# An Investigation into the Suitability of Ordering D-dimers for Patients with Suspected DVT in the A&E at Waterford Hospital

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**ABSTRACT**

Objective: The objectives of this study were to assess the suitability of ordering D-dimer assays and to investigate the need for a validated risk assessment model in the evaluation of patients with a clinical suspicion of deep venous thrombosis in patients attending the Accident and Emergency unit of Waterford Regional Hospital. Methods and Patients: Admission cards of 106 consecutive patients ,for whom D-dimer assays were ordered, were evaluated according to the Wells Criteria to determine whether the patients had a high, medium or low probability risk of having a deep venous thrombosis. (DVT) This information was correlated with initial clinical impression, presenting complaint, the result of the D-dimer test and the results of ultrasonography, if performed. Results: There were 30 positive D-dimer results returned from the 106 analysed. Of those, 19 (63.3%) had a Wells score suggesting low probability of DVT, 10 (33.3%) had a medium probability, and 1 (3%) had a high probability of DVT. For the remaining 76 negative D-dimer results, 59 (77.6%) had a low probability Wells score, 14 (18.4%) were in the medium probability group and 3 (3.9%) were in the high probability group. This study proposes that the introduction of a clinically validated model for the diagnosis of DVT/pulmonary embolism (PE) would rationalise the ordering of D-dimers and make the diagnosis of DVT/PE more evidenced based.

**INTRODUCTION**

D-dimer assays were developed to measure the degradation product of cross-linked fibrin. They have been primarily used to diagnose Deep Vein Thrombosis (DVT) and resultant thrombotic Pulmonary Embolism (PE). They do this by measuring the increase in specific plasma degradation products of fibrin, which is elevated due to the action of plasmin and other endogenous thrombolytic agents. Many different assays have been evaluated for their accuracy

and utility in diagnosing DVT.[1] A D-dimer result of less than 0.2ug/ml is taken to have a negative predictive value for the test. In general, an isolated positive D-dimer (greater than 0.2ug/ml) result is not useful because the test lacks specificity. D-dimer levels are elevated not only in the setting of acute thrombosis, but also in other conditions such as pregnancy, infection and malignancy. In contrast, a negative result using a sensitive D-dimer test is useful for excluding acute DVT. In an overview, Bounameaux et al. (1997) quote an overall sensitivity for D-dimer assays of 82%, with 95% confidence intervals of 77-87%. Unfortunately, commercially available D-dimer assays vary in their sensitivity and specificity and, therefore, the performance of one assay cannot be

extrapolated to another.[2] Currently, the most reliable and extensively evaluated tests are two rapid enzyme-linked immunosorbent assays (ELISAs; Instant-IA D-dimer) and a rapid whole blood assay (SimpliRED D-dimer). The sensitivity of the rapid ELISAs is over 95% and that of the

SimpliRED D-dimer assay is approximately 85%.[3] Currently the ELISA method is the one used in Waterford Regional Hospital.

The incidence of DVT is 5 per 10,000 per annum.[4] The incidence is much lower in the young and higher in the elderly. Although many patients develop DVT in the presence of risk factors, such as malignancy and immobility, DVT can also occur without obvious provocation (idiopathic DVT). Some of the patients with idiopathic DVT have an inherited or acquired thrombophilia, whereas

the remainder have no identifiable biochemical or genetic abnormality.

Making a diagnosis of DVT requires both clinical assessment and objective testing because the clinical features are non-specific and investigations can be either falsely positive or negative. The initial step in the diagnostic process is to stratify patients into high, intermediate or low-risk categories using a validated clinical model. When the clinical probability is intermediate or high and the venous ultrasound result is positive, acute symptomatic DVT is confirmed. Similarly, when the probability is low and the ultrasound result is normal, DVT is ruled out. A low clinical probability combined with a negative D-dimer result can also be used to rule out DVT, thereby obviating the need for ultrasonography. In contrast, when the clinical assessment is discordant with the results of objective testing, serial venous ultrasonography or venography is required to confirm or refute a diagnosis of DVT. Outpatients with classical findings of DVT and at least one risk factor have an 85% probability of having DVT, whereas those with atypical features and no

identifiable risk factors have only about a 5% probability of having thrombosis.[5]

Several clinical models can be found in the literature for the accurate diagnosis of DVT/PE. The important thing is to find one that is accurate and easy to implement in the clinical setting in which it is being used. One such algorithm is presented here for illustrative purposes. The algorithm presented in Figure 1 is used for the diagnosis of DVT. It is important to stress, however, that further research would need to be undertaken to find the most suitable one for Waterford Regional Hospital.

