ventricle end of systole area. LVESD: left ventricle end of systole diameter. MRI: magnetic resonance imaging. PE: pulmonary embolism. PET: positron emission tomography. PLAX: parasternal long axis. POCUS: point of care ultrasound. PSAX: parasternal short axis. RMH: Royal Melbourne Hospital. RV: right ventricle. RVEDD: right ventricle end of diastole diameter.

Declarations

Consent for publication

Written consent was obtained from participants for publication of their personal and health information using only de-identified data. There is no intention of publishing identifying images.

Competing interests

The authors declare that they have no competing interests.

Ethics approval and consent to participate

Ethics approval for this study was obtained from Melbourne Health Human Research Committee on 27th of June of 2018 (protocol reference 2018.200). Participants have given their consent to take part in this research project, which includes having the ultrasound exam and using their personal and health information.

Funding

The trial is conducted without any external funding and is being instead internal funded by the Department of Surgery of the University of Melbourne. There is no grant or individual funding involved in this trial.

Author's contribution

XC contributed to the trial protocol, performed patients screening and recruitment, performed ultrasound, contributed to data analysis and manuscript preparation and submission. CR contributed to the trial protocol and design, ultrasound review, analysis and interpretation of the data and manuscript preparation. AR and DC performed ultrasound review, contributed to analysis of the data, and manuscript preparation. DEA contributed to the protocol and preparation of manuscript. . DJ and ABM contributed to the protocol and manuscript preparation. SCE performed the statistical design and analysis.TF assisted with data collection and analysis.

Acknowledgements:

We acknowledge Lynda Tivendale for her support and contribution to the trial. We also acknowledge the significant role of Internal medicine staffs and trainees of the Royal Melbourne Hospital, who have made this study possible. And Lacey Whelan, who has helped us with the illustrations.

Author's information

XC: Internal medicine specialist in Chile. Candidate for PhD of Medicine confirmed at the University of Melbourne, Australia.

CR: Professor in the Department of Surgery (Royal Melbourne Hospital), University of Melbourne. Consultant anaesthetist in the Department of Anaesthesia and Pain Management of Royal Melbourne Hospital, Australia.

AR: Professor in the Department of Surgery (Royal Melbourne Hospital), University of Melbourne. Consultant Cardiothoracic Surgeon in the Department of Cardiothoracic Surgery of the Royal Melbourne Hospital, Australia

DC: Director of Ultrasound Simulation and Senior lecturer in the Department of Surgery (Royal Melbourne Hospital), University of Melbourne. Consultant anaesthetist at Monash Medical Centre, Department of Medicine, Monash University Australia.

DJ: Associate Professor of the University of Melbourne. Consultant General Medicine and Infectious Disease physician. Head of the Service of General Medicine of the Royal Melbourne Hospital, Australia.

ABM: Professor of Medicine and Aged Care at the University of Melbourne and Professor of Ageing at the Vrije Universiteit, The Netherlands. Consultant Geriatrician and Internal Medicine. Divisional Director of the Department of Medicine and Community Care of the Royal Melbourne Hospital, Australia.

DEA: Course Director of Physiotherapy and Director of Research Development, Department of Health Professions, Faculty of Health, Arts and Design, Swinburne University of Technology. Senior Research Fellow, Department of Surgery, University of Melbourne

SCE: Specialist statistician, Statistical Consulting, The University of Melbourne

TF: Consultant Physician in Metabolic Disease Unit. Clinical informatics lead at the Business Intelligence Unit. Deputy Chief Medical information officer. Royal Melbourne Hospital.

