DOI: 10.23937/2469-5858/1510144

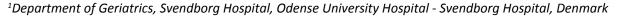
Volume 9 | Issue 1 Open Access



RESEARCH ARTICLE

# Geriatrician-Performed Point-of-Care Ultrasound for Detection of Deep Venous Thrombosis in Geriatric Inpatients – A Proof of Concept Study

Kristoffer Kittelmann Brockhattingen<sup>1,2\*</sup> , Marlene Kvist<sup>1</sup>, Sabine Morris Delhez<sup>3</sup>, Siar Barat<sup>3</sup> and Casper Falster<sup>4,5</sup>



<sup>&</sup>lt;sup>2</sup>Geriatric Research Unit, Department of Clinical Research, University of Southern Denmark, Odense, Denmark

\*Corresponding author: Dr. Kristoffer Kittelmann Brockhattingen, MD, Department of Geriatrics, Svendborg Hospital, Odense University Hospital - Svendborg Hospital, Baagøes Alle 31, 5700 Svendborg, Denmark, Tel: +45-30-89-66-36

### **Abstract**

**Purpose:** To assess the diagnostic accuracy of geriatricianperformed point-of-care ultrasound (PoCUS) on suspicion of deep venous thrombosis (DVT) in geriatric inpatients by comparing findings to a radiologist/specialist performed ultrasound as reference.

**Methods:** This study was conducted as a single-center feasibility study. Patients with suspicion of deep venous thrombosis defined as Well's score of 0-1 with a concomitant elevated D-dimer or a Well's score  $\geq$  2 regardless of D-dimer were eligible for inclusion. In addition, the following inclusion criteria were met: 1)  $\geq$  65 years, and 2) presence of  $\geq$  2 diseases. No current DVT diagnosis or targeted treatment against DVT. Patients first underwent ultrasound examination by a geriatrician and subsequently by a blinded radiologist.

**Results:** A total of 29 (19 women) patients were included. The prevalence of DVT was 3.4%. Analysis of the diagnostic accuracy revealed a sensitivity of 100 (2.5-100), and a specificity of 96.4 (81.7-99.9). Positive predictive value was 50.0 (12.8-87.3) and negative predictive value of 100 (100-100), with an overall diagnostic accuracy of 96.5 (82.2-99.9).  $\chi^2$ -test revealed a non-significant difference in Geriatrician-performed PoCUS and Radiologist-performed ultrasound.

**Conclusion:** Our results suggest a promising diagnostic accuracy of Geriatrician-performed PoCUSfor the examination of deep venous thrombosis which should be further assessed by adequately powered studies. PoCUS, as a tool for clinical examination, could be a great fit for examining geriatric inpatients bedside in a patient-centered and safe environment.

#### **Keywords**

Point-of-care ultrasound, Ultrasound, Deep venous thrombosis, Geriatric

### **Key Points**

- Point-of-care ultrasound is a safe and patient-centered clinical tool for examining geriatric inpatients
- Point-of-care ultrasound show a high diagnostic accuracy when examining geriatric patients for the presence of DVT
- Point-of-care ultrasound offers shielding of frail patients from unnecessary exposure of stressors, thus a great fit for clinical examination of geriatric inpatients



**Citation:** Brockhattingen KK, Kvist M, Delhez SM, Barat S, Falster C (2023) Geriatrician-Performed Point-of-Care Ultrasound for Detection of Deep Venous Thrombosis in Geriatric Inpatients – A Proof of Concept Study. J Geriatr Med Gerontol 9:144. doi.org/10.23937/2469-5858/1510144

Accepted: May 2, 2023: Published: May 24, 2023

**Copyright:** © 2023 Brockhattingen KK, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

<sup>&</sup>lt;sup>3</sup>Department of Radiology, Svendborg Hospital, Odense University Hospital - Svendborg Hospital, Denmark