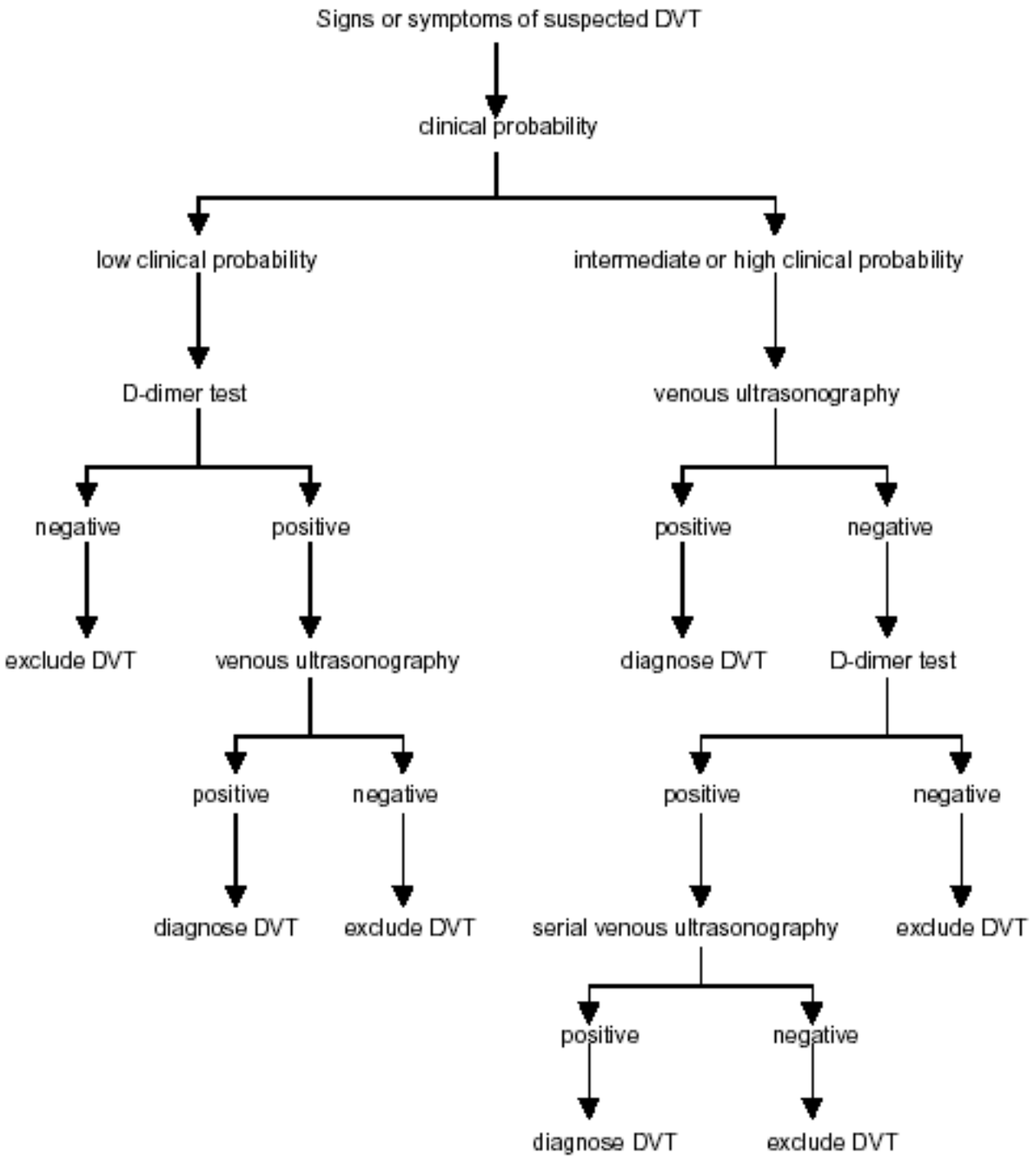
Clinical models exist also for diagnosing PE exclusively. An example is that proposed by Egermayer et. al. (1988) using respiratory rate, arterial oxygen tension and a D-dimer assay produced by the SimpliRED method. With this method a correct diagnosis is made in 95.9% of

