# DEEP VEIN THROMBOSIS: A STUDY IN CLINICAL DIAGNOSIS

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*ABSTRACT*

***Recently, three patients presented with deep vein thrombosis-like symptoms and signs but were negative on venogram. Three questions arose: Was the clinical diagnosis accurate? What is the accuracy of the diagnostic test used? What is the time taken for the clot to lyse? To answer the first question, a retrospective clinical study was done. For the other two I did a literature search. For the clinical study, I analysed thirty patients with venogram proven deep vein thrombosis (DVT) and five patients with DVT-like clinical findings but four were venogram negative and one was ultrasound negative. The results showed that symptoms and almost all the clinical signs were useless in differentiating these two sets of patients. Swelling was very sensitive but not specific and the Homan's sign was very specific for DVT but not very sensitive and would be of use only in a case by case basis. Other significant findings were that DVT was more common in the Chinese than the other races and more common in females. The incidence of DVT is also particularly marked in the 30-39 and 70-79 age groups. It was also found that venograms were very accurate in diagnosing DVT but need to be read by two experienced radiologist. Also it was found that clot lysis can take place as early as 35 hours after starting heparin but vessel changes remain for at least 11 weeks. Thus it is not possible for the five patients with DVT-like symptoms and signs to have DVT missed by the venography or clot lysis that took place so quickly that when the venogram was done the vessel was clear. There could be a new group of patients to be arbitrarily called pseudo-DVT patients.***

*Keywords: deep vein thrombosis, venogram, pseudo-DVT*

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## INTRODUCTION

Recently, there were three cases of deep vein thrombosis (DVT) in which the clinicians were very sure of the diagnosis and started empirical treatment only to discover later that these patients did not have DVT. This group of patients poses a diagnostic problem because they do not fit into known entities of disease but actually mimic the presentation of DVT every closely. Why did the clinical picture not correlate with the actual pathology? To solve this problem, three questions have to be answered:

- Was the clinical diagnosis accurate?
- What is the accuracy of the diagnostic test used?
- What is the time taken for the clot to lyse?

## METHODS

To answer the first question, a clinical retrospective study was carried out to determine the difference in presentation between the patients with DVT and the patients who presented like DVT but on venogram it was negative. The other two questions were answered by a literature survey from a list of journal articles generated using the Medline CD-ROM system.

### Study Subjects

A list of patients' names was generated by the Information Services of Tan Tock Seng Hospital (TTSH) with the International Classification of Diseases (ICD) coding of 4539 which covers all forms of thrombophlebitis. From the original list of 60 patients who had thrombophlebitis, 34 patients who had venograms and one with Doppler ultrasound done identified. Five patients presented with DVT-like symptoms but were found not to have DVT and the other 30 had venogram-confirmed DVT. These patients were admitted to TTSH from April to November 1992. The medical records were search for the relevant information.

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### Data Collection

Standardised forms were used to collect data on 37 clinical items. These items were divided into four main categories, namely symptoms, risk factors, clinical findings and biochemical data. They included symptoms such as pain, swelling, erythema and symptom duration; risk factors of post surgery neoplasm[1,2], immobilisation[3], pregnancy, estrogen or oral contraceptive use, previous history of DVT, family history of DVT, comorbid conditions, ovarian hyperstimulation syndrome[4], atrial fibrillation[5], trauma and hypercoagulable states[6,7], leg signs of swelling, warmth, erythema, pain, palpable cord, superficial vein distension, venous collaterals; calf signs of pain, warmth, increased tissue tugor and Homan's sign; biochemical markers such as fever, white blood cell count, haematocrit and platelet count[8,9]. Obesity has been excluded as a risk factor[10].

### Diagnosis of DVT

The venograms were done in the Radiology Department of TTSH. Each venogram is either read by a medical officer and verified by a radiologist or read by a radiologist alone. The criteria for the diagnosis of DVT are as follows: the presence of filling defects, tramline appearance and presence of collaterals.

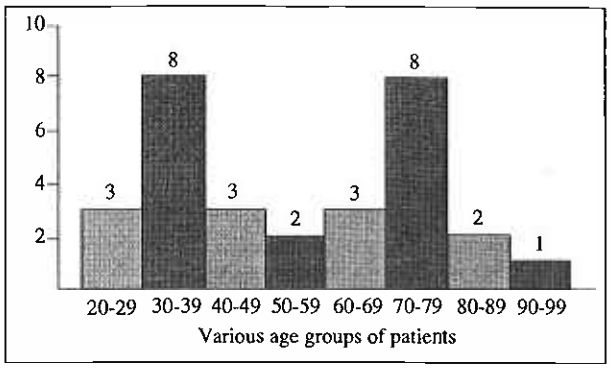
### Data Analysis

For the 30 patients, associations between clinical findings and venographic results were evaluated using the Fisher's exact test of significance with the 5 patients in the group without DVT acting as the control. The Fisher's exact test was used because the cell values in both groups for certain variables were below 10. Variables were considered associated with DVT if the p value for the test of significance is less than 0.05. Sensitivity and specificity were also calculated from the 2 x 2 table for each of the clinical findings.

