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Single whole-leg compression ultrasound for exclusion of deep vein thrombosis in symptomatic ambulatory patients: a prospective observational cohort study

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Summary

International guidance has recently recommended serial proximal compression ultrasound (CUS) as first line imaging for suspected deep vein thrombosis (DVT). Single whole-leg CUS is a routine alternative diagnostic strategy that can reduce repeated attendances and identify alternative pathology. We conducted a prospective observational cohort study. Consecutive ambulatory, adult patients with suspected DVT and negative or inconclusive whole-leg CUS had anticoagulation withheld and were followed for 3 months. The primary outcome was a predefined clinically relevant adverse event rate. Secondary outcomes included technical failure, alternative diagnoses and all cause mortality. 212 patients agreed to participate and completed follow up. One patient was subsequently diagnosed with an isolated distal DVT. The adverse event rate was thus 1/212, 0·47% (95% confidence interval [CI] 0·08–2·62). Technical imaging failure occurred in 11·3% of cases (95% CI 7·7–16·3). Several potential predictors of an inconclusive result were identified on multivariate analysis. 150 (70·8%) patients were provided with a documented alternative diagnosis. Patients who have anticoagulation withheld following a negative or inconclusive whole-leg CUS for suspected DVT have a low rate of adverse events. Technical failure remains an issue: several factors were significantly associated with inconclusive results and may warrant an alternative diagnostic approach.

Keywords: thrombosis, imaging, anticoagulation, whole-leg compression ultrasound.

Deep vein thrombosis (DVT) is an increasingly topical issue in modern healthcare. Clinical signs and symptoms are of limited use in diagnosis (Goodacre *et al*, 2005a). Physicians suspecting disease rely heavily on objective testing.

There is on-going debate regarding the optimal diagnostic approach. Duplex compression ultrasound (CUS) is the initial investigative modality of choice, primarily based on safety, availability and cost (Redman, 1988; Sampson *et al*, 2005). CUS is often limited to imaging of the proximal veins, with serial tests a week apart recommended for those patients deemed at high clinical risk (likely pre-test probability and positive D-dimer). This technique was recently endorsed as first line by the National Institute for Health and Care Excellence (NICE) and the American College of Chest Physicians (ACCP) (Chong *et al*, 2012; Guyatt *et al*, 2012). However, even with the omission of serial imaging for low risk patients, approximately a quarter will be required to return for repeat proximal CUS with this strategy (Wells *et al*, 2003). This can be both time-consuming and costly for patient and clinician. The rationale in support of the second (7 d) scan is also based on low level evidence with a demonstrably low diagnostic yield (Wells *et al*, 2003; Goodacre *et al*, 2005b, 2006). Other limitations include attrition, lack of assessment for alternative pathology and continuing uncertainty for the patient.

Whole-leg CUS evaluates both proximal and distal veins within the leg and, with experience, appears to be reliable (Schwarz *et al*, 2002), increasingly sensitive (Gottlieb *et al*, 1999) and safe (Johnson *et al*, 2010). The technique addresses the majority of concerns with serial proximal

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imaging and saves time for both patient and clinician, as well as providing additional clinical information on which to base management decisions.

Our institution has been operating an ambulatory pathway for suspected DVT using whole-leg CUS for the last decade. In this study, we primarily sought to assess short-term clinical outcomes in patients with a single negative scan who had anticoagulation withheld. We also sought to make a pragmatic assessment of utility through quantifying alternate diagnoses and exploring the issue of technical failure.

Methods

Study design, setting and population

A prospective observational cohort study, conducted within the screening pool of the Anticoagulation of Calf Thrombosis (ACT) project (Horner *et al*, 2011, 2013). We approached a consecutive sample of ambulatory patients with suspected DVT who tested either negative or inconclusive on whole-leg colour duplex ultrasound and had anticoagulation withheld after index visit.