cases.[7]

At present, a standardised, validated clinical model does not exist in Waterford Regional Hospital for the classification of risk in patients with a suspected DVT/PE or the ordering of related tests. The aims of this study were to research the ordering of D-dimer assays in Waterford Regional Hospital and to investigate the need for such a model.

Figure 1. Algorithm for diagnosing DVT using clinical assessment, venous ultrasonography, and

D-dimer testing.[6]




**METHOD**

Over a one month period, 111 A&E admission cards, which contained D-dimer assay orders, were assessed. The Wells criteria were applied to determine whether the patients had a high, medium

or low probability of having a DVT.[5] This was to assess the objective clinical probability of these patients having a DVT/PE. This information was correlated against initial clinical impression, presenting complaint, the result of the D-dimer test and the results of ultrasonography, if performed.

The risk factors for DVT determined by Wells et al. (2001) in the clinical evaluation of DVT are presented in Table 1. Each risk factor constitutes a score of one, and an alternative diagnosis on clinical grounds gives a score of two.5 The total score is achieved by adding these together and allows for risk stratification. Patients with a score of zero are at low risk, those with a score of one or two are at intermediate risk, and those with a score of three or greater are at high risk of having a DVT.

Table 1. Clinical model for predicting pre-test probability for DVT.[5]

| Symptom | Score |
|---|---|
| Active cancer (treatment ongoing or within previous 6 months or palliative) | 1 |
| Paralysis, paresis or recent plaster immobilization of the lower extremities | 1 |
| Recently bedridden > 3 days or major surgery within 4 weeks | 1 |
| Localized tenderness along the distribution of the deep venous system | 1 |
| Entire leg swollen | 1 |
| Calf swelling 3 cm > asymptomatic side (measured 10 cm below tibial tuberosity) | 1 |
| Pitting oedema confined to the symptomatic leg | 1 |
| Collateral superficial veins (non-varicose) | 1 |
| Alternative diagnosis as likely or greater than that of DVT | 2 |

**RESULTS**

Of the 111 admission cards from the A&E department, 5 were excluded, as the cards were illegible. Thus there were 106 patients in this patient cohort. The presenting complaints and clinical impressions given for these patients are displayed in Table 2. Patients with an initial clinical impression other than DVT or PE were those in whom a diagnosis of neither DVT nor PE was explicitly stated on their admission card. Patients with an unspecified clinical impression were those patients who did not have a clinical diagnosis explicitly stated on their admission card.

Wells scores were calculated for all the patients in this study. According to this score system, 78 (73.5%) of the patients studied had a low probability of having a DVT (Wells Score = 0), 24 (22.6%) had a medium probability of having a DVT (Wells Score =1 or 2) and 4 (3.7%) patients had a high probability of having a DVT (Wells Score e"3).

There were 30 positive D-dimer results returned from the 106 analysed. Of those, 19 (63.3%) had a Wells score suggesting low probability of DVT, 10 (33.3%) had a medium probability, and 1 (3%) had a high probability of DVT. For the remaining 76 negative results, 59 (77.6%) had a low probability Wells score, 14 (18.4%) were in the medium probability group and 3 (3.9%) were in the high probability group.

