Point-of-Care Ultrasound for a Deep Venous Thrombosis

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ABSTRACT

Patients presenting to the emergency department with lower extremity symptoms suggestive of venous thromboembolic disease require a diagnostic evaluation. Although contrast venography was the diagnostic standard, this has largely been replaced by duplex ultrasound as the first-line imaging modality. This review presents a summary of the literature on the evolution and performance of B-mode point-of-care compression ultrasound as an alternative to duplex ultrasound evaluation. The 2-point compression and 2-region compression techniques are described. The limitations of point-of-care ultrasound of the lower extremity as a diagnostic modality for this disease entity, the role of a D-dimer assay in the emergency department evaluation and future directions for this diagnostic modality are discussed.

The annual incidence of lower extremity deep venous thrombosis (DVT) in the United States is approximately 300,000 to 600,000 cases per year [1]. This disease process leads to 60,000 to 100,000 deaths annually due to pulmonary embolism [1]. To help prevent a venous thromboembolic event, it is important to diagnose a DVT. Because the treatment for a venous thrombosis is not without its risk, making an accurate diagnosis is imperative.

The focus of this paper is to provide a review of the literature on the evolution of the use of point-of-care lower extremity ultrasound for the diagnosis of DVT. In 2006, the American College of Emergency Physicians published an ultrasound imaging compendium that described a point-of-care compression technique for the detection of lower extremity DVT [2]. Subsequently, the 2009 American College of Emergency Physicians ultrasound policy statement listed this examination as 1 of 11 core applications for the practicing emergency physician [3]. We describe the literature on the evolution of point-of-care lower extremity ultrasound. This review is limited to adult patients as very few publications to date describe the detection of DVT in pediatric patients by emergency physicians [4].

Patients presenting to the emergency department with lower extremity symptoms suggestive of thromboembolic disease require a diagnostic evaluation. Although contrast venography is the diagnostic reference standard, it has been largely replaced by duplex sonography as the first-line imaging modality and reference standard imaging test in clinical practice [5]. A duplex ultrasound examination performed in a vascular laboratory or in the department of radiology is not always obtainable due to time of day or day of week. A complete examination by duplex ultrasound involves not only an assessment of vessel compressibility with B-mode but also a Doppler evaluation including the presence of spectral and color flow signals, respiratory phasicity, and augmentation. Reportedly, a lower extremity duplex examination takes an average of 37 min and usually results in the patient leaving the acute care area for a much longer period of time [6]. During off-hours, for example, nights and weekends, some institutions may have on-call technicians; however, the reimbursement for these examinations has decreased, may in some cases be below operating expenses, and may eventually limit the availability of these tests [7]. In light of these and other challenges, the published literature has focused on the utility of abbreviated examinations and on the performance of the examinations by nontechnician sonographers.

TWO-POINT VERSUS 2-REGION POINT-OF-CARE LOWER EXTREMITY ULTRASOUND TECHNIQUE

There is variability in the point-of-care lower extremity ultrasound literature in terms of compression technique and protocol. Compression-only 2-point sonography evaluates for thrombosis in the common femoral vein and in the popliteal vein at the popliteal fossa. A 2-region technique, which, for example, is described in the study by Poppiti et al. [6], compares the accuracy of a limited B-mode compression-only technique of 2 regions (the femoral veins 1 to 2 cm above and below the saphenofemoral junction and the popliteal veins including the calf veins confluence) to a complete color-flow duplex venous examination. This whole-leg duplex ultrasound visualizes the entire deep venous system from the inguinal region to ankle. In the Poppiti et al. study [6], the compression-only studies for proximal DVT were performed by vascular technologists and had a sensitivity of 100%, a specificity of 98%, and an overall accuracy of 99%. In the popliteal region, the compressibility-only study yielded 2 false positive results. In both cases, there was anatomic transposition of the artery and vein, which would have been identified during a complete duplex examination. The investigators concluded that 2-region compression-only ultrasound was an acceptable technique for the diagnosis of proximal lower extremity venous thrombosis [6].

In 2010, Crisp et al. [8] reported their results from a prospective convenience sample of patients with a suspected

The authors report no relationships that could be construed as a conflict of interest.
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GLOBAL HEART

VOL. 8, NO. 4, 2013
ISSN 2211-8160
http://dx.doi.org/10.1016/j.gheart.2013.11.002

DVT. They compared the findings of department of radiology studies with the results of 2-point compression ultrasound examinations performed by emergency medicine residents and attending physicians. The physicians used a portable vascular ultrasound machine after a 10-min training session [8].