<sup>&</sup>lt;sup>4</sup>Department of Geriatrics, Odense University Hospital, Odense University Hospital - Svendborg Hospital, Denmark

<sup>&</sup>lt;sup>5</sup>Department of Respiratory Medicine, Odense University Hospital, Denmark

<sup>&</sup>lt;sup>6</sup>Odense Respiratory Research Unit (ODIN), Department of Clinical Research, SDU, Denmark

DOI: 10.23937/2469-5858/1510144 ISSN: 2469-5858

### Introduction

Deep venous thrombosis (DVT) is a common condition in patients ≥ 80 years of age, with an estimated prevalence of 1/100 in Denmark [1]. Several studies have estimated a prevalence lower extremity DVT of 15% in geriatric patients aged > 70 years admitted to the emergency department [2,3]. Typical symptoms encompass swollen/painful leg(s), tenderness along the deep veins, superficial venous configuration, and pitting edema [4]. For assessment of pre-test probability, clinical scores such as Well's score (Table 1) in addition to measurement of D-dimer are commonly utilized as recommended by The European Society of Cardiology [5,6].

The primary and chief life-threatening complication of DVT is pulmonary embolism (PE), which occurs when a DVT dislodges from its site of origin and travels to the pulmonary vasculature, obstructing blood flow. Multiple studies have reported a presence of residual deep venous thrombotic material in approximately 50% of patients with PE [7-9]. In these cases, an undetected residual DVT may aggravate an already potentially life-threatening condition by dislodging and migrating to the already embolized pulmonary vessels, further adding to the occlusion [10]. Aside from complications like PE, nearly half of patients with DVT develop postthrombotic syndrome (PTS). This condition arises due to venous valvular incompetence and venous hypertension as a result of thrombotic obstruction, manifesting as symptoms such as swelling, cramping, itching, and pain [11].

Point-of-care ultrasound (PoCUS) is a safe, non-invasive, and patient-centered bedside method for assessing and diagnosing various conditions including DVT [12,13]. With an evidence-based education and continuous supervised training, PoCUS has been shown to enhance clinical decision-making [14,15]. This makes it ideal for examining geriatric patients suspected of critical illness, which are among the most frequent users

of the healthcare system in the western world [16,17]. As disease presentation is often atypical in the geriatric patient, the clinician must be able to interpret clinical information while considering that these patients are hallmarked by: 1) Vague symptoms, 2) A decreased ability to explain symptoms, 3) A decreasing cognition, and 4) A decreasing physical function [18].

These circumstances often complicate assessment of pre-test probability of present DVT. As such, ultrasound investigations performed by the geriatrician could save both time for the clinician and of even greater importance alleviate the need for transporting a potentially frail geriatric patient to another ward, thereby avoiding the unnecessary exposure of potential stressor, hence lowering the risk of delirium.

In recent years, several studies have emerged which evaluates PoCUS protocols, performed by surgeons who underwent a training course in US technics, physics, anatomy and hands-on training under supervision, in comparison with radiologist performed ultrasound. These studies showed an accuracy of 94% in detecting gallstones, an accuracy of 93.3% in detecting acute cholecystitis, and an accuracy of 77.3% in detecting appendicitis [19,20]. However, to our knowledge, no study has evaluated the diagnostic accuracy of geriatrician-performed PoCUS in regards to lower extremity DVT occurrence, in comparison with radiologist-performed ultrasound.

To assess the clinical utility of geriatrician performed deep venous ultrasound, this study aims to approximate the diagnostic accuracy of geriatrician-performed PoCUS on suspicion of deep venous thrombosis in geriatric inpatients by comparing findings to a radiologist/specialist performed ultrasound as reference test.

#### **Materials and Methods**

The study was a quality assurance project, which entails that no personal data were collected that could identify participating patients. The authors

Table 1: Wells score.