According to Figure 2, 27% of the patient group were in the medium to high risk group of having a DVT/PE. According to the algorithm proposed by Hirsh et al. (2002), this group of patients should have had venous ultrasonography performed in the first instance. The 73% of patients in the low risk group are the patients who would most benefit from D-dimer assays in the study.[6]

Information regarding the patients with a primary diagnosis of DVT/PE on clinical grounds is presented in Table 3. Of these patients only one was admitted. The eventual outcome of one other patient is unknown. All others were discharged from A&E. Venous ultrasonography of the lower limbs was performed in four of these patients. The author was unable to establish why this was the case, although it may be because clinicians do not see D-dimers as a useful test in this situation, despite having ordered them. None of these patients had a final diagnosis of DVT/PE.

Figure 2. Wells Score Rick vs. Total D-dimers ordered.

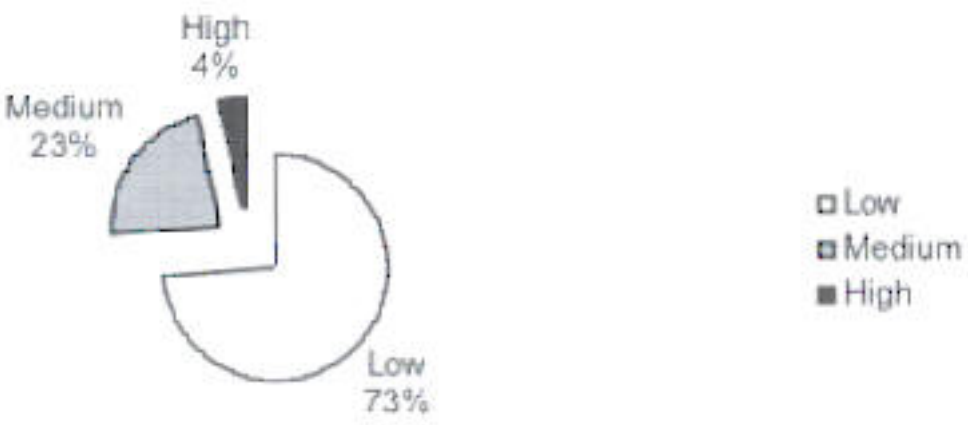



Table 2.Patients' presenting complaints and clinical impressions.

| Presenting Complaint | Total Number of Patients | Patients with an Initially Indicated Clinical Impression Other than DVT/PE | Patients with an Initially Indicated Impression of DVT/PE | Unspecified Clinical Impression |
|---|---|---|---|---|
| Abdominal pain | 18 | 11 | 0 | 7 |
| Chest Pain/SOB | 51 | 30 | 1 | 20 |
| Leg pain | 11 | 4 | 6 | 1 |
| Musculoskeletal pain | 3 | 2 | 0 | 1 |
| Other | 4 | 4 | 0 | 0 |
| Paralysis/Weakness | 11 | 4 | 0 | 7 |
| Collapse | 3 | 2 | 0 | 1 |
| Haemorrhage | 5 | 1 | 0 | 4 |
| Total | 106 | 58 | 7 | 41 |

Table 3. Patients suspected of having DVT/PE

| D-dimer result | Risk (from Wells Score) | Admitted to Hospital | Doppler Performed | Presenting Complaint |
|---|---|---|---|---|
| <0.2 (negative) | Low | No | | Chest pain/ dyspnoea |
| <0.2 (negative) | Intermediate | No | | Leg pain |
| <0.2 (negative) | Intermediate | No | Negative | Leg pain |
| <0.2 (negative) | Intermediate | NO | | Leg pain |
| <0.2 (negative) | Intermediate | Unknown | Negative | Leg pain |
| 0.52 (positive) | High | Yes | Negative | Leg pain |
| <0.2 (negative) | High | No | Negative | Leg pain |

## DISCUSSION

This study was undertaken to assess the suitability of ordering D-dimer assays and to investigate the need for a validated risk assessment model in the evaluation of patients with a clinical suspicion of DVT in patients attending the A&E unit of Waterford Regional Hospital.

