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Research

Deep vein thrombosis: validation of a patient-reported leg symptom index

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Abstract

Introduction: Deep vein thrombosis (DVT) is a serious health problem that affects more than 2 million people annually in the United States. Many of these patients develop asymptomatic DVT, but months to years later may experience symptomatic post-thrombotic syndrome (PTS). It is not known how many cases of PTS can be traced to "asymptomatic" DVT because venography is no longer routinely done and ultrasonography (US) may miss some asymptomatic clots. As a result, a clinical tool in addition to US to detect symptom emergence or exacerbation in patients after DVT would be of value.

Methods: Seventy-seven patients hospitalized with an acute DVT interviewed by telephone at 3–7 days, 30–40 days, and 12-months following discharge were included in this report. All were treated with a standard anticoagulation "Clinical Pathway Protocol" between April 1999 and January 2000. Using a 14-item Deep Vein Thrombosis Leg Symptom Index (DVT-LSI), patients were queried regarding leg pain, swelling, skin discoloration, cosmetic appearance, activity tolerance, emotional distress, and leg-related sleep problems.

Results: The DVT-LSI for each leg was reliable at all assessments, with instrument reliability (alpha coefficients) greater than 0.70 at all time points (range 0.71–0.87). DVT-LSI scores, and the percentage of patients exhibiting symptoms, were higher in the DVT-affected leg at all time points. Among patients with unilateral disease, symptom severity ratings were significantly worse for patients in the affected leg compared to the normal leg at all time points, with the exception of those with a right-leg DVT at 12 months. Patients with bilateral thrombi did not have different scores on one leg compared to the other.

Conclusion: The DVT-LSI is useful in assessing symptomatic clinical outcomes in patients after diagnosis of DVT, and may represent a surrogate marker for DVT otherwise presumed to be asymptomatic.

Background

Deep vein thrombosis (DVT) is a condition involving the formation of a thrombus within a deep vein [1-6]. It is often under-diagnosed and, therefore, under-treated [7].

DVT affects approximately 160 per 100,000 people annually, with relative yearly cost exceeding one billion dollars [1,2,6,8]. The incidence of pulmonary embolus (PE) in patients with DVT ranges from 5% to 20%, and it can be fatal [1,4,5,7,12]. Although typically brought on by injury, radiation or surgery, it can also be caused by a variety of other problems, including some forms of cancer [1]. Common treatment for DVT is non-operative supportive therapy (i.e., bed rest, leg elevation, etc.), drug treatment (i.e., anticoagulants, etc.), or rarely thrombectomy [5]. However, even with effective treatment, patients who survive the initial episode of DVT are prone to recurrence, as well as chronic symptoms and life-threatening complications related to the thrombotic process [2,5,8,9].

Most cases of DVT that occur following surgery are labeled "asymptomatic"; since these occurrences go unnoticed, they are often believed to be clinically insignificant [19]. However, 35–70% of patients will develop PTS by 3 years after DVT, increasing to 49–100% at 5–10 years after the event [1,2,11]. Also referred to as post-phlebitic syndrome, PTS can be permanently disabling, accounting for 2,000,000 work days lost annually [12]. Much of it may be preventable if thrombosis prophylaxis is routinely employed. PTS is caused by venous hypertension, which results in chronic pain and swelling [6]. Patients who have suffered a DVT are at a higher risk for PTS than patients who have suffered PE alone [9]. PTS diagnosis is based on duplex US and includes evidence of severe venous insufficiency. PTS develops in 40% to 60% of patients who have suffered a DVT [10,15] and typically manifests itself within 2 years following the first diagnosis of DVT.

In order to understand the relationship between DVT and PTS, it is important to screen postoperative patients over time for symptoms. Screening methods include venography, duplex US, impedance plethysmography, computed tomography, and magnetic resonance imaging [3,4]. When all postoperative patients are screened with sensitive tests, such as venography or US, many cases of asymptomatic thrombosis are discovered [20]. In asymptomatic patients, approximately 24% will develop PTS within 3 years [21]. If DVT is recognized early and treated properly, it will usually resolve without complication [1]. Venography, which is no longer routinely done, will detect asymptomatic DVT, but it is unpopular because of discomfort, dye injection, and expense to the patient.