Variable	Points
Paralysis, paresis or recent immobilization of the lower extremity	+1
Bedridden recent for > 3 days or major surgery within 12 weeks	+1
Active cancer (treatment or palliation > 6 months)	+1
Previously documented DVT	+1
Tenderness along the deep veins	+1
Unilateral swollen leg	+1
Unilateral swollen calf > 3 cm	+1
Unilateral pitting edema	+1
Collateral superficial veins (nonvaricose)	+1
Alternative diagnosis to DVT as likely or more likely	-2

Wells score for DVT where a score of 0 is associated with a low risk of DVT. A score 1-2 is associated with an intermediary risk and a score of  $\geq$  3 is associated with a high risk of DVT [24].

made inquiries to the local ethics committee and no formal approval from the committee was required (ID: S-20212000-18 Acadre 21/209). All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions.

Informed consent was obtained from all patients for being included in the study.

### Study setting

This study was carried out as a single center feasibility study at Svendborg Hospital, Region of Southern Denmark, Denmark. The hospital is the second largest referral center, covering the southern part of the region of Funen, with an annual emergency census of approximately 1400 geriatric patients. Following initial diagnostic and clinical work-up in the emergency department, geriatric patients are referred to the department of geriatrics for further treatment.

### Patient population

Geriatric patients with clinical suspicion of DVT in lower extremities, exhibiting either a Well's score of 0-1 with a concomitant elevated D-dimer or a Well's score ≥ 2 regardless of D-dimer were eligible for inclusion if they fulfilled the following inclusion criteria:

- Geriatric patients referred to the department of geriatrics defined as: 1) aged ≥ 65 years, and 2) presence of ≥ 2 diseases (multimorbidity).
- One of the following symptoms: Uni- and/or bilateral swollen leg, pain, increased venous prominence, and/or edema.
- 3) No recent prior DVT diagnostics (6 months) upon hospital admission.
- 4) No current DVT diagnosis or targeted treatment against DVT.

Further, in accordance with Danish legislation, patients suffering from cognitive impairment were also not eligible.

## Deep venous ultrasound investigations

Patients meeting the inclusion criteria would undergo extended compression ultrasound (ECUS) by one of two geriatricians certified in PoCUS by an educated instructor with several years of teaching and experience in PoCUS-research. Subsequently, the patients were referred to the department of radiology, where they were subject to a complete duplex ultrasound scan (CDUS) performed by a physician employed in the ultrasound section as a reference standard. The investigating physicians at the department of radiology were blinded to geriatrician findings and were only provided information regarding which extremity to scan. In case of DVT found by ECUS, patients would immediately receive treatment

according to hospital guidelines (e.g., either treatment with Dalteparin (low molecular weight heparin) or direct oral anticoagulants).

### **Extended compression ultrasound scan (ECUS)**

According to a recent report published in Circulation, a journal under the American Heart Association (AHA), for PoCUS examination for DVT, the extended compression ultrasound (ECUS) scan is favored over the frequently used 2-point compression ultrasound (2-CUS) scan [12].

With the patient in the supine position, the examined leg slightly rotated externally, and with a gentle flexion of the knee, ECUS was performed by compressing the deep veins, starting with the common femoral vein (Figure 1), and compressing for every centimeter, continuing just proximal to the division of the popliteal vein (Figure 2). The linear transducer (3-12 MHZ linear transducer, GE Venue) was used for the examination and was placed transversely, perpendicular throughout the examination [12].

# Complete duplex ultrasound scan (CDUS) performed by the department of radiology

The deep veins were examined from the groin and as far down the lower extremity as possible by using the linear transducer. The patient was first positioned in the supine position with a slight external rotation of the hip. First, the common femoral vein both above and below the inguinal ligament and the sapheno-femoral junction was examined. For examination of the popliteal vein and the crural veins the patient was placed in the lateral decubitus position, or prone with a pillow under their ankles. Hereby, exposing the popliteal vein to examination of the posterior tibial and peroneal veins as far distally as possible were examined. If it was possible to identify the anterior tibial veins these were examined as well. During the whole examination compression and color Doppler were applied along the veins to evaluate the presence of DVT.