Of the 106 D-dimer tests ordered in this study, only 6.6% of them were done for patients with a primary suspicion of DVT/PE (Table 1). The presenting complaint and clinical impression varied widely in this cohort as can be seen in Figure 3 and Figure 4. While the majority of tests were ordered for patients with a presenting complaint of either chest pain or dyspnoea, over half of these patients were suspected to have a condition other than DVT/PE (Table 2). The high testing rates for chest pain and a clinical impression of cardiac pathology suggests that D-dimer testing is being used as a "safety net" to exclude pulmonary embolism in patients with symptoms of cardiac pathology. The very low rate of venous ultrasonography would back this up. Of the 7 patients in whom DVT/PE was suspected, 6 of them were in intermediate or high probability groups. These

six presented with leg pain, while the remaining patient with low probability presented with chest pain. This was perhaps the sole patient who presented with chest pain who would have benefited from the D-dimer assay, as he presented with low probability of having a DVT and therefore a negative D-dimer assay result would put his risk of having a DVT/PE in the next 3 months at less

than 2%.[8]

As can be seen in Figure 2, 73% of all D-dimers ordered were for patients with a low probability of DVT/PE. Only 4% of those ordered were done so for patients with a high probability of DVT/PE. If D-dimers are to be used as a primary test for the exclusion of PE, they should be correlated with

arterial oxygen tension less than 80mmHg or respiration rate greater than 20.[6] However, only 3 patients in the study group presented with a respiration rate of over 20 breaths per minute and arterial oxygen tension was not recorded.

According to the Wells score, 6.6% of the patients in the study were suspected of having a DVT/PE as their primary pathology, and 4% were in the high probability category. Ultrasonography is indicated for those patients with a high clinical probability, therefore only 2.6%of the patients in the study would have benefited from D-dimer assays for a primary suspicion of DVT/PE.

An explicit initial clinical impression of DVT/PE was only expressed in seven of the patients in the study group. However, 28 of the patients were in the medium to high risk groups as calculated by the Wells score (Table 1). This illustrates that DVT/PE is a very difficult diagnosis to make. The introduction of the clinical model would standardise the diagnostic process, which ultimately would lead to increased diagnosis of DVT/PE. If the clinical model proposed by Hirsh et al. (2002) had been used in the A&E department of Waterford Regional Hospital for the duration of the study, the number of D-dimers ordered would have been reduced by 27%. The trade off is that, if the model proposed earlier (Figure 1) were used, the 28 patients in the medium and high risk groups would have had venous ultrasonography performed which is a more expensive test.

The ordering of D-dimers in patients presenting to A&E in this study seems to be poorly selective. It is not influencing further testing procedures and presumably patient outcomes. The implementation of a validated clinical model would standardise the ordering procedure and lead to greater confidence in the diagnosis of DVT/PE.