The study was conducted in the Emergency Department (ED) of an academic teaching hospital, located within the city centre of Manchester. The segregated adult ED has an annual attendance of approximately 100 000. A dedicated research team conducted the study, enrolling patients over a 10-month period between July 2011 and April 2012.

Study protocol

All ambulatory patients attending the ED with suspected DVT, who were subsequently referred for CUS imaging were screened for inclusion. All clinical management decisions, including referral for CUS, were made principally by non-research emergency physicians using an internationally-agreed ambulatory protocol. This protocol incorporated the Wells clinical prediction model and a highly sensitive D-dimer assay, with imaging recommended in the event of either likely pretest probability (Wells score >1) or unlikely pretest probability (Wells score <2) but raised D-dimer assay (Wells *et al*, 2003).

Patients with a negative or inconclusive result on whole-leg CUS were approached for participation. Patients testing positive for acute or chronic disease, those requiring inpatient admission, with confirmed PE, superficial thrombophlebitis, unable to provide informed consent, unable to perform follow-up (non-UK resident), previously enrolled or on any form of ongoing formal prophylactic or therapeutic anticoagulation (warfarin, heparin, low molecular weight heparin, dabigatran, rivaroxaban) were excluded. All participants provided full and informed written consent. Demographic, risk factor and clinical data were collected at index assessment.

Follow up was performed at 3 months in line with previous research (Birdwell *et al*, 1998; Johnson *et al*, 2010). Patient records, regional imaging databases and referral data were comprehensively reviewed. All patients were additionally contacted by telephone to complete a short standardized questionnaire, enquiring specifically about new episodes of investigation, diagnosis or management of VTE. For those patients not responding to telephone contact after multiple attempts, the research team contacted the primary care provider or next of kin to complete the questionnaire and obtain any relevant further information.

Clinical, imaging and laboratory protocols

Whole leg CUS imaging was performed by an external vascular sonography service. All sonographers within the vascular laboratory are vocationally trained in Vascular Sciences to postgraduate level and accredited to standards set by the Society for Vascular Technology of Great Britain and Ireland. Patients were scanned using a 9–4 MHz linear and 5–2 MHz curvilinear transducer to a standard proforma. This includes documented assessment of all proximal, muscular calf and deep calf veins using B mode, colour Doppler and spectral Doppler including compression, augmentation and Valsalva manoeuvre.

All D-dimer measurements were conducted using a rapid and quantitative immunoturbidometric assay (STA Liatest; Diagnostica Stago, Paris, France).

Key outcome measures

The primary safety outcome was a composite of subsequent venous thromboembolic events and/or death related to VTE, during the 3-month follow up period. Events were objectively defined using repeat duplex examination (Birdwell *et al*, 1998; Cogo *et al*, 1998), Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED)-reported ventilation/perfusion imaging (PIOPED Investigators, 1990) or computerized tomography Pulmonary Angiogram (Stein *et al*, 2006). Clinical outcomes were considered by a central adjudication committee with full access to medical records. Disagreements were resolved by consensus discussion. Deaths during the follow up period were classed within an ordinal scale of 1: probably related to VTE, 2: potentially related to VTE and 3: Unrelated to VTE. Outcomes 1 or 2 were both classed as positive primary endpoints in line with previous studies (Sevestre *et al*, 2009).

Secondary outcomes included an assessment of technical failure rate (calculated as the total number of initial scans reported as inconclusive/total number of scans performed), all cause mortality and alternate diagnoses attributable to CUS. Both primary and secondary outcomes were also evaluated within subgroups of *a priori* moderate or high pre-test clinical probability, using the original Wells score (Wells *et al*, 1997). Lastly, we attempted to compare categorical variables using multivariate analysis to assess those characteristics that predicted technical failure of whole-leg CUS, as determined by inconclusive scan result.