Because the ECUS protocol does not include the crural part of the lower extremity, the department of radiology noted if the patients had DVT according to the area included by the ECUS and/or DVT in the region not included by the ECUS.

# Divergence among geriatrician-performed PoCUS and radiologist-performed CDUS

In case of divergence in DVT-diagnosis, defined as the presence of DVT in a patient by geriatrician-performed ECUS but absence of DVT in the same patient by CDUS, patients were offered a new scan 5-7 days after their latest scan, to evaluate if a DVT was present. As the department of radiology was the reference standard, patients would not receive treatment prior to the additional CDUS.

DOI: 10.23937/2469-5858/1510144 ISSN: 2469-5858

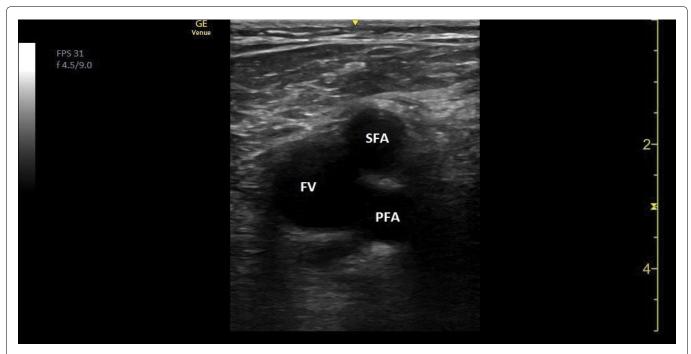


Figure 1: Ultrasound image showing the left femoral vein (FV) and the superficial (SFA) and profound (PFA) femoral artery.

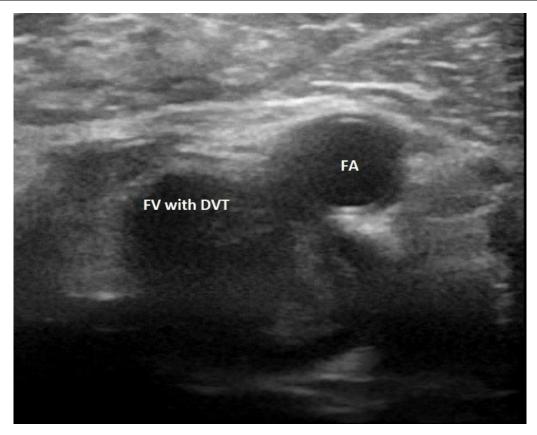


Figure 2: Ultrasound image showing the left femoral vein (FV) containing thrombosis and the femoral artery (FA).

# Sample size

The prevalence of DVT among geriatric patients varies immensely, in general and according to the clinical setting. For example, as a part of a focused examination during admission to the emergency department [3], or as a coincidently finding at a geriatric department. Thus, a valid expected prevalence of DVT among geriatric inpatients as usage for power-calculation was

challenging to estimate. There for it was decided to include all inpatients suspected for DVT over the course of a year.

# Statistical analysis

All statistical analyses were performed in GraphPad Prism 9.0.0. (GraphPad Software, San Diego, California USA). Diagnostic accuracy of geriatrician performed

DOI: 10.23937/2469-5858/1510144 ISSN: 2469-5858

ultrasound was assessed through calculation of sensitivity and specificity, positive and negative predictive values as well as accuracy. 95% confidence intervals were calculated as Clopper-Pearson intervals [21]. Normality was assessed using the Shapiro-Wilk test [22]. Normally distributed data are presented as mean ± SD. Non-normally distributed data are presented as median with interquartile range (IQR), χ<sup>2</sup>test was performed to assess differences in diagnosing DVT and non-DVT patients between Geriatricianperformed **PoCUS** and Radiologist-performed ultrasound. A P-value below 0.05 was considered statistically significant.