In his 2010 editorial in response to the report by Crisp et al. [6], Blaivas [9] clarified that the 2-point compression (common femoral vein and popliteal vein as described by Crisp et al.) technique in the evaluation of point-of-care lower extremity ultrasound does not and should not mean only 2 compressions with the probe. The intention is to interrogate 2 regions, the first including the region from the greater saphenous vein junction with the common femoral vein extending to the confluence of the deep and superficial femoral veins—an area 3 to 4 cm in length. The second area surveyed is behind the knee extending from the proximal popliteal vein to the confluence of the calf veins—also an area 3 to 4 cm in length. Albeit rare, it is possible that small segmental thrombi will be missed with this technique. Blaivas cautioned that "10 minutes and you are ready to go" is not quite sufficient for training; however, he echoed that with proper training, emergency physicians can accurately diagnose DVT in the emergency department and decrease length of stay [8,9].

POINT-OF-CARE LOWER EXTREMITY ULTRASOUND IN THE EMERGENCY DEPARTMENT

Several papers have described the ability of emergency physicians to perform point-of-care ultrasound of the lower extremity in the diagnosis of DVT. One of the earliest, by Jolly et al. [10], from 1997, evaluated 2 emergency physicians' accuracy in performing duplex ultrasound as compared to the accuracy of vascular laboratory studies. The physicians were trained by the vascular laboratory technicians and were required to complete 25 to 30 technically adequate examinations prior to performing studies in the emergency department. Interestingly, these physicians were trained in order to provide this diagnostic modality during off-hours, when vascular laboratory services were not available. Although the investigators reported a high sensitivity (100%), this study involved extensively trained physicians performing lengthy complete duplex examinations.

In 2000, Blaivas et al. [11] performed examinations using duplex evaluation, however, in 2 locations only: the femoral and popliteal veins. The 5 emergency medicine physicians who participated all had significant ultrasound experience (>350 previous scans, not related to the lower extremity veins). Their training session consisted of 2 h of didactic education followed by 3 h of hands-on learning [11]. The time dedicated to training seemed more achievable and therefore made the results more generalizable. This 2-location duplex technique, when compared with studies performed in the vascular laboratory, demonstrated a high correlation (kappa = 0.9), 98% agreement, and required a median time of 3 min 28 s to complete.

The Jolly et al. [10] and Blaivas et al. [11] studies both studied physicians with a significant amount of previous ultrasound experience. A third study by Magazzini et al. [12] from 2007 enrolled patients to receive a study by 1 of 2 emergency department physicians, who each completed a 30-h training, followed by a formal duplex ultrasound in a vascular laboratory within 24 to 48 h of discharge. The emergency department ultrasound had a sensitivity of 100%, specificity of 98.4%, a positive predictive value of 94.9%, and a negative predictive value of 100%, giving an overall accuracy of 98.7% [12]. Whereas this study was encouraging regarding the ability of emergency physicians to accurately perform and lower extremity ultrasound for the diagnosis of DVT, its applicability and generalizability was questionable given the extensive training provided to those involved and the time needed to perform such a comprehensive examination.

In 2008, Burnside et al. [13] published a systematic review of pooled data from 6 studies that met their inclusion criteria. The investigators assessed emergency physician–performed versus department of radiology–performed ultrasounds. The pooled summary estimate of the 6 studies included in this analysis produced a sensitivity of 95% and specificity of 96% [13]. Although these results were promising, the investigators discussed a variety of concerns complicating the interpretation of the data, including small sample sizes and methodological issues. Most of the reviewed studies lacked details involving patient enrollment and used a small number of highly skilled ultrasonographers to perform the examinations.

In a similar fashion and with similar limitations, a 2010 study by Shriver et al. [14] described the results of a prospective convenience sample study comparing emergency department–performed ultrasound with computed tomography venography, as a gold standard, in patients with symptoms of pulmonary embolism. Of 61 patients enrolled, 10 had a DVT. Emergency department ultrasound detected all of those detected by computed tomography except for 1, which was located in the external iliac vein. Their evidence added to the literature supporting the correlation between emergency department–performed ultrasound and computed tomography venography. Noted limitations of this study included the detection of DVT in regions other than the femoropopliteal region and the difficulty in differentiating between acute and chronic thrombi. Moreover, the sample size was small and operator experience with this particular examination extensive [14].

POINT-OF-CARE LOWER EXTREMITY ULTRASOUND IN THE EMERGENCY DEPARTMENT BY RESIDENT PHYSICIANS

In 2004, Jang et al. [15] studied the ability of emergency medicine residents to perform a compression-only examination of the entire proximal leg including the popliteal fossa [15]. Eight residents received a 1-h lecture and a

demonstration of the technique on 2 healthy volunteers. Contrast venography, duplex ultrasound, or computed tomography venogram was used as the reference standard. The resident physician examination findings were 100% sensitive and 91.8% specific in diagnosing proximal vein thromboses. The 11.7 min average required to complete the examination was self-reported. These investigators concluded that residents with limited training could quickly and accurately perform compression ultrasound for proximal vein thrombosis.