Sample size calculation

Based on previous research, we estimated the prevalence of the primary safety outcome to be approximately 0·5% within our cohort (Sevestre *et al*, 2009; Johnson *et al*, 2010). In line with previous authors, we considered an adverse event rate of more than 3% (upper boundary of 95% Confidence Interval) to be unsafe (Gibson *et al*, 2009). Thus, in a sample of 200 patients receiving no anticoagulation following a negative/inconclusive whole-leg ultrasound scan, we would expect to see a single VTE event. This would provide an upper limit 95% confidence interval [CI] of 2·8% for any VTE occurring within a 3-month period.

Data analysis

Categorical data were summarized by percentage and compared using Fishers exact test. Non-parametric data were summarized by the median (interquartile range, IQR) and compared using the Mann–Whitney *U* test. Multivariate analysis was performed using binary logistic regression. Confidence intervals were calculated to 95% using the Wilson method. All *P* values reported are two tailed, with <0·05 considered statistically significant. All analyses were performed using SPSS version 20 (IBM, NY, USA). Statistical advice was ongoing throughout data collection and analysis.

Ethical review

The study was approved by the North West Greater Manchester Central Research Ethics Committee (ref: 10/H1008/97) and the institutional Research and Innovation department. All data presented conform to the STROBE recommendations on reporting of observational cohort data (von Elm *et al*, 2007).

Results

Patient flow and demographics

During the recruitment period, 610 ambulatory patients attended the ED with suspected DVT and were referred for diagnostic imaging. The median delay to duplex ultrasound was 1 d (IQR 1–2). At least one dose of therapeutic dalteparin prior to scan was received by 91·2% (95% CI 86·4–94·3) patients, with a median of one dose administered (IQR 1–2).

Of 432 patients with negative or inconclusive ultrasound imaging, 214 eligible subjects agreed to participate in the study. Two patients were subsequently withdrawn, leaving 212 suitable for analysis. Reasons for exclusion prior to and post-recruitment are listed in the patient flow chart (Fig 1).

Follow up was completed for all patients, principally by direct telephone contact with the subject (N = 188, 88·7%). Those uncontactable after multiple attempts were followed up through their primary care practitioner/next of kin where possible (N = 16). In addition, a regional database and medical record search were conducted for evidence of further attendance/investigation. Participant demographics and baseline characteristics are shown in Table I, with stratification by CUS result and comparison to missed patients.

Primary outcome

During the follow up period, only one patient received a subsequent objective diagnosis of VTE. This patient was a 95-year-old female with an initial negative ultrasound, who had an unplanned re-attendance with ongoing symptoms at 2 weeks post-recruitment. She underwent repeat duplex examination, which recorded the presence of isolated distal deep vein thrombosis (IDDVT) within a single posterior tibial vein. The clot was chronic in appearance. No anticoagulation was prescribed by the attending clinician and the patient was alive and well at the 3-month follow-up. We also noted one death during the study period. This patient had known renal carcinoma and was diagnosed with metastatic disease 10 d after presentation to the ED and recruitment to the trial. She was later transferred to a hospice for palliation. Cause of death was recorded by the coroner as disseminated metastatic cancer. This event was ruled as unrelated to VTE by the central adjudication committee.

The subsequent incidence of the composite primary outcome in our population following withheld anticoagulation after single whole-leg CUS was 1/212 = 0·47% (95% CI 0·08–2·62).

Secondary outcomes

Technical failure occurred within 11·3% (95% CI 7·7–16·3) of our study population. This rate was replicated within the original screening cohort (70/610 – 11·5%, 95% CI 9·1–14·3) – Fig 1. Obesity, acute infection, immobilization and active cancer were all significantly associated with technical failure on multivariate analysis (Table I). All cause mortality within 3 months was 0·47% (95% CI 0·08–0·26), due to the single death noted above.

All patients with completed Wells score data were subsequently analysed as a pre-specified subgroup for both primary and secondary outcomes. 163 patients had complete data suitable for analysis (76·9%). No significant differences were found on direct comparison between patients deemed at high risk or otherwise. Stratification is shown in Table II. The composite primary outcome for those patients with a high pre-test probability was achieved in 2·1% (95% CI 0·4–11·1).