Figure 3. Patients' presenting complaints

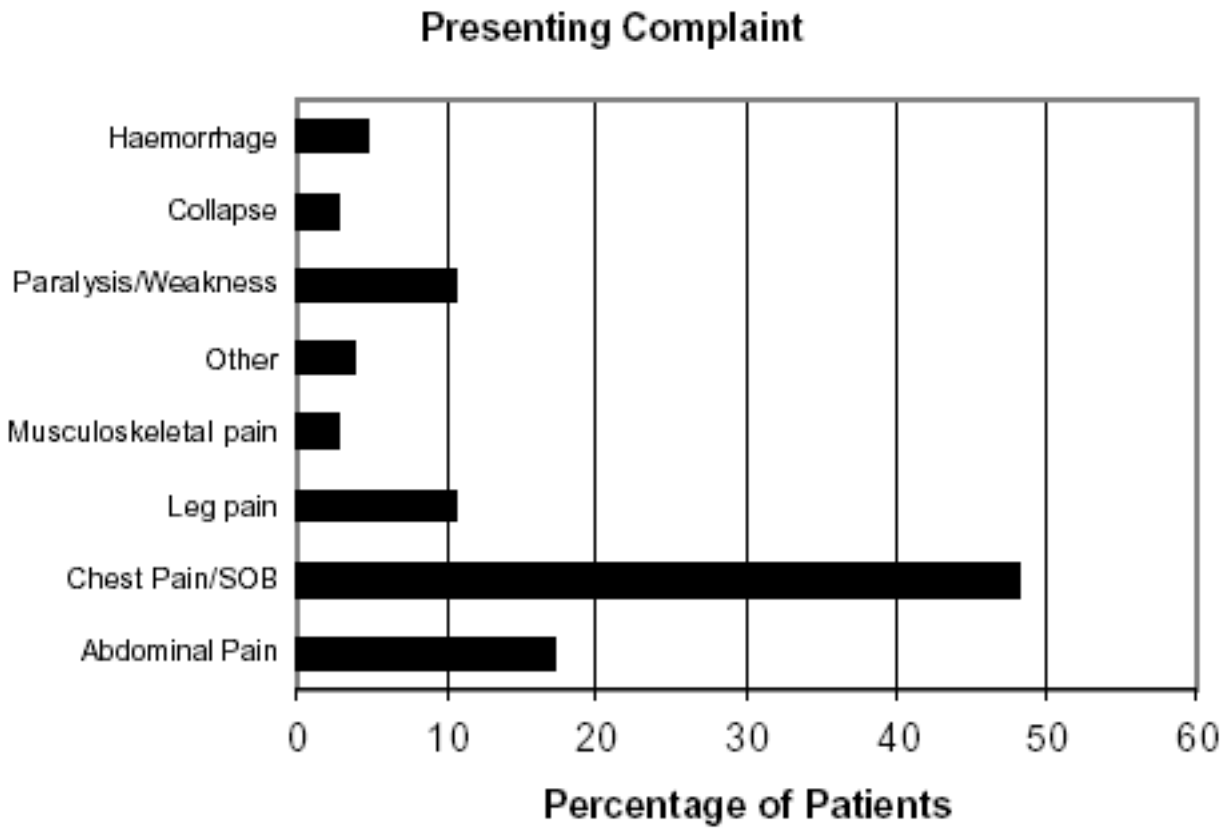
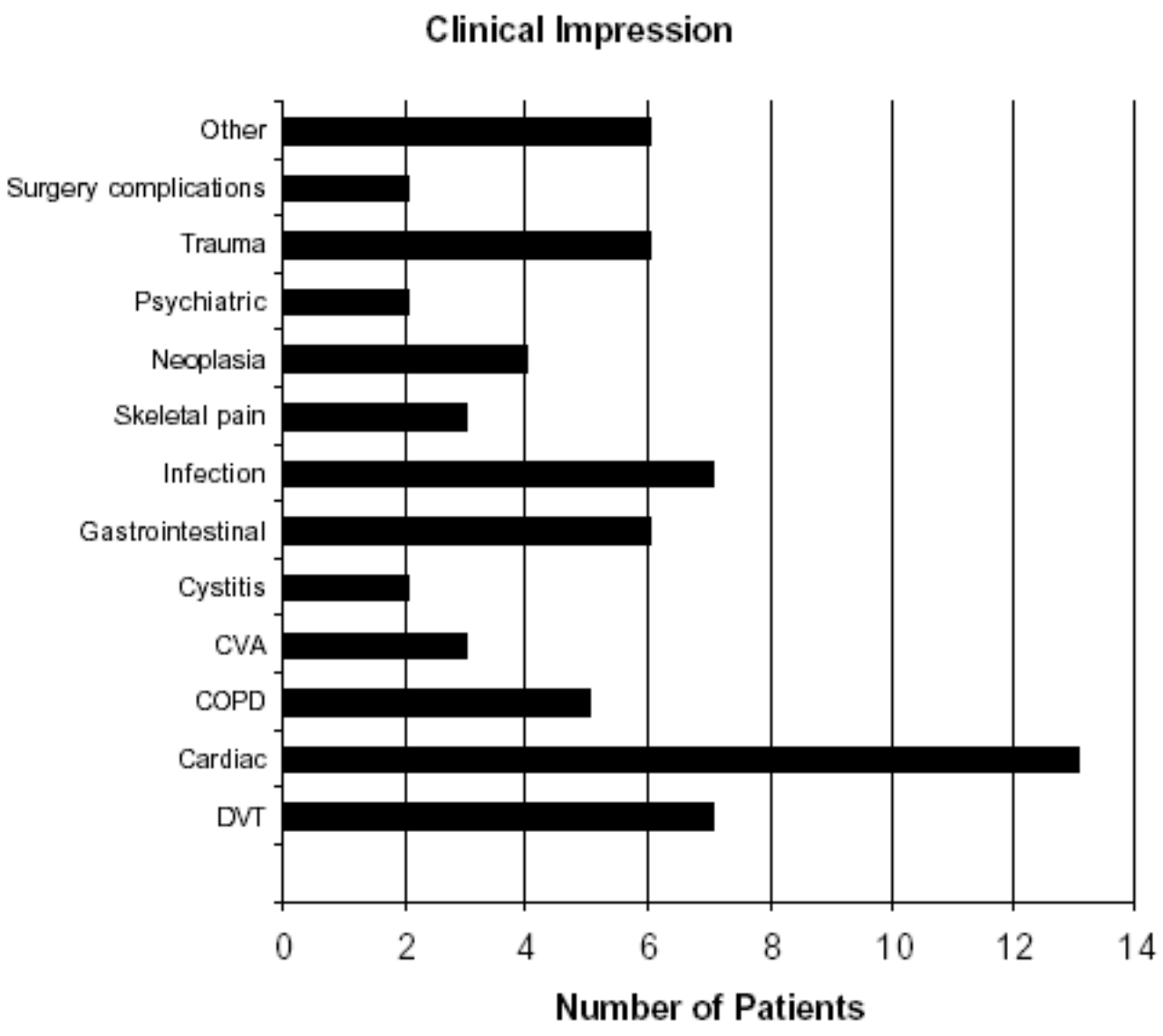