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Figures

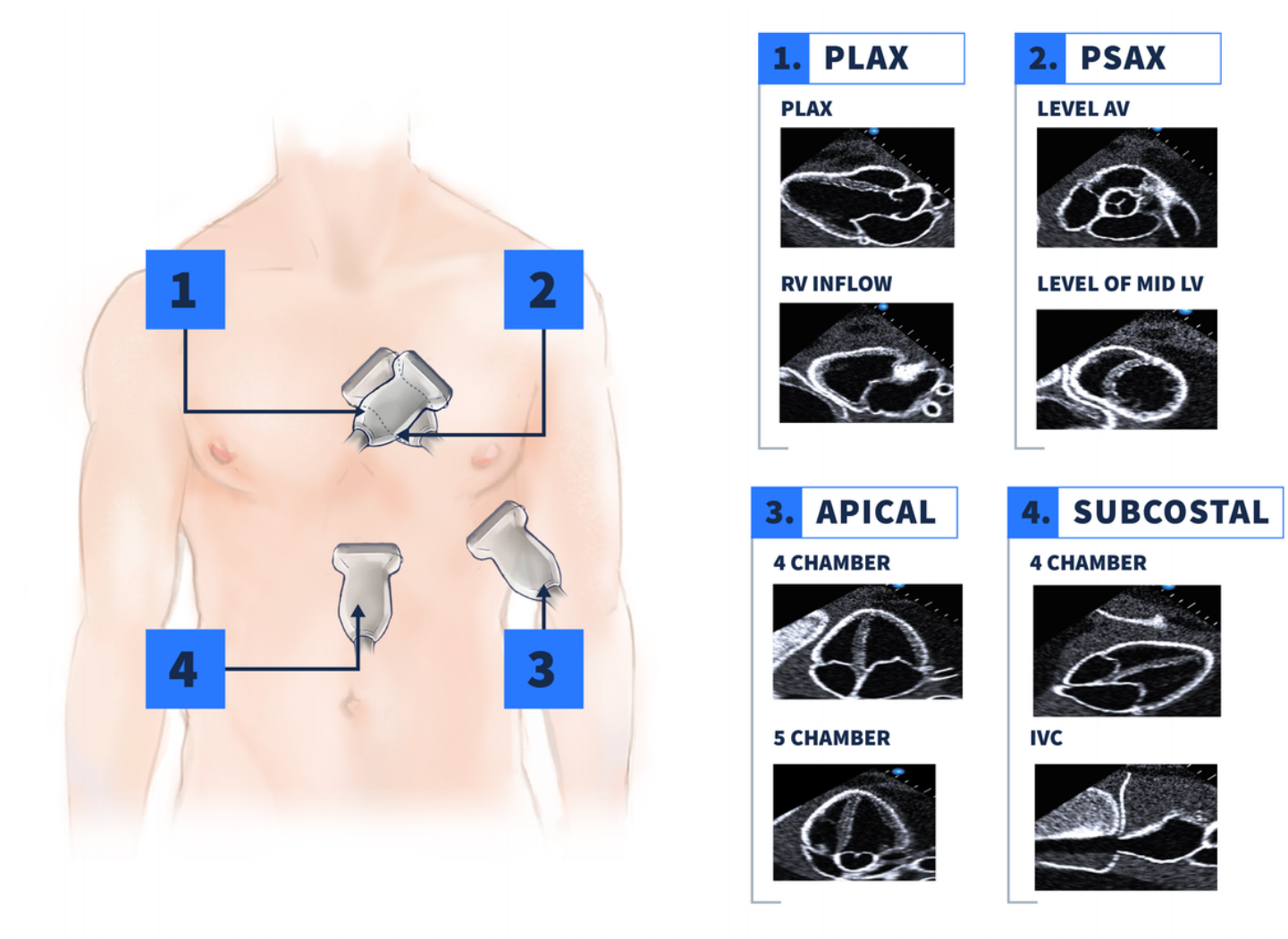

Figure 1

Four anatomical windows are used to assess eight views of the heart. 1) At the level of the fourth intercostal space lateral to the left border of the sternum, parasternal long axis (PLAX) and right ventricle inflow are recorded. 2) Second window is technically the same than the first, from PLAX the probe is rotated in clock direction ending in the parasternal short axis (PSAX). Two views are recorded at this point, one at the level of the aortic valve and other at the level of papillary muscle or mid left ventricle. 3) Apical window is found about the fifth intercostal space between the mid clavicular line ant the anterior axillary line. In this window the views assessed are apical four-chamber and apical five-chamber. 4) Subcostal window involves two views: subcostal four-chamber view of the heart and the inferior vena cava (IVC) view where the IVC can be identified ending in the right atrium.