### Results

A total of 29 patients (19 women) were included in the study. Demographic baseline characteristics are listed in Table 2. Median age was 85.3 years and body composition measures revealed mean BMI of 29.2 ± 6.4 kg/m^2. Median Charlson Comorbidity Index (CCI)score of 4 (IQR: 2-5.5). Median Well's score was1 (IQR: 0-2) with a median D-dimer of 2.0 mg/L (IQR: 1.1-5.0). A median of 4 admission days (IQR: 2-6) went by before patients received their initial ultrasound scan. Five patients were admitted with erysipelas, six patients were admitted with other infections (pneumonia, urinary tract infections unspecified bacterial infection),

Table 2: Baseline characteristics.

Baseline characteristics			
Age (IQR)	85.3 years (78.7 to 88.5)		
Female sex, n (%)	19 (65.5)		
Body mass index	29.2 ± 6.4 kg/m <sup>2</sup>		
CharlsonComorbidity Index (IQR)	4 (2 to 5.5)		
Well's score (IQR)	1 (0 to 2)		
Length of admission prior to inclusion (IQR)	4 days (2 to 6)		
D-dimer (IQR)	2.0 mg/L (1.1 to 5.0)		
Diagnosis upon admission (%)			
Erysipelas	5 (17.2)		
Oedema, unspecified	4 (13.7)		
Other infections (pneumoni, urinary tract infection, cystitis)	6 (20.7)		
Traumatic muscle ischemia	2 (6.8)		
Osteoporosis	1 (3.4)		
Anemia	1 (3.4)		
Hyperkalemia	1 (3.4)		
Malignancy	1 (3.4)		
Dorsopathy	1 (3.4)		
Dyspnea	1 (3.4)		
Constipation	1 (3.4)		
Septicemia, unspecified	1 (3.4)		
Abnormal weight loss	1 (3.4)		
Erysipeloid	1 (3.4)		
Fluid-electrolyte disorder, unspecified	1 (3.4)		
Urinary tract infection, unspecified	1 (3.4)		
Limb pain	1 (3.4)		

Baseline characteristics. Data are presented as n (%), mean  $\pm$  standard deviation (SD) or median with associated interquartile range (IQR).

Table 3: Diagnostic accuracy.

Diagnosticaccuracy (95% CI)	Sensitivity	Specificity	PPV	NPV	Accuracy
Geriatrician-performed PoCUS	100 (2.5 to 100)	96.4 (81.7 to 99.9)	50.0 (12.8 to 87.3)	100 (100 to 100)	96.5 (82.2 to 99.9

	True positive	False positive	False negative	True negative
Geriatrician-performed PoCUS	1	1	0	27

Diagnostic accuracy- Data are presented as sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy for geriatrician-performed PoCUS. Lastly, the number of true positive, false positive, false negative and true negative cases are presented.

four patients with unspecified oedema, two patients were admitted with traumatic muscle ischemia after falling. Other diagnoses upon admission are listed in Table 2.

The prevalence of DVT was 3.4% (1/29). Analysis of diagnostic accuracy regarding Geriatrician-performed PoCUS, as listed in Table 3, revealed a sensitivity of 100 (2.5-100), and a specificity of 96.4 (81.7-99.9). Positive predictive value was 50.0 (12.8-87.3) and negative predictive value was100 (100-100), yielding an overall diagnostic accuracy of 96.5 (82.2-99.9). Geriatricianperformed PoCUS revealed 1 true positive, 1 false positive, 0 false negatives and 27 true negatives patients. A  $\chi^2$ -test was performed to examine differences in DVT and non-DVT patients when patients underwent Geriatrician-performed **PoCUS** and Radiologistperformed ultrasound.  $\chi^2$ -test revealed a p-value of 0.5532, thereby showing a non-significant difference.

