Accuracy of three-point compression ultrasound for the diagnosis of proximal deep-vein thrombosis in emergency department

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Background: This study aimed to assess the accuracy of three-point compression ultrasonography (3PCUS) performed for the diagnosis of proximal deep-vein thrombosis (DVT) in Emergency Department (ED) compared with the results of duplex US (DUS) (whole-leg compression ultrasonound). Materials and Methods: The current prospective cross-sectional study with diagnostic test assessment was conducted on adult patients who were referred to the ED of a general teaching hospital in Shiraz, southern part of Iran (September 2016–May 2017), suspected of lower-extremity DVT, using a convenience sampling. The results of 3PCUS performed by ED residents were compared with the results of DUS performed by the radiology residents, which was considered as a criterion standard. Results: A total of 240 patients were enrolled, with a mean (standard deviation) age of 59.46 (16.58). 3PCUS has a sensitivity and a specificity of 100% (95% confidence interval [CI], 96.55%–100%) and 93.33% (95% CI, 87.72%–96.91%), respectively, in comparison with DUS (whole-leg compression ultrasonound). Negative predictive value and positive predictive value were 100% and 92.11% (95% CI, 86.12%–95.64%), respectively, with an accuracy of 96.25% (95% CI, 93%–98.27%). Conclusion: The results of this study showed that 3PCUS of the lower extremities with a portable US machine, performed by the ED's residents, can accurately identify the presence or absence of lower-extremity DVT.

Key words: Compression ultrasound, deep-vein thrombosis, emergency department

INTRODUCTION

Lower-limb pain and swelling is a usual complication seen in patients referring to emergency department (ED). Among differential diagnosis of this condition, deep-vein thrombosis (DVT) is the most serious because it can result in pulmonary embolism (PE). DVT is a common disorder that can be difficult to diagnose clinically but carries significant morbidity and mortality if unrecognized or untreated.[1] It was reported that the incidence rate for DVT is 45–117/100,000 persons, annually,[2] and venous thromboembolism can increase disability-adjusted life-years and also lead to high health-care cost.[3] Failure to promptly diagnose and treat DVT can directly bring about serious morbidity and mortality.[4] Early diagnosis and treatment of cases with DVT can considerably reduce PE and its hemodynamic complications. The clinical diagnosis of lower-extremity DVT needs to be confirmed by imaging study before preparing the patients for anticoagulation therapy.[5]

In ED, the D-dimer assay can help physicians to exclude the diagnosis of DVT; however, it is merely helpful in less than half of the cases and cannot confirm the diagnosis.[6] Venography is considered the most accurate test, which can confirm or rule out DVT. Even though venography is the gold standard for the diagnosis of DVT, it is invasive and requires contrast agents.[7] On the other hand, duplex ultrasonography (DUS) is a
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Patients with a history of trauma to
and the absence
In both
In compression ultrasound, the ability
Previous studies showed that
The convenience
DVT; inaccessibility to venography and DUS in ED; adverse
cost for both patients and the health-care
Therefore, simpler and cost-effective modalities are preferred for timely diagnosis in EDs.

Ultrasonography (US) as a noninvasive, accurate, and widely available modality is an alternative choice for detecting proximal DVT.[7] Previous studies showed that 99% of cases suspected of DVT have femoral and popliteal vein involvement.[12] In compression ultrasound, the ability of the examiner is important in using the US probe to compress and assess the veins using B-mode imaging at point-of-care in ED,[12,13] and it is not required to transfer the patients to radiology department.

Up to now, no technique has been defined as a choice, and the decision as which method to use is center dependent. On the other hand, increasing number of referral cases suspected of DVT; inaccessibility to venography and DUS in ED; adverse events of anti-coagulant medications;[14] and the absence of accurate, simple, quick, user-friendly, and cost-effective modality, made us to assess the diagnostic value of three-point compression US (3PCUS) performed by emergency medicine residents for the diagnosis of proximal lower-extremity DVT in ED. In addition, we aimed to determine if gender differences exist in the results of diagnostic tests.

MATERIALS AND METHODS

Study design
The current study used a prospective cross-sectional design (September 2016–May 2017) with diagnostic test assessment, which assessed the diagnostic value of 3PCUS performed by emergency medicine residents for the diagnosis of proximal lower-extremity DVT in suspected patients, in comparison with DUS (whole-leg compression ultrasound).

Setting
This study was conducted in a single center at ED of Namazi Hospital, a tertiary university-affiliated hospital in the southern part of Iran, with residency training program, and about 90,000 EDs admissions, annually.