Another concern of PTS is the impact on patients' quality of life. Quality of life (QoL) may be considerably reduced in patients who are suffering from chronic lower limb venous insufficiency [2,11], yet there are few existing tools for measuring patients' specific complaints of leg symptoms [2,14]. Existing instruments specifically designed to measure QoL and symptoms in patients suffering from PTS include the Venous Insufficiency Epidemiologic and Economic Study of Quality-of-Life questionnaire scale (VEINES-QoL [2,11,18]), the Villalta scale [11,17], and the Chronic Venous Insufficiency Questionnaire (CIVIQ [14]). The VEINES-QoL is a well-validated, 25-item scale that contains 10 questions specific to venous symptoms (VEINES-Sym). The Villalta Scale is a physician-assessed symptom scale designed to measure QoL in patients suffering PTS. The CIVIQ is a validated, 20-item scale developed to measure QoL in patients suffering chronic venous insufficiency across four dimensions (psychological repercussions, physical repercussions, pain repercussions, social repercussions), as well as the overall impact. While these instruments have value in depicting the overall multidimensional impact of DVT, what remains lacking is a brief, targeted, stand-alone instrument focusing on leg symptoms associated with PTS.

Monitoring symptoms of patients with known DVT over time may offer insight into disease onset or severity. If a questionnaire accurately reflects the symptoms of DVT in patients with clots, it might also reflect occult or silent thrombi in these patients when the questionnaire is applied postoperatively. This may be manifested as measurable symptoms in the affected leg long after surgery. Establishing a symptomatic link between PTS and "asymptomatic" thrombi could shed a new light on thrombosis prophylaxis in surgical patients.

The DVT Leg Symptom Index (DVT-LSI)

The Deep Vein Thrombosis-Leg Symptom Index (DVT-LSI) is a 14-item questionnaire assessing the severity of a patient's leg symptoms due to DVT (see additional file: Appendix A.doc). It was developed to measure the specific leg symptoms experienced by patients after DVT [12]. The scale queries patients on the following symptoms: leg pain, swelling, leg-related sleep problems, skin discoloration, cosmetic appearance, activity limitation, and emotional distress. For swelling, discomfort/pain, and leg-related sleep problems, patients are instructed to rate these items for each leg on a 5-point Likert scale (0 = no problem to 4 = very much a problem). For the items regarding skin discoloration, cosmetic appearance, activity limitations, and emotional distress, patients rate each leg based on "how true" the statement is for them (0 = not at all to 4 = very much). This paper reports on the validation of the DVT-LSI.

Table 1: Follow-up Group Information (n = 77)

DVT Location	n	History of DVT/PE	Deaths During Study
Left Leg	37	11 (29.7%)	2 (5.4%)
Right Leg	32	11 (34.4%)	2 (6.3%)
Bilateral	8	3 (37.5%)	2 (25.0%)

Methods

Data collection procedure and sample

One hundred and four patients admitted to the hospital with acute DVT and/or PE were eligible for the follow-up interviews. All were treated with a standard anticoagulation clinical pathway protocol between April 1999 and January 2000. Average length of stay was 5.1 days (sd = 4.0, range = 1 to 27 days). The pathway protocol called for telephone assessment of leg symptom status with the DVT-LSI at 3–7 days, 30–40 days and 12 months following discharge. Of 104 eligible patients, 88 (85%) participated in at least one of the three assessments. Medical chart review was used to ascertain the DVT location (left, right, bilateral, pulmonary embolism). A Registered Nurse supervised the chart reviews whereby leg involvement was determined according to test results (e.g., venous Doppler) and/or physician documentation. Of the 88 patients who completed one or more telephone interviews, 37 suffered DVT in the left leg, 32 suffered DVT in the right leg, 8 had bilateral thrombi, and 11 were diagnosed with pulmonary embolus alone. Patients with a PE alone were not asked to complete the DVT-LSI because they had no leg involvement. Consequently, 77 patients with left, right or bilateral thrombi form the focus of this report (see Table 1). Of the 77 patients in this report, 63 (82%) completed the 3–7 day interview, 61 (79%) completed the 30–40 day interview, and 40 (52%) completed the 1-year interview. Of these patients, 25 (32.5%) had a history of DVT or PE prior to involvement in the project.