An alternative diagnosis was provided by the attending clinician in 150/212 cases. Clinicians providing diagnostic labels operated outside the research team and were of registrar or consultant grade. The alternate diagnosis was felt to be directly identified or confirmed by CUS in 55 of these cases, such that 25·9% (95% CI 20·0–31·8) of the original cohort were provided with a conclusive diagnosis and appropriate

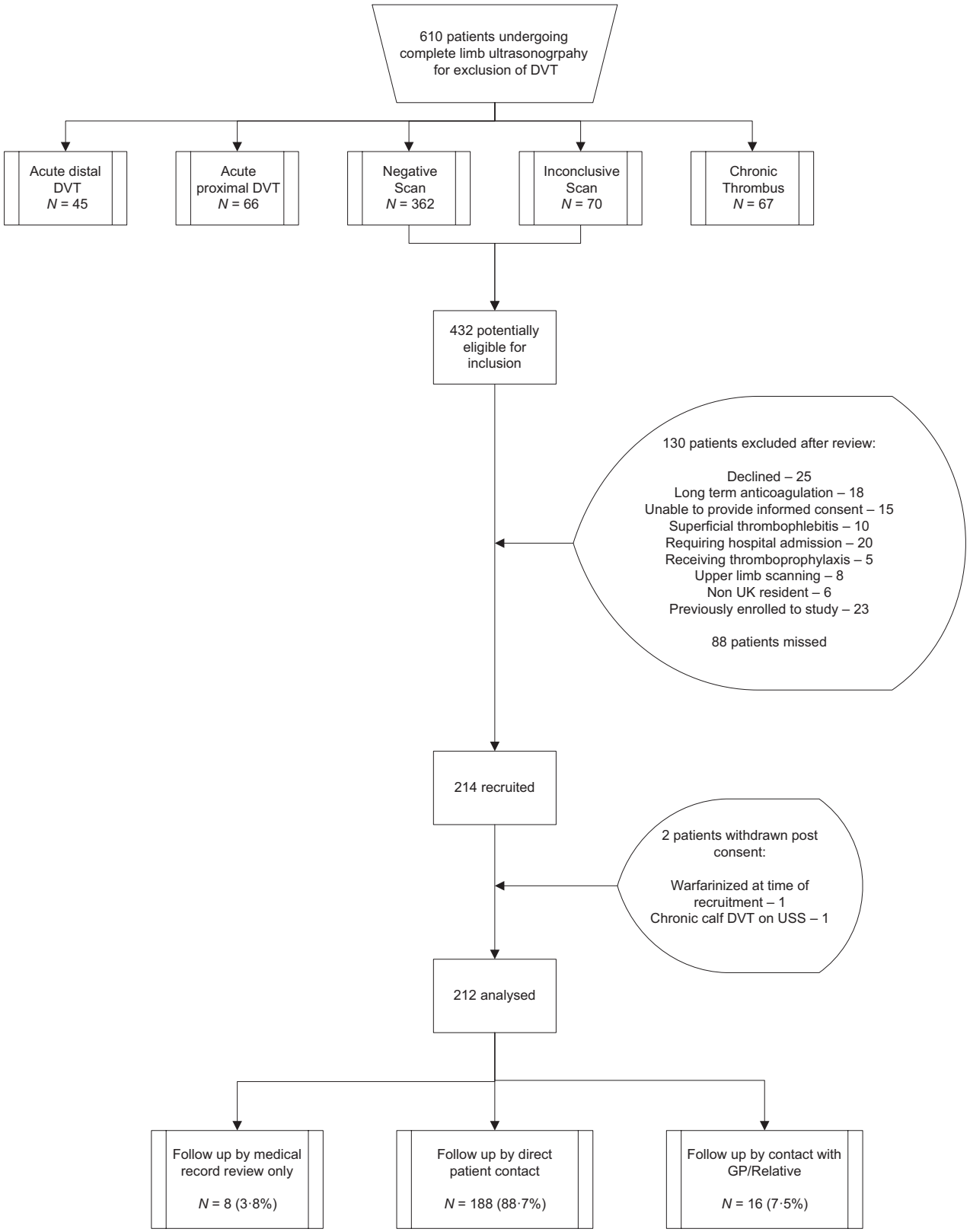

Fig 1. A recruitment flow chart delineating the number of screened, excluded and recruited participants. Also shown are cumulative positive results over the study period and methods of follow up, with proportions. DVT, deep vein thrombosis; USS, ultrasound scan; GP, general practitioner.

Table I. Demographic and clinical presentation data, with stratification by result.

	Recruited patients $N = 212$	Missed patients $N = 218$	Inconclusive ultrasound $N = 24$	Negative ultrasound $N = 188$	Univariate analysis (P value)	Multivariate analysis (OR and P value)
Demographics						
Age, years	56·7 (18·8)	55·7 (18·9)	59·5 (19·6)	56·4 (18·7)	0·84	–
Female	137 (64·2)	134 (61·5)	20 (83·3)	117 (62·3)	0·04	OR 6·9 (0·5–90·3), $P = 0·13$
Left sided	107 (50·5)	95 (43·6)	11 (45·8)	96 (51·1)	0·66	–
Right sided	79 (37·3)	97 (44·5)	9 (37·5)	70 (37·2)		