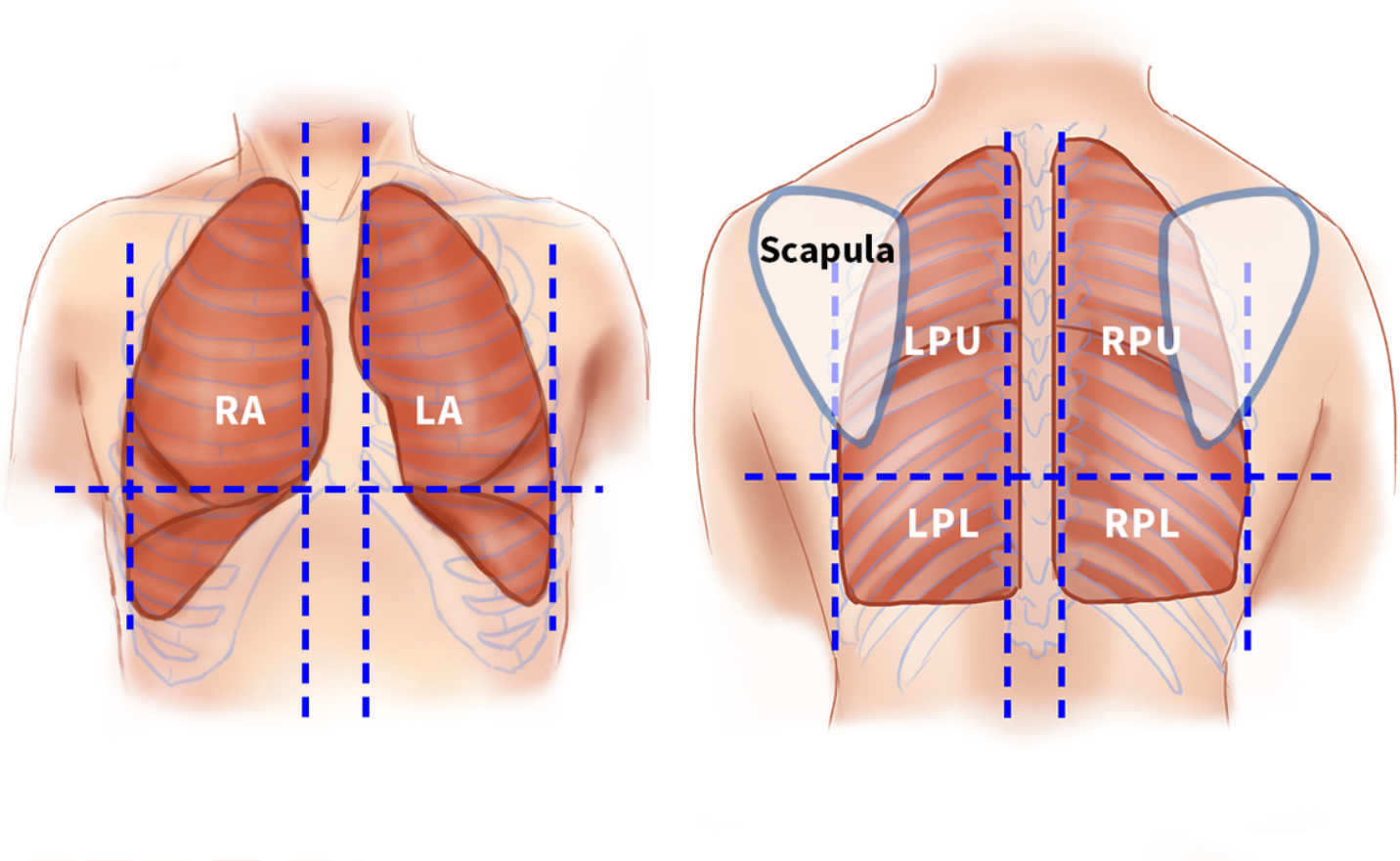

Figure 2

Illustrations of the front (left) and back (right) of the chest showing the six anatomical zones scanned. RA: right anterior. LA: left anterior. LPU: left posterior upper. LPL: left posterior lower. RPU: right posterior upper. RPL: right posterior lower.