Reasons for incomplete interviews included death, patient refusal, patient illness, family member refusal, inability to reach patient after several attempts, and administrative error (see Table 2). Patients excluded from the interviews had one or more of the following medical conditions: advanced-stage cancer, severe pulmonary, cardiac, renal or hepatic diseases, dementia, or Alzheimer's disease. This was determined at the time of call using a hospital-based diagnosis and procedure database. Patients were not contacted to complete the 12-month assessment if they did not answer an earlier assessment.

The telephone interviewer followed research guidelines regarding the manner (courtesy and the ability to put the respondent at ease), conduct (ability to conduct the interview in an unbiased manner and to read each question exactly as worded), and completeness for each interview. The telephone interviewer used a Computer Assisted Telephone Interview (CATI) program whereby patient responses were entered directly into the database during the interview. The database used for analytical purposes contained no identifying information.

Hypothesis and outline of analysis

To assess instrument reliability, Cronbach's alpha was calculated for the right leg symptoms (7 items) and left leg symptoms (7 items) at all three time points. Moderate to high alpha coefficients for each leg scale and the overall instrument were expected (a widely-accepted criterion is that alpha should be 0.70 or higher for a set of items to be considered a scale. Values at or above this level are considered moderate to high [16]). The DVT-LSI's ability to differentiate and localize symptom reports was assessed on each leg symptom index regardless of leg involvement. Paired-sample t-tests were calculated between each leg symptom index within leg involvement groups to test the ability of the instrument to discriminate patients according to laterality of leg involvement. SAS statistical programming software was used for the statistical analysis of these data. We defined statistical significance as $p < 0.05$.

Results

Intrument Reliability

The scores for the Left and Right Leg Symptom indexes were calculated by dividing the sum (range 0–28) of the symptom responses within each leg by the total number

Table 2: Leg Symptom Index Compliance Table (N = 77)

	3–7 Days	30–40 Days	12-month follow-up
Initial Sample	77	77	77
Missing evaluations	14	16	37
Reason missing			
Death	0	0	6
Too ill	0	3	4
Unable to Reach	6	9	14
Site Error	6	1	1
Patient Refusal	1	1	1
Not Required*	0	0	8
Other Reason	1	2	3

*Patients not assessed before one year were not called for the one-year assessment

of symptoms (range 0–7) reported. Alpha coefficients were 0.86 (Left-LSI) and 0.87 (Right-LSI) at baseline, 0.73 and 0.71 at 30–40 days, and 0.82 and 0.87 at 12-month follow-up. The DVT-LSI for assessment of symptoms in both legs exceeded standards for adequate reliability at all assessments [12].

Validity

LSI scores and the percentage of patients exhibiting symptoms were higher in the DVT-affected leg at all time points (Tables 3,4). Symptom severity ratings were significantly worse for patients in the affected leg compared to the normal leg at all time points, with the exception of those with a right-leg DVT at 12 months. As expected, DVT-LSI scores of patients with bilateral thrombi did not discriminate between legs at any point in time.

Patients interviewed who had a right or left leg DVT reported significantly worse symptom scores in their affected leg, when compared to their opposing leg, at 3–7 days and 30–40 days (see Table 3: average difference of 4 points). These patients were also more likely to report having no symptoms in their opposing leg when compared with those of their affected leg (Table 4).