Bilateral	26 (12·3)	26 (11·9)	4 (16·7)	22 (11·7)		
White	169 (79·7)	168 (77)	19 (79·2)	150 (79·8)	0·99	–
Afro-Caribbean	24 (11·2)	15 (6·9)	3 (12·5)	21 (11·2)		
Asian	12 (5·6)	30 (13·8)	1 (4·2)	11 (5·9)		
Other	7 (3·4)	5 (2·3)	1 (4·2)	6 (3·2)		
Risk factors						
Family history VTE	36 (17·0)	20 (9·2)	4 (16·7)	32 (17·0)	0·57	–
Past history VTE	35 (16·5)	42 (19·3)	4 (16·7)	31 (16·5)	0·47	–
Thrombophilia	8 (3·8)	8 (3·7)	0 (0)	8 (4·3)	1·00	–
Obesity	43 (20·3)	52 (23·9)	12 (50)	31 (16·6)	<0·01	OR 4·15 (95% CI 1·5–11·2) $P < 0·01$
Smoker	63 (29·7)	78 (35·8)	6 (25·0)	57 (30·5)	0·59	–
Acute infection	49 (23·1)	Unrecorded	10 (43·5)	39 (20·7)	0·02	OR 2·9 (95% CI 1·1–8·0) $P = 0·04$
Immobilization	20 (9·4)	17 (7·8)	6 (25·0)	14 (7·4)	0·02	OR 4·9 (95% CI 1·5–16·2) $P = 0·01$
Active cancer	9 (4·2)	6 (2·8)	3 (12·5)	6 (3·2)	0·05	OR 7·9 (95% CI 1·5–41·7, $P = 0·01$
Oestrogen use	14 (6·6)	6 (2·8)	1 (4·2)	13 (6·9)	0·94	–
Recent surgery	30 (14·2)	27 (12·4)	3 (12·5)	27 (14·4)	0·74	–
Clinical presentation						
Wells high	47 (28·8)	68 (31·2)	9 (41·0)	38 (27·0)	0·66	–
Wells intermediate	73 (44·8)	85 (39·0)	7 (31·8)	66 (46·8)	0·64	–
Wells low	43 (26·4))	65 (29·8)	6 (27·2)	37 (26·2)	0·84	–
Symptom duration	7 (3–14)	6 (3–14)	7 (3–21)	7 (3–14)	0·07	–
NRS pain score	3 (2–5)	3 (2–5)	4 (2·75–5·25)	3 (2–5)	NS	–