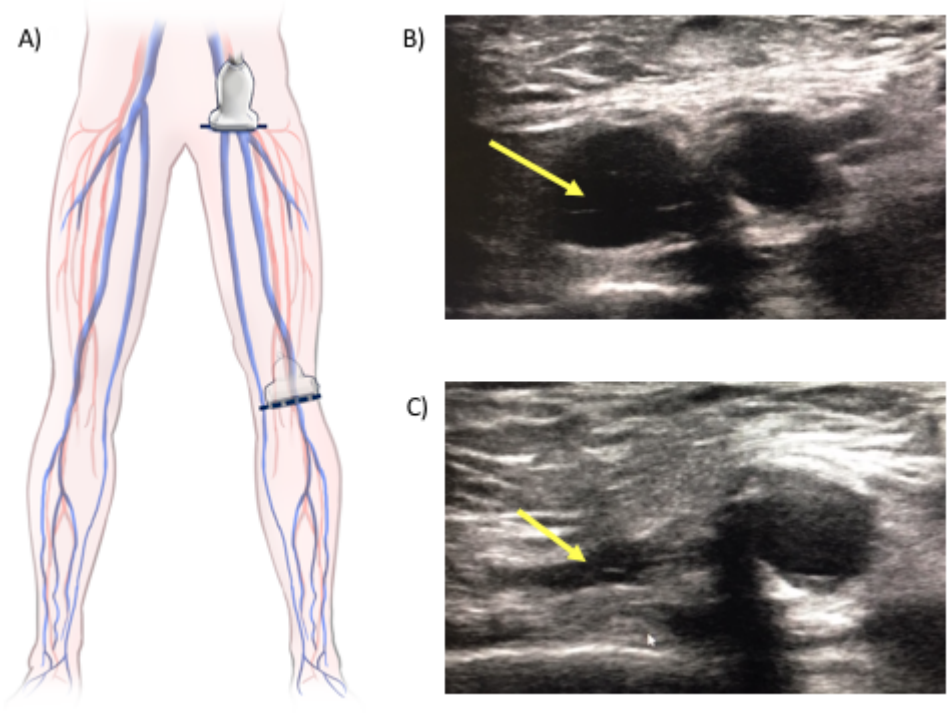

Figure 3

A) The illustration shows the two points of the lower extremities assessed for deep venous thrombosis: The common femoral vein at the groin level and popliteal vein at the popliteal fossa. B) and C) are ultrasound images showing the vein marked with yellow arrows before (B) and after (C) external compression has been applied. In this case, the vein is entirely collapsible, consistent with absence of a deep venous thrombosis.