### **Discussion**

To our knowledge this is the first study comparing Geriatrician-performed **PoCUS** with performed by radiologists. Our results showed a nonsignificant difference between Geriatrician-performed PoCUS and Radiologist-performed ultrasound in diagnosing patients with or without DVT. Furthermore, a specificity of 96.4% and a promising diagnostic accuracy of Geriatrician-performed PoCUS of 96.5%. These findings suggest that geriatrician-performed PoCUS, as a tool for clinical examination, could be a great fit for examining geriatric inpatients bedside in a patientcentered and safe environment. Because PoCUS allows for a patient-centered approach and potentially could be performed by the same physician who initially sees the patient, it is not only a patient-friendly method but also a time saving method that shields the potentially frail patient from unnecessary exposure of stressors.

However, this study has some limitation which should be considered when interpreting the results. First, the prevalence of DVT was lower than previously reported [3]. Several factors could have contributed to this. One factor is the high presence of atrial fibrillation (AFLI) among the studied population (data not shown) and the corresponding treatment with direct oral anticoagulants (DOAC) such as Rivaroxaban and Apixaban. These medications are also the recommended treatment for DVT [23], and although the indication for treatment was not DVT but thromboprophylaxis in AFLI, there is a great probability that it did affect the results. However, the prevalence of DVT among geriatric patients might still be high despite prophylactic treatment with anticoagulants [3]. Second, in the hospital where the study was performed, geriatric patients are not directly admitted to the department of geriatrics but admitted to the department of emergency medicine and after initial diagnosis then referred to the department of geriatrics. This could influence the overall prevalence of DVT among geriatric patients since potential patients with DVT would not be seen by a geriatrician but rather referred to the outpatient clinic of cardiology for further diagnosis and treatment. Third, the median Well's score among the studied population was 1 (IQR: 0-2), hence the risk of DVT low, and therefore the portion of patents with a low risk of DVT high, and thereby a potential confounder.

As such, further large-scale studies are warranted to confirm the promising use of geriatrician-performed PoCUS for the detection of DVT. The limited but promising diagnostic accuracy of 96.5% in this study could be an impetus for a movement in geriatric medicine for enhancing the use of PoCUS among geriatricians, given sufficient supervision and after undergoing a certified education program.

### **Acknowledgement**

The authors would like to acknowledge Open Patient data Explorative Network (OPEN) at Odense University Hospital, for their support during this project.

### **Conflict of Interest Statement**

None declared.

### **Funding**

This project did not receive funding of any kind.

### **Authors' Contribution**

All authors participated equally in the conduct of this study.

### References

- Schultz J, Kjærgaard J, Olesen JB, Poulsen MH, Würtz M, et al. (2022) Lungeemboli og dyb venetrombose. National Behandlings veiledning.
- Stein PD, Hull RD, Kayali F, Ghali WA, Alshab AK, et al. (2004) Venous thromboembolism according to age: The impact of an aging population. Arch Intern Med 164: 2260-2265.
- Bosson JL, Labarere J, Sevestre MA, Belmin J, Beyssier L, et al. (2003) Deep vein thrombosis in elderly patients hospitalized in subacute care facilities: A multicenter crosssectional study of risk factors, prophylaxis, and prevalence. Arch Intern Med 163: 2613-2618.
- 4. Kahn SR (1998) The clinical diagnosis of deep venous thrombosis: Integrating incidence, risk factors, and symptoms and signs. Arch Intern Med 158: 2315-2323.
- Ljungqvist M, Söderberg M, Moritz P, Ahlgren A, Lärfars G (2008) Evaluation of Wells score and repeated D-dimer in diagnosing venous thromboembolism. Eur J Intern Med 19: 285-288.
- Mazzolai L, Aboyans V, Ageno W, Agnelli G, Alatri A, et al. (2017) Diagnosis and management of acute deep vein thrombosis: A joint consensus document from the European Society of Cardiology working groups of aorta and peripheral vascular diseases and pulmonary circulation and right ventricular function. Eur Heart J 39: 4208-4218.