## RESULTS

The mean age of the 30 patients with DVT were 55 years and the racial distribution was 87% Chinese, 10% Malays and 3.3% Indians. The majority of the patients were females at 70% as compared to males at 30%. The age distribution of the DVT patients as shown in Fig 1 shows that patients in the age groups of 30-39 and 70-79 are particularly prone to DVT. The patients in the 30-39 age group are females who underwent caesarean sections or had a hypercoagulable state like systemic lupus erythematosus. The patients in the 70-79 age group are those with co-morbid conditions like diabetes or hypertension or are post surgery.

**Fig 1 – Distribution of 30 patients with DVT in the various age groups**



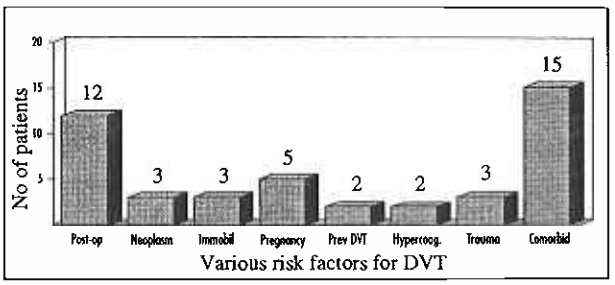

Among the patients who had DVT, 45% of them had acute symptoms ie symptoms lasting for less than 2 days. Another 50% presented with symptoms lasting 2 days to a month. The difference in the duration of symptoms between the DVT group and non-DVT group was not significant. At presentation, 50% (15) of the patients had complained of pain and 63.3% (19) had complained of swelling in one leg. Further breakdown of the analysis showed that 20% (6) of the patients had complained of pain in the whole leg, 20% (6) below the knee and 20% (6) of the patients did not complain of any pain at all. Only 3.3% of patients had complained of pain above the knee at presentation. Patients who were totally asymptomatic but were found to have clinical signs of DVT and later venographic signs made up 33.3% (10) of the total of 30 patients. None of the patients presented with the complaint of redness of the leg (erythema) and it is not included in the summary of the data in Table I. Fisher's exact test was carried out between each of the symptoms found in the DVT and that found in the group without DVT. The figures were not significant. The sensitivity and specificity of each symptom are too marginal to be of any value in helping to diagnose DVT since the variables hover about the 50-60% mark and the specificity for leg swelling is only 20% – many false positives would result.

**Table I – Association of symptoms with venographic findings**

| Symptoms | Status | DVT | No DVT | Significance | |
|---|---|---|---|---|---|
| Pain | Present | 15 | 2 | p=0.5 | sensitivity 50% |
| | Absent | 15 | 3 | | specificity 60% |
| Swelling | Present | 19 | 4 | p=0.43 | sensitivity 63% |
| | Absent | 11 | 1 | | specificity 20% |

Of the patients with DVT, 66.7% of them had one risk factor and 26.7% had two risk factors. In the group without DVT, 40% had one risk factor and 20% had two risk factors. The difference is not significant. The data for risk factors is summarised in Fig 2. The two most important risk factors found are post-surgery and co-morbid conditions. Forty percent (12) of DVT patients were post-operative and 50% had co-morbid conditions. In the postoperative group, 25% (3) had undergone orthopaedic surgery and 42% (5) had undergone a caesarean section. Abdominal surgery (1), thoracic surgery (1), head surgery (1) and gynaecological surgery (1) made up 8.3% each.

**Fig 2 – Distribution of 30 DVT patients with the various risk factors**




Note: Some of the patients had more than one risk factor therefore the figures exceed the total number of patients.

The clinical signs elicited in the DVT patients were mainly swelling and warmth for proximal DVT and swelling, warmth, tenderness, increased tissue tugor, Homan's sign and superficial vein distension for calf DVT. Table II shows the data in greater detail. Signs like erythema, a palpable cord, venous collaterals and phlegmasia cerula dolens were not present in our sample of DVT patients. Due to the small sample of patients who did not have DVT, the Fisher's exact test found th difference between the signs in the DVT group and the group without DVT to be not significant.

The sensitivity and specificity figures show two prominent results. Leg swelling is a very sensitive marker (83%) for presence of DVT but will give many false positives as the specificity is 0%. Homan's sign, a clinical entity long panned by clinicians, is very specific for DVT (80%) but there would be many false negatives as it is not a sensitive marker (16%). The rest of the clinical signs are practically useless for diagnosing DVT as the figures for sensitivity and specificity hover about 40-60%. It is like flipping a coin.