NRS, Numerical Rating Scale for pain; VTE, Venous Thromboembolism; OR, odds ratio; 95% CI, 95% confidence interval.
Age is presented as mean (SD). All other data is presented as categorical (%). Valid percentages are given in the context of missing data. Obesity was defined as Body Mass Index >30. Recent surgery was defined as operative intervention within the last 3 months. Data on Wells scoring is recorded as valid percentages only (163 patients total). Logistic regression analysis compares characteristics of patients with inconclusive ultrasound results against those with negative results. Missed patients comprise the 130 patients excluded from the study after review and the 88 cases who were not screened by the research team during the study period.

management as a result of whole-leg CUS. A list of alternate diagnoses stratified by CUS is given in Table III.

Discussion

These findings support previously published low adverse event rates after withholding anticoagulation following a single negative whole-leg CUS examination in suspected DVT. Our data validates this approach within an ambulatory ED setting, basing clinical decision making on imaging performed by qualified ultrasonographers, rather than after clinical assessment and imaging performed by vascular specialists.

We also highlight several new points regarding process measures: the technical failure rate of whole-leg CUS was 11·3% (95% CI 7·7–16·3) in our study population. Obesity, acute infection (any site), active cancer and immobilization were all potentially associated with technical failure on multivariate analysis.

This study has a number of strengths. Our cohort was similar at baseline to previous ambulatory populations, suggesting external validity. A 29% pre-test probability of disease is also in keeping with other sample estimates, ranging from 13·7 to 32·7% at recent systematic review (Johnson *et al*, 2010). This study was pragmatic and used existing healthcare resources. This should ensure that our findings can be generalized to other centres performing whole-leg CUS.

We made a deliberate *a priori* decision to include patients with an inconclusive scan result, as we deemed it vital to evaluating the pathway. Technical failure is a real concern with whole-leg CUS, with previous studies quoting a wide variation in failure rates between 9·3 and 82·7% (Gottlieb *et al*, 1999). As such, our study is one of the few to provide an open assessment of the caveats with whole-leg CUS and the characteristics associated with technical failure.

Finally, we attempted to standardize all interventions and outcomes in an objective manner. Protocolized scanning

Table II. Primary outcome data stratified by clinical pretest probability scoring.

	High risk $N = 47$	Moderate risk $N = 73$	Low risk $N = 43$	Non-high (<3) $N = 116$	Comparison high vs non-high
Primary outcome					
VTE event	1 (2·1)	0 (0)	0 (0)	0 (0)	NS
VTE-related death	0 (0)	0 (0)	0 (0)	0 (0)	NS
Secondary outcome					
All cause mortality	1 (2·1)	0 (0)	0 (0)	0 (0)	NS
Reattendance	13 (27·7)	11 (15·1)	8 (18·6)	19 (16·4)	NS
VTE-related re-attendance	6 (12·8)	6 (8·2)	3 (7·0)	9 (7·8)	NS
Therapeutic intervention	2 (4·3)	1 (1·4)	3 (7·0)	4 (3·4)	NS
Repeat imaging	7 (14·9)	7 (9·6)	6 (14·0)	13 (11·2)	NS
Scan result					
Negative	38 (80·9)	69 (94·5)	37 (86·0)	106 (91·4)	NS
Inconclusive	9 (19·1)	4 (5·5)	6 (14·0)	10 (8·6)	NS

VTE, Venous Thromboembolism.
All data is recorded as n/N (%). Data on Wells scoring was available for 163 patients.

Table III. Alternative diagnoses provided to patients during the study, stratified by the contribution of whole-leg CUS.