Figure 4. Clinical impression of patients




**CONCLUSION**

This study aimed to outline the ordering practices of D-dimer assays in Waterford Regional Hospital's A&E department. The shortcomings of this study were the relatively small sample size and the fact that the clinical outcomes of the patients in the cohort were not analysed. Despite these, it is clear that the "safety net" status of D-dimer ordering needs to be examined and more

evidenced-based ordering strategies implemented.

The impact of this is that in a nine-month period in 2001 there was an overshoot of 78,234 euro for the D-dimer budget of Waterford regional hospital. The implementation of a standard practice for ordering D-dimer assays or even a DVT/PE algorithm such as that proposed by Hirsh et.al., would regulate the investigation of DVT/PE and ultimately increase the detection rate while

decreasing budgetary overruns.[6]

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REFERENCES

1. Dixon AK, Coulden RA, Peters AM. The non-invasive diagnosis of pulmonary embolism. BMJ 2001; 323(7310):412-3.

2. Bounameaux H,de Moerloose P,Perrier A,Miron MJ D-dimer testing in suspected venous thrombo-embolism:an update. Quarterly Journal of Medicine 1997; 90:437-442.

3. Lee AY, Ginsberg JS. Laboratory diagnosis of venous thromboembolism, Baillieres Clin Haematol 1998; 11:587-604.

4. Fowkes FJ, Price JF, Fowkes FG. Incidence of diagnosed deep vein thrombosis in the general population: systematic review. Eur J of Vasc Endovasc Surg 2003; 25(1):1-5.

5. Wells PS, Anderson DR, Rodger M. Excluding pulmonary embolism at the bedside without diagnostic imaging: management of patients with suspected pulmonary embolism presenting to the emergency department by using a simple clinical model and D-dimer. Annals of Internal Medicine 2001; 135(2):98-107.

6. Hirsh J, Lee AY. How we diagnose and treat deep vein thrombsis. Blood 2002; 99(9):3102-3110.

7. Egermayer P, Town GI, Turner JG. Usefulness of D-dimer, blood gas, and respiratory rate measurements for excluding pulmonary embolism. Thorax 1998; 53(10):830-4.

8. Janes S, Ashford N. Use of a simplified clinical scoring system and D-dimer testing can reduce the requirement for radiology in the exclusion of deep vein thrombosis by over 20%. Br J Haematology 2001; 112:1079-1082.