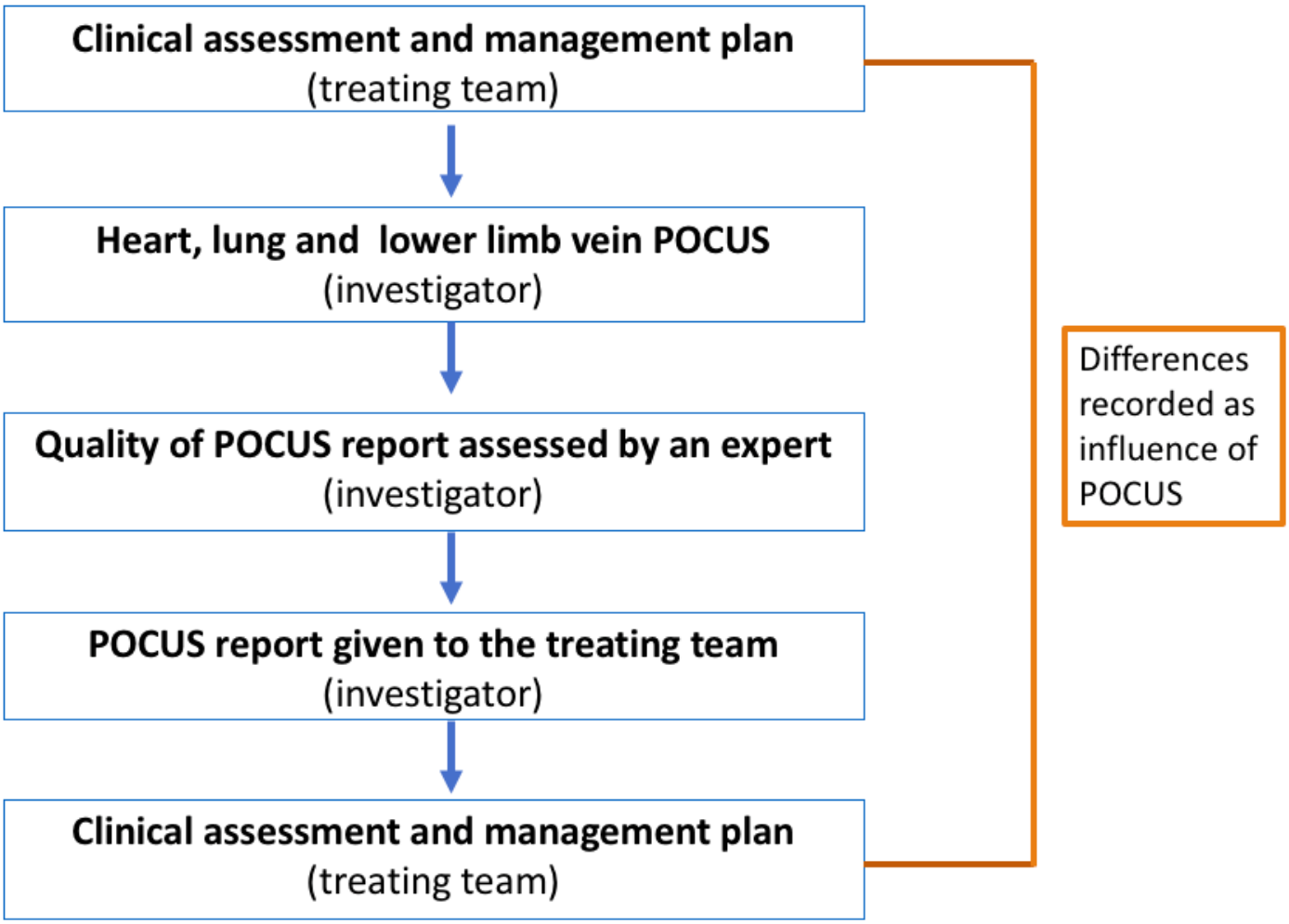

Figure 4

: In the intervention group a point-of-care ultrasound (POCUS) of the heart, lungs, femoral and popliteal veins is performed bedside the patient. The report summarizing the main findings is assessed by a second expert in POCUS before it is given to the treating team. The treating team is requested to fill out forms about their clinical assessment and management plan before and after receiving the POCUS report. Difference between forms will be recorded as influence of POCUS.

	STUDY PERIOD					
	First 24 hours					
	Enrolment	Allocation	Post-allocation			
TIMEPOINT	***-1***	**0**	***1***	***2***	***3***	***Recruitment completed***
ENROLMENT:						
Eligibility screen	X					
Informed consent	X					
Allocation		X				
INTERVENTIONS:						
POCUS				X		
ASSESSMENTS:						
Clinical assessment and management plan			X		X	
Length of hospital stay						X
30-day readmission						X
Health costs						X

Figure 5

Schedule of enrolment, intervention, and assessments.