	Patients with negative or inconclusive whole-leg CUS $N = 212$
Alternate diagnosis provided	150/212 (70·8%)
Yes	150
No (idiopathic/unknown)	38
Inconclusive scan recorded – no diagnosis offered	24
Diagnosis directly attributable to or confirmed by whole-leg CUS	55/150 (36·7%)
Severe arterial vascular disease	1 (0·7%)
Bakers cyst	13 (8·7%)
Musculoskeletal (including calf haematoma, tendonitis and muscle rupture)	32 (21·3%)
Superficial thrombophlebitis	4 (2·7%)
Post thrombotic syndrome/venous incompetence	5 (3·3%)
Diagnosis unassisted by whole-leg CUS	95/150 (63·3%)
Crystal arthropathy	2 (1·3%)
Dependent oedema (Cardiac/pregnancy/liver failure)	27 (18·0%)
Diabetic neuropathy	1 (0·7%)
Infective process	43 (28·7%)
Meralgia parasthetica	2 (1·3%)
Post-operative swelling	13 (8·7%)
Arthritic disease	5 (3·3%)
Lymphoedma	1 (0·7%)
Bony injury	2 (1·3%)
Venous eczema/lipodermatosclerosis	2 (1·3%)
Sciatica	2 (1·3%)

CUS, compression ultrasound.

allows reproduction of whole-leg ultrasound within external research environments and thus renders our intervention transparent and reproducible. Also, use of an independent central adjudication committee promotes unbiased dialogue regarding potentially subjective endpoints (Bernardi *et al*, 2008). This is essential for a study with few expected positive outcomes.

The potential benefits of whole-leg CUS are well established and include a reduction in re-attendance/repeat imaging; thorough assessment of the deep calf veins to allow risk stratification and fully informed discussion in the event of IDDVT; detection of additional pathology in the lower limb such as calf haematoma, Bakers cyst or thrombophlebitis; and the opportunity to clarify the diagnosis at the initial visit. This last point is especially important for a mobile emergency department population, who will often have even higher rates of non-return than seen with vascular outpatients (Birdwell *et al*, 1998).

However, whole-leg CUS is not without caveats. Principle issues include limited robust sensitivity data, longer scanning time and a concern that imaging of the calf veins will lead to overzealous anticoagulation for no proven benefit. Indeed, two diagnostic randomized controlled trials have recently shown no significant clinical benefit to use of whole-leg CUS *versus* serial proximal imaging, but noted a substantial increase in the proportion of anticoagulated patients (Bernardi *et al*, 2008; Gibson *et al*, 2009). In these trials, all calf thrombi in the whole-leg CUS cohort received full therapeutic dose anticoagulation. The issue of propagation and complication in calf DVT remains challenging.

The 0·47% (95% CI 0·08–2·62) composite primary outcome that we report is similar to that published in a recent meta-analysis of seven studies and over 4700 patients (Johnson *et al*, 2010). The authors reported a VTE event rate following negative whole-leg CUS of 0·57% (95% CI

0·25–0·89), in patients with suspected DVT after a 3-month follow-up. This data includes inpatient studies and several cohorts managed exclusively by vascular specialists. Our results thus externally validate these findings within an ambulatory protocol using ultrasound performed by qualified non-physicians.

Three studies have now previously analysed outcomes in patients with high pre-test probability and documented higher adverse event rates in those with negative whole-leg CUS results (Stevens *et al*, 2004, 2012; Sevestre *et al*, 2009) over a 3-month follow-up. Our data support this increased risk, albeit with similarly broad confidence intervals due to the modest sample size. The reproducibility shown here argues for further robust study within a larger cohort of patients. If higher adverse event rates are proven, this may suggest a benefit to further clinical review or serial imaging after negative whole-leg CUS in patients with high pre-test probability. This is currently not recommended practice (Bates *et al*, 2012).