- Lee JS, Moon T, Kim TH, Kim SY, Choi JY, et al. (2016) Deep vein thrombosis in patients with pulmonary embolism: Prevalance, clinical significance and outcome. Vasc Specialist Int 32: 166-174.
- Becattini C, Cohen AT, Agnelli G, Howard L, Castejón B, et al. (2016) Risk stratification of patients with acute symptomatic pulmonary embolism based on presence or absence of lower extremity DVT: Systematic review and meta-analysis. Chest 149: 192-200.
- Falster C, Jacobsen N, Coman KE, Højlund M, Gaist TA, et al. (2022) Diagnostic accuracy of focused deep venous, lung, cardiac and multiorgan ultrasound in suspected pulmonary embolism: A systematic review and metaanalysis. Thorax 77: 679-689.
- 10. Konstantinides SV, Meyer G, Becattini C, Bueno H, Geersing GJ, et al. (2019) 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS): The task force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC). Eur Heart J 41: 543-603.
- 11. Sara R Vazquez, Kahn SR (2016) Postthrombotic syndrome. Circ 121: e217-e219.
- 12. Needleman L, Cronan JJ, Lilly MP, Merli GJ, Adhikari S, et al. (2018) Ultrasound for lower extremity deep venous thrombosis. Circ 137: 1505-1515.
- 13. Moore CL, Copel JA (2011) Point-of-care ultrasonography. N Engl J Med 364: 749-757.
- 14. Weile J, Frederiksen CA, Laursen CB, Graumann O, Sloth E, et al. (2020) Point-of-care ultrasound induced changes in management of unselected patients in the emergency department A prospective single-blinded observational trial. Scand J Trauma Resusc Emerg Med 28: 47.
- Moussa M, Stausmire JM (2018) Do emergency physicians rely on point-of-care ultrasound for clinical decision making without additional confirmatory testing? J Clin Ultrasound 46: 437-441.

- 16. Bonnel AR, Baston CM, Wallace P, Panebianco N, Kinosian B (2019) Using point-of-care ultrasound on home visits: The home-oriented ultrasound examination (HOUSE). J Am Geriatr Soc 67: 2662-2663.
- 17. Ukkonen M, Jämsen E, Zeitlin R, Pauniaho SL (2019) Emergency department visits in older patients: A populationbased survey. BMC Emerg Med 19: 20.
- 18. Limpawattana P, Phungoen P, Mitsungnern T, Laosuangkoon W, Tansangworn N (2016) Atypical presentations of older adults at the emergency department and associated factors. Arch Gerontol Geriatr 62: 97-102.
- Gustafsson C, Lindelius A, Törngren S, Järnbert-Pettersson H, Sondén A (2018) Surgeon-performed ultrasound in diagnosing acute cholecystitis and appendicitis. World J Surg 42: 3551-3559.
- Gustafsson C, McNicholas A, Sondén A, Törngren S, Järnbert-Pettersson H, et al. (2016) Accuracy of surgeonperformed ultrasound in detecting gallstones: A validation study. World J Surg 40: 1688-1694.
- 21. Clopper CJ, Pearson ES (1934) The use of confidence or fiducial limits illustrated in the case of the binomial. Biometrika 26: 404-413.
- 22. Shapiro SS, Wilk MB (1965) An analysis of variance test for normality (Complete Samples). Biometrika 52: 591-611.
- 23. Burnett AE, Mahan CE, Vazquez SR, Oertel LB, Garcia DA, et al. (2016) Guidance for the practical management of the direct oral anticoagulants (DOACs) in VTE treatment. J Thrombo Thrombolysis 41: 206-232.
- 24. Wells PS, Anderson DR, Rodger M, Forgie M, Kearon C, et al. (2003) Evaluation of D-dimer in the diagnosis of suspected deep-vein thrombosis. N Engl J Med 349: 1227-1235.