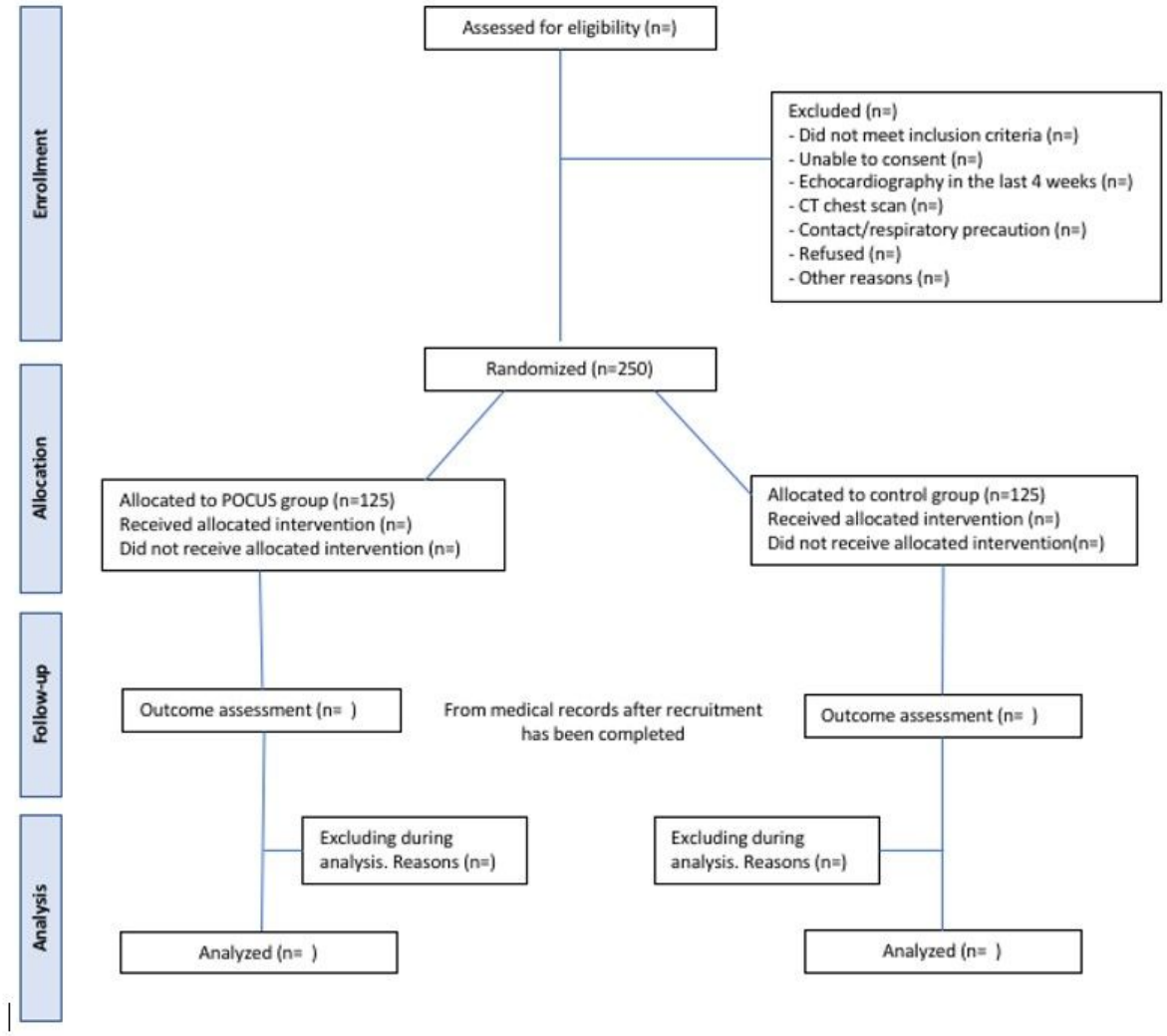

Figure 6

Proposed of Consolidated Standard of Reporting Trials (CONSORT) flow-chart for IMFCU-1 study.

Supplementary Files

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