**Table II – Association of clinical signs with venographic results**

| Clinical Signs | Status | DVT | No DVT | Significance | |
|---|---|---|---|---|---|
| Swelling | Present | 20 | 5 | p=0.44 | sensitivity 83% |
| | Absent | 4 | 0 | | specificity 0% |
| Warmth | Present | 10 | 4 | p=0.19 | sensitivity 45% |
| | Absent | 12 | 1 | | specificity 20% |
| Tenderness | Present | 13 | 3 | p=0.68 | sensitivity 59% |
| | Absent | 9 | 2 | | specificity 40% |
| Increased | Present | 10 | 3 | p=0.46 | sensitivity 45% |
| Tissue Tugor | Absent | 12 | 2 | | specificity 40% |
| Homan's | Present | 3 | 1 | p=0.58 | sensitivity 16% |
| Sign | Absent | 19 | 4 | | specificity 80% |

Note: Figures do not add up to the total number of thirty patients in the DVT group as some patients were left out due to incomplete documentation in the records.

With regard to the biochemical data analysis, most of the patients (80%) with DVT were afebrile ie a temperature range defined as between 36.5°C and 37.4°C. Also 45% of the patients

had a total white cell count of 10000-14999 cells/mm$^3$ and 28% had a count of 15000-19999 cells/mm$^3$ and 24.1% had normal white blood cell counts. The haematocrit and platelet counts were not analysed because data were lacking in many of the patients.

## DISCUSSION AND ANALYSIS

### 1. Was the clinical diagnosis accurate?

The sample sizes of both the DVT group and the group without DVT were too small. This affected the results of significance tests carried out to test the association between clinical features and venographic signs. The group without DVT is a biased group as all of them have symptoms and signs suggestive of DVT and was worked up as such. This would result in clinical features between the DVT and non-DVT group to be similar thus affecting significance testing. Being a retrospective study, many of the patients had incomplete descriptions of the leg findings and those findings not documented in the case-notes were presumed to be absent. This might underestimate the frequency of some of the clinical signs.

In comparison with overseas studies, the mean age of our sample is very similar to that found in a Hong Kong study[11] and a US study[9]. However, the distribution in the age groups is not weighted towards the older age group as found in Hong Kong but has two peaks – one at 30-39 and the other 70-79. This is due to the fact that different risk factors are prevalent in different age groups with the elderly being more affected by co-morbid conditions like diabetes and hypertension. There is also a preponderance of female patients in all the three studies making sex a significant risk factor.

Presenting symptoms do not seem to be very predictive of DVT as a third of the patients were totally asymptomatic, ie admitted for a different problem and discovered in the ward to have leg swelling and investigated and found to have DVT. The symptom that could be discounted from consideration is erythema as all the patients did not have it. Pain and swelling of the leg are commonly found in DVT patients but our tests have shown that these can also be found in those without DVT. A study by Landefeld et al also concurred[9]. The duration of symptoms seem more important as 45% of the patients presented acutely ie less than 2 days and the rest of the patients presented within a week as was also found by Landefield et al.

No clinical findings were significantly associated with DVT unfortunately. Only the clinical findings of leg swelling and Homan's sign are of any use. Although the high likelihood of false positives and negatives respectively present for these signs precludes their use in mass screening, on a case by case basis, they can actually be very accurate in picking up DVT.

It is evident by the data presented that it is insufficient to rely on clinical findings to predict the occurrence of actual DVT pathology in persons who present with symptoms and signs of DVT.

### 2. What is the accuracy of the diagnostic tests used?

Of the 5 patients who did not have DVT, venograms were used to diagnose 4 patients whilst in the fifth patient, Doppler ultrasound was used. Could it be that DVT in these patients was not detected because of the inaccuracy or error in the diagnostic tests used?

Venography carries an accuracy of 90% to 98% which means that a normal venogram virtually rules out the diagnosis of DVT[12]. However, in a recent study of venography in recurrent DVT, venograms did not show DVT in 10% of limbs with chronic DVT and in 20% of limited/initial DVTs[13]. Venograms are more likely to miss thrombi in iliac, femoral and popliteal regions. Another area of doubt is in the interpretation of the venograms. In a study by de Valois et al, the inter-observer agreement was 96%[14]. In another study comparing conventional films and phosphor plates, significantly better results with venograms on phosphor plates show room for error in reading conventional films[15]. Thus venograms are reasonably accurate for the diagnosis of DVT.