Farahmand et al. [16] also focused on emergency medicine resident diagnostic ability by point-of-care ultrasound. In a study of 71 patients presenting with symptoms suggestive of a DVT, the whole leg was not interrogated. Two regions, "the iliofemoral segment from saphenofemoral junction up to 10 cm below it and the popliteal segment from saphenopopliteal junction up to tibial vein confluence," were evaluated with a reported 100% sensitivity, specificity, and accuracy. As in the Jang study [15], a B-mode compression-only technique was compared to color-flow duplex ultrasound [16]. In a third study, Jacoby et al. [17] in 1997 also looked at the emergency medicine resident accuracy in the diagnosis of DVT by ultrasound using the 2-region compression technique. The residents had the option, but were not required, to use color Doppler respiratory variation and augmentation. The results of these scans by residents, who completed a 90-min training session, were then compared with those of a whole-leg study performed by a vascular technician within 30 min of the resident's study. Here, the sensitivity for resident-performed ultrasound was 89%, with a resident examiner missing 1 of the 9 DVT diagnosed by the technician-performed study. Three false positives were diagnosed by the resident examiners, generating a specificity of 97%. In the Jacoby study [17], emergency medicine resident accuracy and the interpretation of their results was limited given a small sample size and a low prevalence of disease.

TIME EFFICIENCY OF POINT-OF-CARE ULTRASOUND OF THE LOWER EXTREMITY

Subsequently, Theodoro et al. [18] sought to address the question of how these studies influenced the time-to-department disposition when patients presented with signs or symptoms concerning for a DVT. The time the emergency physician made the diagnosis was used as the emergency physician disposition time and the time the report was received from the radiology department was used as the radiology disposition time. The mean time from triage to disposition was 95 min for patients who had their ultrasound performed by the emergency physician, whereas the mean time from triage to disposition was 220 min for patients who had their study performed by the radiology department. There was a high correlation (kappa = 0.9) and 99% agreement of the emergency physician–performed studies with radiology department results.

LIMITATIONS OF POINT-OF-CARE LOWER EXTREMITY ULTRASOUND

Contrast venography, which remains the gold standard, is invasive, involves the use of ionizing radiation, requires specialized personnel to perform and interpret the study, and requires that the patient leave the acute care area. In 1989, Lensing et al. [19] were the first to publish a large study on the accuracy of compression ultrasound versus contrast venography in symptomatic outpatients. Using the single criterion of vein compressibility of the common femoral and the popliteal veins, they were able to diagnose proximal venous thrombosis (above the calf) with a sensitivity of 100%. In patients with isolated calf vein thrombosis, the sensitivity was low at 36%. This region of the calf, including the 3 smaller, deeper, more difficult to identify calf veins to their region of confluence into the popliteal vein is a known area of limitation for sonographic evaluation. In studies that used the reference standard test to diagnose calf vein thrombosis, the investigators noted that the thrombi only became clinically important when they extended into the proximal veins [20,21]. Due to the limitation of ultrasound in this setting, when an isolated calf vein thrombosis is suspected, an interval diagnostic study is usually performed to evaluate for proximal propagation. In addition to the calf region, sonographic evaluation for thrombosis is limited in the pelvis as portions of the iliac veins are not visualized or easily compressible. Although only 1% to 2% of deep venous thromboses are isolated to the iliac veins, the clinician must be cautious if abnormal compression is encountered in the femoral region as this should raise suspicion for a DVT more proximally in this location [22].

With regard to the safety of performing point-of-care lower extremity ultrasound, a literature review from 2007 addressed the question of whether an ultrasound compression test could in fact cause harm to the patient by precipitating a thromboembolic event. A search of the literature at that time revealed no articles that directly answered this question. It was concluded that there was no evidence to suggest that compressing vessels in order to diagnose a DVT would cause an embolic event [23].