Study population
The study was performed on eligible patients who were referred to the ED and suspected of lower-extremity DVT over a period of 9 months. The inclusion criteria were adult patients aged more than 18 years, who were suspected of lower-extremity DVT based on their medical history (cramp, pain, or swelling in the lower extremities beginning in the preceding 7 days), or physical examination (swelling, asymmetry in lower extremities size, color changes, or calf tenderness).[7] Patients with a history of trauma to the affected extremity, indwelling femoral catheters, and a history of vascular surgery in the same extremity were excluded from the study. In addition, patients who refused to participate in the study and who did not understand and refused to sign the written informed consent for ultrasound were excluded.

Sample size and sampling method
Using MedCalc Statistical Software version 13.3.3 (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2014), a sample size of 240 patients was calculated to obtain a 95% confidence interval (CI) (standard deviation [SD] = 5%) with an estimation of 96% specificity for ultrasound diagnosis of DVT (α = 5%, β = 20%).[15] The convenience sampling method was used to collect the participants.

Study protocol and interventions
Following clinical and laboratory assessment, trained third-year residents supervised by an ED-attending physician who was an Iranian board certified in emergency medicine, a faculty member, and who was an expert in performing 3PCUS evaluated the proximal veins of the patients suspected to DVT using portable ultrasonography machine (Fujifilm SonoSite, Inc., USA) with high-frequency linear probe (6–15 MHz). Point-of-care US is one of the topics that is part of emergency medicine curriculum, and is taught to emergency medicine residents in Iran, during their residency periods. In addition, the residents who participated in this study had attended a 2-day workshop on vascular ultrasound.

Three-point compression means doing compression US in three regions with higher turbulence and at the greatest risk of developing thrombosis. These regions were tested more than once by adequate compression until the veins were compressed fully, including: (1) the common femoral vein at the level of inguinal crease, (2) the superficial femoral vein superior to the adductor canal, and (3) the popliteal vein in the popliteal fossa.[16,17] Each 3PCUS lasted about 5–7 min.[17] An ultrasound study was defined normal if the vein was completely compressed and abnormal if the vein was incompressible or an occlusive clot was detected in these target areas. Compressibility of veins was evaluated in the transverse view. The vein was defined “noncompressible” (indicating the presence of DVT) if the vein remained open while the adjacent artery
was obliterated by applying pressure. The results were reported as positive for DVT (noncompressible or not visualized veins in one or more target points) or negative for DVT (compressible veins in all the three target points).

After recording the results, the patients were referred to the radiology department for DUS (whole-leg compression ultrasound) by second-year residents of radiology, supervised by a radiology attending, who was an Iranian board certified in radiology and a faculty member. The radiologists were blinded to the results of the US which were obtained in the ED. The DUS includes color Doppler, wave Doppler, and augmentation (color flow). The radiologists’ report was considered as criterion standard.

Demographic variables (such as age and gender), body mass index, history of DVT, and risk factors (obesity, physical inactivity, dyslipidemia, smoking, and familial history of DVT), as well as the results of both 3PCUS and DUS, were recorded in a data-gathering form. In addition, all the participants signed the written informed consent.

**Statistical analysis**
All statistical analyses were performed by IBM SPSS statistics for Windows, version 20.0. (IBM Corp, New York, USA), and MedCalc Statistical Software version 13.3.3 (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2014) for Windows, using Chi-square and Fisher’s exact tests for proportions, and independent *t*-test for the means. Results were presented as mean (SD) for continuous variables and were summarized in number (percentage) for categorical ones. Two-sided *P* < 0.05 and CI of 95% were considered to be statistically significant. For calculating the diagnostic tests, such as sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (PLR), negative likelihood ratio (NLR), and accuracy, the MedCalc software was used. Receiver operating characteristics (ROC) curve was drawn for compression ultrasound of lower extremities in the suspected patients to DVT to obtain the area under the curve.

**Ethical consideration**
The current study was supported by Shiraz University of Medical Sciences, which was conducted in accordance with the Declaration of Helsinki, and was approved by the vice-chancellor of research and technology, as well as the local ethics committee of Shiraz University of Medical Sciences (IR.sums.med.rec. 1396.s240). To consider ethical issue, the collected data were not revealed to anyone, except for the researchers; hence, patients’ names were kept confidential.

**RESULTS**
A total of 240 patients were enrolled, and the mean (SD) of age was 59.46 (16.58) (range, 18–89) years, and 120 (50%) of them were male. The patients’ characteristics are shown in Table 1. There was no difference between gender and risk factors of DVT, except smoking (*P* = 0.01) and family history of DVT (*P* = 0.029), which were higher in male. 3PCUS of proximal lower extremities in the suspected patients to DVT were positive in 114 (47.5%) and were negative in 126 (52.5%) patients. While DUS showed that 105 (43.75%) patients were positive to DVT and 135 (56.25%) patients were negative to DVT [Table 2].