In one patient, ultrasound diagnosis was used. In various studies, the overall sensitivity of ultrasound imaging as compared to venography was 95% and specificity was 92%[16]. The rates vary for different areas of veins visualised. The sensitivity and specificity of ultrasound for the diagnosis of femoral and popliteal vein thromboses were 100% and 97% respectively. The sensitivity and specificity for calf thromboses were 85% and 83% respectively. The patient had swelling of the right ankle and calf – the use of ultrasound imaging for detecting DVT in this area is not very good as the sensitivity is only 85%[17]. The study by Fletcher et al from which the above figures are quoted recommended that the scan be performed by an experienced vascular technologist. Such a person is definitely lacking in our local context. Therefore, the reliability of ultrasound imaging for the diagnosis of DVT in TTSH is to be questioned.

### 3. What is the time taken for the clot to lyse?

Another variable in this study is that the clot could have lysed before the diagnostic test was done thus giving a negative result. It is interesting to note that in two patients heparin was started empirically and the venograms were done one day three and day eleven after the clinical diagnosis of DVT was made.

In a study in which streptokinase was used to treat DVT with the duration of treatment ranging from 35 to 198 hours, complete (>90%) or moderate (50% – 90%) lysis occurred in 9 of 15 patients[18]. In another study in which heparin was used, repeat venograms 5 – 7 days after standard heparin was started showed improvement in 61% of patients[19]. A third study in which patients were treated with unfractionated heparin for 10 days showed reperfusion of the deep vein system in 75% of the patients[20]. Moreover, the period of normalisation of the venous system which ranges from 11 weeks up to 1 year, seems to depend on the number of sites affected, whether the pelvic veins were unaffected, whether the affected leg was the left, whether the initial clot was non-occlusive, whether there was a history of DVT and whether the symptoms lasted for less than twenty-four hours[21].

It is thus possible that in the 5 patients that tested negative for DVT, their clots could have lysed before the venograms were done as the shortest documented time is 35 hours and the average time is about 5-7 days. However, even with the clot lysed, lingering changes in the veins should have been present in the venograms for at least 11 weeks. This reduces the possibility that these women had DVT as the venograms were essentially normal with the above-mentioned error in venograms taken in consideration.

## CONCLUSION

When a patient presents with a swollen leg, a list of differentials come to mind and amongst them are congestive heart failure, thrombophlebitis, cellulitis and lymphedema[22]. It is easy to differentiate amongst them as these conditions have their unique features.

The problem arises when trying to differentiate between DVT and a small subgroup of patients who have presentations very much like DVT ie pain and swelling and clinical signs of warmth and tenderness and some of the known risk factors for DVT. The clinical study done above showed that it is not possible to predict actual DVT with accuracy on clinical findings alone. Therefore, it is wise to do a venogram in each clinically suspected case of DVT. Supporting this is a review of cost effectiveness of basing therapeutic decisions on clinical diagnosis where it was

found that venography was cost effective whilst relying on clinical diagnosis alone was not[23]. The only drawback is the possibility of venography induced DVT in a small percentage of patients.

The clinical study does show that DVT is a much more common problem in the Chinese than the Malays or Indians. The population census 1980 records that the proportion of Chinese, Malays and Indians to be 77%, 15% and 6% respectively whilst the proportion of Chinese in the study group is 87% and the proportion of Malays and Indians are less as compared to the population proportions. Another fact is that females are much more at risk of developing DVT irregardless of presence or absence of risk factors. The age distribution of the DVT patients is fairly even except for the two age groups most prone to it because of the prevailing risk factors in those two age groups. It means that the elderly are not more prone to DVT. The clinical study also showed that of all the clinical signs, the two most definitive are swelling and Homan's sign. Swelling is useful in picking up patients with DVT in a non-specific way whilst the Homan's sign is good selecting patients with actual DVT.

The venogram is a very accurate test to determine actual DVT pathology. The onus here is on the radiological department to ensure accurate reading of the venograms ie the venograms must be ready by two experienced radiologists. For example, in two of the patients with pseudo-DVT and risk factors such as atrial fibrillation and ovarian hyperstimulation syndrome, the venograms were read as normal. It could have been due to the inability to get a good visualisation of the venous system and error in reading the venogram film. The use of ultrasound should be avoided when it comes to differentiating between patients with actual DVT and those with pseudo-DVT as the sensitivity is only 83%.

The shortest time taken for a clot to lyse with heparin treatment is 35 hours and even then vessel wall changes remain for at least 11 weeks. Therefore it was not possible in the five patients with DVT-like clinical findings to have DVT missed by venography. Therefore it remains that there is a group of patients who would not have DVT but present with DVT-like clinical findings and I arbitarily call them pseudo-DVT patients. In this group of patients, it has been found to be safe to withhold treatment[24].

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