POINT-OF-CARE LOWER EXTREMITY ULTRASOUND AND D-DIMER

In 2008, Bernardi et al. [24] compared 2 diagnostic strategies for lower extremity DVT evaluation—serial 2-point ultrasound plus D-dimer testing and whole-leg color-coded Doppler ultrasound. Patients were randomized to either strategy, and those who had negative initial workups (negative whole-leg duplex, negative 2-point ultrasound plus negative D-dimer, or negative 2-point ultrasound with positive D-dimer and negative follow-up scan) were followed for 3 months. During this period, the incidence of objectively confirmed symptomatic venous thromboembolism was similar between the 2 groups, with the 0.3% difference being within the chosen equivalence limit. The

investigators concluded, therefore, that these 2 strategies were equivalent for the management of patients with suspected DVT [24]. Of note, the whole-leg group had a significantly higher initial prevalence of DVT than did the 2-point compression group. This was entirely due to isolated calf DVT, perhaps challenging the clinical significance of diagnosing and treating patients with these thrombi. The 2-point method eliminated the need for a repeat study for normal initial findings, but required more time to complete, more training, and newer equipment. The investigators concluded that in cases of negative 2-point compression, a negative D-dimer may help avoid necessity for a repeat study [24].

In the same year, Kline et al. [25] examined the applicability of clinician-performed ultrasound diagnosis of DVT by including emergency department faculty, residents, fellows, and mid-level providers in their analysis. Here, the clinicians performed a 3-point compression (common femoral vein, superficial femoral vein, and popliteal vein) examination of the lower extremity. All patients then underwent a reference ultrasound in the department of radiology within 12 h of enrollment and were followed for 30 days to establish any evidence of DVT or pulmonary embolism during this period. They reported a lower sensitivity and diagnostic accuracy than in previous studies. For this group of heterogeneous emergency clinicians, emergency department ultrasound had a sensitivity of 70%, specificity of 89%, and diagnostic accuracy of 85%. The diagnostic accuracy improved with experience, remaining relatively constant (at 81%) for the first 3 examinations performed by a practitioner, but increasing thereafter. When only including those studies performed by clinicians with $\geq$3 completed examinations, the diagnostic accuracy rose to 95.5% [25].

Relatedly, Fox and Bertolio [26] called for a more uniform and universal training of emergency physicians for the detection of DVT. These investigators also made recommendations regarding the adjunctive role a D-dimer test plays in clinical decision making. A high-risk patient with a negative ultrasound and positive D-dimer should have a repeat ultrasound examination within 1 week. They also described a 2-region compression ultrasound technique that can be accurate and time efficient. They cautioned that other imaging modalities should be employed when there is a suspicion for calf, pelvic, or abdominal DVT [26].

Most recently, in a 2012 meta-analysis, Pomero et al. [5] reviewed 16 studies (>2,000 patients) that compared emergency physician–performed B-mode ultrasound to color-flow duplex ultrasound or to angiography. The investigators reported a weighted mean sensitivity of 96.1% and specificity of 96.8%. The clinical implications of this review support the role of emergency physician–performed point-of-care ultrasound as an alternative to a department of radiology or vascular laboratory–performed study. These investigators suggested the need for further studies to confirm their findings as well as to evaluate the examination with pre-test probability and D-dimer assay assessments [5].

POINT-OF-CARE LOWER EXTREMITY ULTRASOUND IN THE ICU

Blaivas [27] advocated for clinician-performed ultrasound in the intensive care unit (ICU), asserting that by eliminating reliance on radiologists or vascular technologists to perform and interpret the examination, efficiency is improved, convenience is afforded, and accuracy is preserved. With the interest of reducing time to diagnosis in the ICU setting, 2 studies examined how accurate internal medicine physicians were when performing this modality. In a prospective cohort study, Caronia et al. [28] reported that a 2-point compression technique performed by internal medicine residents was not adequate for detecting DVT. Notably, 6 of the 12 DVT were isolated to the superficial femoral vein. In contrast, Kory et al. [29] studied intensivist fellows and faculty who performed a protocol compression technique that compared favorably in terms of accuracy with the complete vascular laboratory study [28,29].

CONCLUSIONS

Point-of-care ultrasound of the lower extremity for suspected DVT is becoming increasingly common and relevant due to multiple forces influencing the availability and feasibility of obtaining traditional department of radiology or vascular laboratory examinations. The current literature is promising for this application of point-of-care ultrasound performed by emergency physicians, but limitations must be fully acknowledged and accounted for when making patient care decisions. There is support for both emergency department and ICU physicians using B-mode compression-only ultrasound to diagnose lower extremity DVT, excluding isolated calf or pelvic thromboses. The accuracy of examinations increases with increased clinician ultrasound experience and training. Most literature to date argues for using a technique of compression-only B-mode ultrasound focused in 2 regions (femoral and popliteal), not 2 points. Some investigators suggest an adjunctive role for D-dimer testing. This use of point-of-care ultrasound has the potential to decrease length of stay for patients in the emergency department and has important clinical implications given the consequences of both unnecessary treatment and missed diagnoses of the venous thromboembolic disease process.

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