At 12-month follow-up, there was a trend for all patients to exhibit more problems in both legs (Table 3). For patients suffering a left-leg DVT, the difference, when compared to the opposing leg, was significant, yet the difference between DVT-LSI right- and left-leg scores was smaller than previous assessments (mean difference of 2.7 points). There was also a decrease in the proportion of patients reporting no symptoms in their unaffected leg (Table 4). Scores of patients who suffered a right-leg DVT did not discriminate between legs at 12 months (Table 3: difference < 1 point). Within this group of 14 patients, 4 patients reported a left-leg score greater than 11, raising the overall mean. For these patients, skin discoloration, discomfort, and overall appearance of their left leg caused substantial problems (i.e., symptom severity ratings of 3 or 4). Two patients in this group had a history of DVT prior to the index hospitalization. The remaining patients in the right-leg DVT group reported 12-month left-leg DVT-LSI scores ranging from 0 to 2.

Conclusion

Venous insufficiency is a chronic, debilitating disease with side-effects that impact a person's daily functioning and quality of life. Monitoring patients suffering from venous insufficiency requires better tools for recognizing the symptomatology of the disease. Symptoms can be quantified by the CEAP (Clinical Epidemiological Anatomic and Physiologic) classification in order to measure outcomes typically experienced by patients suffering with this disease [13] and can aid in the early diagnosis of asymptomatic clots in postoperative patients. Symptoms of venous insufficiency are not always associated with objective signs such as varicosities, dilated veins, ulcers or other lesions [14]. CEAP classification symptoms are based on clinical signs, etiologic classification, anatomic distribution and pathophysiologic dysfunction, and include: leg pain, swelling, leg-related sleep problems, skin discoloration, cosmetic appearance, activity limitation, and emotional distress [5,13]. Patients with these symptoms also report impaired mobility and functionality, which may adversely affect their quality of life.

Although patients can identify and report chronic symptoms and functional difficulty, these problems may not be related to a prior DVT; therefore, the physician must be able to quantify and classify symptoms for appropriate treatment [14]. This is important because DVT and PE

Table 3: DVT-LSI Scores at each Assessment According to Location of Admission DVT

Time post-DVT	DVT location	n	Left leg score mean (sd)	Right leg score mean (sd)	p-value*
3–7 days	Left	28	5.4 (5.8)	1.2 (2.9)	0.001
	Right	28	1.0 (2.7)	6.4 (6.6)	<0.001
	Bilateral	7	1.2 (1.6)	1.9 (3.1)	0.695
	Total	63	3.1 (4.9)	3.4 (5.4)	0.704
30–40 days	Left	31	6.0 (5.3)	1.6 (2.7)	<0.001
	Right	24	1.3 (2.7)	5.5 (5.1)	0.001
	Bilateral	6	3.8 (4.7)	1.8 (3.4)	0.205
	Total	61	4.0 (4.9)	3.1 (4.3)	0.270
12-month follow-up	Left	22	4.7 (5.3)	2.0 (3.7)	0.014
	Right	14	4.6 (6.0)	5.0 (6.1)	0.847
	Bilateral	4	6.5 (2.4)	9.3 (7.5)	0.523
	Total	40	4.9 (5.2)	3.9 (5.5)	0.332

*p value is for t-test comparing left leg score to right leg score

Table 4: Number (percent) of Patients with No Symptoms*

Time Post DVT	DVT Location	Left leg proportion* (%)	Right leg proportion* (%)
3–7 Days	Left	6 (**24.0**)	17 (**68.0**)
	Right	15 (**71.4**)	6 (**27.3**)
	Bilateral	3 (**50.0**)	3 (**50.0**)
	Total	24 (46.2)	26 (49.1)
30–40 Days	Left	7 (**25.9**)	16 (**59.3**)
	Right	15 (**75.0**)	6 (**28.6**)
	Bilateral	3 (**50.0**)	4 (**66.7**)
	Total	25 (47.2)	26 (48.2)
12-month follow-up	Left	4 (**21.1**)	9 (**47.4**)
	Right	5 (**41.7**)	3 (**25.0**)
	Bilateral	0 (**0.0**)	0 (**0.0**)
	Total	9 (25.7)	12 (34.3)