3PCUS has a sensitivity and specificity of 100% (95% CI, 96.55%–100%) and 93.33% (95% CI, 87.72%–96.91%), respectively, in comparison with DUS (whole-leg compression ultrasound), which is considered as the criterion standard for the diagnosis of DVT. NPV was 100% and PPV was 92.11% (95% CI, 86.12%–95.64%). In total, the accuracy of the compression ultrasound was 96.4% (95% CI, 93%–98.27%). The accuracy of 3PCUS in males and females is shown in Table 3. The sensitivity of 3PCUS was higher in men (*P* = 0.0002, 95% CI, 6.91%–21.44%), but the specificity of 3PCUS was higher in women (*P* = 0.0171, 95% CI, 0.76%–11.91%). Figure 1 shows the ROC curve of 3PCUS in patients suspected of lower-extremity DVT. The area under the curve was 0.967 (95% CI, 0.942–0.992, *P* < 0.0001).

**DISCUSSION**
In ED patients with unexplained lower-limb pain and swelling, it is essential to rule out DVT by ultrasound before patients’ disposition. In most centers, lower-limb ultrasound is done by the Radiology Department, which
might delay timely diagnosis and disposition, especially during off hours when technicians are not readily available. In addition, sometimes, it is not possible to send a suspected case of DVT to the radiology department because of instability in vital signs and hemodynamic conditions. However, portable ultrasound devices applied by ED residents are small, have low cost, and can be used by relatively small hours of training, which reduces the time of diagnosis, does not require many personnel, and can be life-saving. Although DUS continues to be widely used by radiology departments to assess DVT, earlier literature clearly shows that compression ultrasound examination of symptomatic ambulatory patients when done by an expert sonographer, is highly accurate in excluding or confirming the diagnosis.\[13,16,17]\n
In the current study, the diagnostic value of 3PCUS at the point-of-care in ED was assessed, which was performed by emergency medicine residents for the diagnosis of lower-extremity DVT compared to DUS. The results showed that 3PCUS had a sensitivity of 100%, a specificity of 93.33%, and an accuracy of 96.4% \( (P < 0.0001) \) in comparison with DUS (whole-leg compression ultrasound). A systematic review in 2008 of six studies showed that emergency physician-performed US could accurately diagnose lower-extremity DVT compared with radiology-performed ultrasound.\[18]\n
Frazee et al.\[13\] found a sensitivity and specificity of 89% and 76%, respectively, in the evaluation of 76 patients, using compression ultrasound of the common femoral and popliteal veins, which was done by six emergency physicians. Jang et al.\[19\] assessed the accuracy of compression ultrasound in the diagnosis of proximal lower-extremity DVT in 72 patients. It was the first study in which emergency residents performed compression ultrasound. They found a sensitivity of 100% and a specificity of 91.8%, with an average scan time of 11.7 min. In a recent study, Crisp et al.\[13\] evaluated the sensitivity and specificity of bedside two-point compression (2PCUS) ultrasound (including common femoral and popliteal veins) in ED for the diagnosis of proximal lower-extremity DVT. Their results showed that the sensitivity and specificity of compression US for DVT were 100% and 99%, respectively. Furthermore, Jacoby et al.\[20\] found that 2PCUS which was done by six emergency medicine residents on 121 patients had a sensitivity and specificity of 89% and 97%, respectively. A meta-analysis in 2013 showed that the mean sensitivity and specificity of 2PCUS test compared to DUS were 96.1% and 96.8%, respectively, and the researchers concluded that this diagnostic method is useful for patients suspected of DVT.\[21\] Another study concluded that 2PCUS performed by residents had a sensitivity of 57.1% and a specificity

### Table 1: The patients’ characteristics suspected to lower-extremity deep-vein thrombosis

| Variables (years) | Patients suspected of DVT \( n=240 \) | Gender \( n=120 \) | \( P \) |
|-------------------|--------------------------------------|--------------------|------|
| Age (years)       | 59.46 (16.58)                        | 60.15 (17.05)      | 58.78 (16.01) | 0.52 (−2.831, 5581) |
| Median            | 59.5                                |                    |      |
| Range             | 18–89                                |                    |      |
| Obesity BMI>30, \( n \% \) | 66 (27.5)                          | 30                  | 36   | 0.470 |
| Physical inactivity, \( n \% \) | 177 (73.8)                          | 87                  | 90   | 0.769 |
| Dyslipidemia, \( n \% \) | 114 (47.5)                          | 57                  | 57   | 1     |
| Diabetes mellitus, \( n \% \) | 87 (36.2)                           | 45                  | 42   | 0.788 |
| Hypertension, \( n \% \) | 84 (35)                             | 42                  | 42   | 1     |
| Smoking, \( n \% \) | 117 (48.8)                           | 69                  | 48   | 0.01* |
| History of previous DVT, \( n \% \) | 30 (12.5)                           | 18                  | 12   | 0.329 |
| History of trauma, \( n \% \) | 33 (13.8)                           | 15                  | 18   | 0.708 |
| History of lower-extremity fracture, \( n \% \) | 33 (13.8)                           | 15                  | 18   | 0.708 |
| History of CVA, \( n \% \) | 21 (8.8)                            | 9                   | 12   | 0.649 |
| History of cancer, \( n \% \) | 18 (7.5)                            | 12                  | 6    | 0.22  |
| Family history of DVT, \( n \% \) | 6 (2.5)                             | 6                   | 0    | 0.029* |