We saw a higher rate of technical failure than perhaps expected with whole-leg CUS. However, rates have been shown to vary significantly throughout the literature. The most recent assessments range from 0 to 5% (Elias *et al*, 2003; Bernardi *et al*, 2008; Gibson *et al*, 2009), but it is notable that these three studies assess technical failure in the hands of non-blinded accredited vascular physicians: all examinations within our study were performed by dedicated ultrasonographers. Our findings are therefore less likely to be influenced by conscious or subconscious bias as a result and as such, this is not a limitation in our study *per se*. Most emergency departments utilize external imaging services for confirmation of venous disease: modern protocols must be assessed in light of this.

Our study does not assess the cost effectiveness of an ambulatory pathway utilizing single whole-leg CUS assessment. This is an area in pressing need of further research, yet limited by the equipoise regarding therapeutic approach to IDDVT.

Several limitations of this study must be acknowledged. Although we strived for a consecutive sample, the research team did not screen 15% of patients. In addition, we restricted recruitment to those patients we believed would be able to provide robust follow-up data (exclusion of non-UK residents). Although we had a high rate of direct patient contact for follow-up and a comprehensive protocol designed to identify adverse events, there is always a potential to miss outcomes without face-to-face appointments. As such, generalizability may be limited.

Vascular ultrasonography was also performed and reported by non-physicians. A decade of whole-leg scanning implies our vascular laboratory is both practiced and experienced. This is particularly pertinent with regard to our technical failure rates – these rates may well be higher in centres with limited experience. However, we do not consider this a limitation as such: whole-leg CUS is used internationally and modern protocols have shown good inter-rater reliability. We attempted to standardize results. As such, our data should be reflective of any institution using whole-leg CUS with adequate governance and oversight.

Whilst the majority of imaging was ordered by non-research clinicians within the context of an internationally agreed protocol for assessment of suspected DVT, there is potential for confounding by indication within the study results.

Only symptomatic individuals who re-attended the department were assessed for further disease. This could potentially lead to verification bias in our results. However, we would suggest that an alternative approach would fail to accurately test the study hypothesis: screening for incidental disease and detection of future spontaneous DVT may lead to unwarranted concern with whole-leg CUS. We were interested in a pragmatic assessment looking chiefly for symptomatic returns, as we would be in clinical practice. Screening and treatment for asymptomatic DVT remains controversial, even in at-risk groups (Haut *et al*, 2011).

Lastly, it must be acknowledged that our multivariate analysis was not adequately powered to provide definitive evidence of characteristics associated with technical failure. This was always a secondary outcome and aimed to be hypothesis generating, rather than conclusive.

The future direction of research in this area needs to focus on several key issues. The on-going management of patients with technical failure of whole-leg CUS, further study of outcome in patients with high pre-test probability and a negative whole-leg CUS and an assessment of cost effectiveness comparing whole-leg to serial above-knee ultrasound. The latter is urgently needed and has recently been the subject of a national research call (NICE, 2012). Such a trial would need to provide standardized care for IDDVT patients and focus not just on short term outcomes, but also those relevant to conservative treatment of non propagating IDDVT, such as post thrombotic syndrome, symptomatology, representation and recurrence.

Conclusion

In conclusion, patients who have anticoagulation withheld following a negative or inconclusive whole-leg CUS for suspected DVT, within the context of an ambulatory service, have a low rate of adverse events at 3 months. In addition, whole-leg CUS can offer or confirm an alternative diagnosis in roughly one out of every four patients. Several factors are potentially associated with technical failure, including obesity, immobilization, active cancer and acute infection. Further comparative study is warranted to confirm these findings and determine whether such patients could benefit from alternative diagnostic strategy.

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Author contributions

DH and KH conceived the study and drafted the protocol. MN and KM-J advised on the protocol. DH and RB recruited patients and supervized the active research team. KH, RB, SJ, MN and KM-J advised on the manuscript and suggested revisions. DH was responsible for the drafting of this paper, although all authors read and approved the final version.

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Conflicts of interest

All authors declare that they have no conflicts of interest.

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