* Proportion of patients who report "not at all" to all DVT-LSI symptoms. These proportions are based on the number of patients at each assessment, which decreased to 40 patients by month 12.

complications from surgical treatment or from medical illnesses carry increased risk of hospitalization, healthcare costs, patient morbidity, and mortality [6]. Early identification by the physician may reduce symptom distress, which may, in turn, reduce the above-mentioned complications.

Symptom management for patients after DVT is difficult because they are often classified as "asymptomatic," and yet exhibit signs of recurrent DVT [3]. Patients may also develop thromboneurosis, which is the fear affiliated with recurrent DVT [6]. When DVT symptoms are left untreated, there is a significant impact on morbidity and mortality rates [7] due to the increased risk of PTS and fatal PE. Rarely, these thrombi can result in fatal PE or less severe long-term leg or lung problems. The most definitive way to prevent PE and PTS in patients suffering an acute episode of DVT is to prevent recurrence by appropriate treatment and careful attention to risk factor analysis [8].

Currently, postoperative screening involves objective tools, such as venography and US, which are considered useful and can identify "asymptomatic" DVT [3]. However, the use of subjective outcome measures, prior to objective measures, to screen postoperative DVT patients may have a significant impact on the incidence of PTS. The tool reported herein assesses the subjective (patient-reported) components of symptoms mentioned above.

The DVT-LSI is a focused, compact assessment of leg symptoms and related concerns that has potential value in monitoring symptoms related to PTS. It was designed for use in research and clinical settings to evaluate the natural history of leg-associated symptoms over time following an acute episode of DVT. As applied in this clinical setting, the DVT-LSI indicated good reliability for one year following DVT requiring hospitalization. Patients reported symptom severity consistent with the site of their prior DVT. Leg symptoms were related in a predictable fashion to the location of the DVT, lending support to the view that this instrument accurately assesses PTS-specific symptomatology, apart from general (background) leg symptomatology in this population.

The Index may be important for its ability to point out the extent DVT has on a person's ability to function that has heretofore not necessarily been attributed to previous thrombotic events. This assessment of DVT symptoms could also be used prospectively to estimate the patient-experienced impact of DVT after a particular surgical procedure or medical complication. The instrument may, therefore, be a useful clinical guide during treatment and follow-up. When used postoperatively, this instrument could be used as a screening tool after particularly high-risk surgical procedures to identify symptoms suggestive of thrombi that might otherwise remain undetected by objective screening tools. It may also signal new problems in the previously unaffected leg.

As noted in Table 4, although not definitive, the reduction in proportion of patients who report no symptoms in their (presumably) unaffected leg suggests that they may have experienced a silent DVT late during the follow-up period. At the very least, it seems clear there is an increase in leg symptoms over time which may warrant clinical attention. This is especially apparent in those patients suffering a right DVT one year after hospitalization. Although 5 (41.7%) of these patients remained asymptomatic, the majority reported leg symptoms to a degree where, by one year, their "unaffected" leg was as symptomatic as their "affected" leg. We cannot deny the possibility that some of

these patients may have suffered a recurrence in their "unaffected" leg.

These findings are limited by the relatively small sample size and some missing follow-up information. Nevertheless, evidence in support of this brief symptom index suggests it would be of value in or for following symptoms over time in patients after DVT. Use of this tool in identifying emerging leg symptoms and perhaps indicating new DVT events will require further study. Additionally, we feel that if the validity of this instrument to reflect PTS symptoms in patients following a DVT could be further documented in a larger patient population; a powerful tool would be available for both clinicians and researchers. For example, this instrument could be administered to patients one year after participation in thrombosis prophylaxis trials to assess the effectiveness of a study drug in preventing PTS.

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