*Statistically significant. BMI=Body mass index; CVA=Cerebrovascular accident; DVT=Deep-vein thrombosis; SD=Standard deviation

### Table 2: The results of emergency department three-point compression ultrasonography and duplex ultrasound (whole-leg compression ultrasound) in the suspected patients of lower-extremity deep-vein thrombosis

| ED compression ultrasound | Positive | Negative | Total |
|---------------------------|----------|----------|-------|
| Positive                  | 105      | 9        | 114   |
| Negative                  | 0        | 126      | 126   |
| Total                     | 105      | 135      | 240   |

ED=Emergency department
of 96.1%. One important methodological difference between our study and previous researches was that we used 3PCUS (common femoral, superficial femoral, and popliteal veins) as opposed to 2PCUS (common femoral and popliteal veins).

Kline et al. found that the sensitivity and specificity of 3PCUS by emergency clinician-performed ultrasound were 70% and 89%, respectively. Another study involving 15 emergency physicians and 178 patients showed that 3PCUS had a sensitivity of 77.8%, a specificity of 91.4%, and an accuracy of 89.6%. This study which was conducted at an urban academic ED with a heterogeneous group of ED clinicians revealed that the sensitivity of 3PCUS was higher than that of 2PCUS, significantly, with similar specificity. Moreover, Zuker-Herman et al. found similar results (sensitivity and specificity of 90.57% and 98.52% in 3PCUS vs. 82.76% and 98.52% in 2PCUS, respectively). They concluded that 2PCUS was not sufficient in the management of patients with lower-extremity DVT.

A study by Kim et al. that evaluated the accuracy of compression ultrasound for lower-extremity DVT in the common femoral, superficial femoral, popliteal, and calf veins demonstrated a lower sensitivity and specificity of 86% and 93%, respectively. The diagnostic values which were obtained in the current study with larger sample size were much more than that of previous studies. It should be considered that the obtained results show PLR more than 1 (15 [95% CI, 7.98–28.20]). It means that higher probability of DVT is present in a patient with a positive 3PCUS, and 3PCUS can be considered as a suitable diagnostic procedure in routine practice.

Furthermore, we calculated the sensitivity and specificity of 3PCUS in men and women separately, which were not observed in previous researches. Our reason was that previous studies have shown that the risk factors of DVT in female population are more than male population, such as estrogen and hormone replacement therapy, immobility, obesity, and pregnancy (and postpartum status). In addition, the risk of osteoporosis and fracture of femoral neck, as well as bedridden, is higher in women. The sensitivity and accuracy, which were obtained in women, were lower than that of men. It could be due to that females were more obese, especially in pelvic area, but no statistical difference between both genders was found about obesity. In addition, it might be because of less cooperation in performing US in females, especially during femoral examination. However, the obtained specificity and PPV were higher in women. It can be concluded that 3PCUS is a more specified tool in diagnosing DVT and a good instrument to confirm this disease in women who were suspected to DVT. PLR more than 1 in men (18 [95% CI, 5.99–54.06]) and NLR <1 in women (0.13 [95% CI, 0.06–0.28]).
mean that higher probability of DVT is present in men with a positive 3PCUS and lower probability of DVT is present in women with a negative 3PCUS, respectively.

**Limitations and suggestions**

This study had several limitations such as small sample size, single-center nature with convenience sampling, as well as not providing specific information about the location of DVT. In addition, we did not follow the patients, and also the average time needed to complete each 3PCUS examination was not recorded. It took more time for obese patients. Furthermore, we did not define any special maneuver in performing US. Future studies using cohort or randomized controlled trial designs with randomized sampling are suggested, accompanied by specifying the location of DVT, time of ED 3PCUS, the role of D-dimer, the types of ultrasound machines, and probes’ resolutions. Researches with a larger population to determine the cost-effectiveness and efficacy are recommended.

**CONCLUSION**

The results of the current study showed that 3PCUS of the lower extremities with a portable US machine, performed in ED by emergency physicians, can accurately identify the presence or absence of lower-extremity DVT in suspected patients.

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**Conflicts of interest**

There are no conflicts of interest.

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