Diagnosis of Deep Vein Thrombosis (DVT) using Color Duplex Imaging (CDI) versus D Dimer Test

Nadia A. Salih[1], Bushra H. Almalik[2], Abu Naib BaderEldin[3]

Abstract: ***Several diagnostic strategies using ultrasound imaging, measurement of D-dimer, and assessment of clinical probability of disease have proved safe in patients with suspected deep-vein thrombosis,. The purpose of this review is to discuss the utility of venous ultrasonography as the foundation for diagnosis of lower extremity DVT. The effectiveness and practicality of venous ultrasonography as a stand-alone examination versus D-dimer testing in the diagnosis of DVT. Inpatients and Outpatients presenting with suspected lower-extremity deep-vein thrombosis were potentially eligible. Using a clinical model, physicians evaluated the patients and categorized them as likely or unlikely to have deep-vein thrombosis. The patients were then randomly assigned to undergo ultrasound imaging alone (control group) or to undergo D-dimer testing (D-dimer group) followed by ultrasound imaging unless the D-dimer test was negative and the patient was considered clinically unlikely to have deep-vein thrombosis, in which case ultrasound imaging was not performed.The study consisted of 300 Saudi patients were 121 males (40.3%) and 179 females (59.7%).In our study D- Dimer test was positive in 286 (95.3 %) with sensitivity (95.3%) and specificity (83.3%). comparison with Color Duplex Imaging (CDI) showed that 274 positive patients 91.3 % had sensitivity (91.7%) and specificity (97.1%).***

Keywords: Diagnosis, Clinical, Ultra Sonography, Patients, D-Dimer group

1. Introduction

Deep veins thrombosis (DVT) is a blood clot in a deep vein, also known veins thromboembolism (DVT). DVT predominantly occurs in the legs and may have no symptoms. When symptoms are present, the non-specific signs include pain, swelling, redness, warmness, and engorged superficial veins in the leg. DVT can go away naturally, but the most serious complication is when a thrombosis dislodges and travels to the lungs to become a life-threatening pulmonary embolism. The term veins thromboembolism is used to refer to DVT and/or pulmonary embolism. The most frequent complication of DVT is the post-thrombotic syndrome, which can cause swelling (edema), pain, and rarely, leg ulcers. These symptoms make post-thrombotic syndrome a significant contributor to the health care costs of DVT. About 1 in 1000 adults develops DVT annually, and aging increases its rate of occurrence. [1]

DVT is a serious medical event associated with a substantial risk of adverse outcomes [2]. The 30-day case fatality rate (i.e. proportion of patients who die) is about 5% for DVT and 10% for PE; the one-year case fatality rate is approximately 20% for both DVT and PE[3]. The 10-year recurrence rate of is 30%21-24. Predictors of DVT recurrence are male sex, idiopathic DVT, and persistent risk factors. The recurrence rates of DVT and PE are similar [4].

The initial clinical presentation of DVT or PE predicts the manifestation of a recurrence; hence, patients that had a previous PE event tend to have a recurrence of PE more frequently than patients that had a previous DVT event [5]. Furthermore, DVT is associated with long- term complications. The post-thrombotic syndrome is a chronic, progressive condition that occurs despite optimal anticoagulant therapy. This syndrome occurs years after the DVT event, thus, it may not be interpreted as a result of thrombosis. The symptoms include pain, heaviness, swelling, and cramping in the leg; these symptoms are aggravated during standing or walking. In severe cases, a venous ulcer may develop. The post-thrombotic syndrome occurs in 20-50% of DVT patients within 10 years of the DVT, and severe post-thrombotic syndrome with an ulcer occurs in 3-7% of DVT patients[6]. D-dimer (DD) units are generated by the action of factor XIIIa on fibrin monomers and polymers and when the endogenous fibrinolytic system degrades cross-linked fibrin present in the organism. These units consist of two identical subunits derived from two fibrin molecules. DD is the final fragment of the plasmin-mediated degradation of cross-linked fibrin and its molecular weight is around 180 000 Da. Unlike fibrin/fibrinogen degradation products, which are derived from both fibrinogen and fibrin, DD fragments are end products of the action of plasmin on cross-linked fibrin; however, monoclonal antibodies used in the so-called DD assays also recognize many fragments from cross-linked fibrin without prior proteolysis by plasmin [7] Because 2 – 3% of plasma fibrinogen is physiologically converted to fibrin and then degraded, small amounts of D-dimer-containing species are detectable in the plasma of healthy individuals. However, the D-dimer concentration in blood is increased under all conditions associated with enhanced fibrin formation and subsequent degradation by plasmin. D-dimer represents the most frequently used laboratory marker of coagulation and fibrinolysis activation [8]. Plasma levels demonstrate anaverage 8-fold increase in patients with proven VTE compared with controls, with a level falling to approximately one-quarter of the initial value between week 1 and 2 following the acute event, especially on anticoagulant treatment [9]. The plasma half-life of DD fragments is approx- imately 8 hours and clearance occurs via the kidney and the reticuloendothelial system [10] (Figure 1).

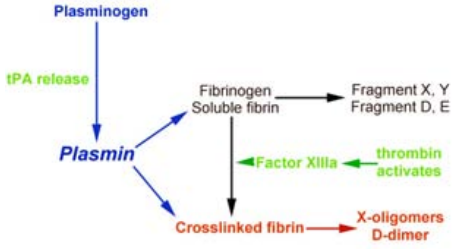

Figure 1: The Degradation of Fibrin into D-dimer

Figure 2: The Degradation of Fibrin into D-dimer

2. Methodology

The study was performed In Kingdom of Saudi Arabia, in Aseer Hospital(Abha city) and King Khalid Hospital (Hail city) in duration (February 2010- January 2013).The study is performed in 121 males (40.3%) and 179 females (59.7%). The mean age of all patients is 45years ranging (15-75) years .Inpatients & Outpatients presenting with suspected lower-extremity deep-vein thrombosis were potentially eligible. Using a clinical model, physicians evaluated the patients and categorized them as likely or unlikely to have deep-vein thrombosis. The patients were undergo D-dimer testing (D-dimer group) .The former consist of latex agglutination assays (semiquantitative and qualitative) followed by ultrasound imaging unless the D-dimer test was negative and the patient was considered clinically unlikely to have deep-vein thrombosis, in which case ultrasound imaging was not performed .the protocols technique of D Dimer testing include . Patient plasma is tested undiluted. Control group is thirty six healthy volunteers (21 male, 16 female).All the reagents must at a room temperature.. In each appropriately identified circle on the test card place 20µL of the test sample (patients undiluted, the reagent3 (lyophilized human negative)and the reagent and 4(positive plasmas for use as control.). Shake the reagent 1 vial (latex particles coated with mouse monoclonal anti-human D-dimer antibodies) survival times. Place 20µL of reagent 1 (latex particles coated with mouse monoclonal anti-human D-dimer antibodies) next to the test sample in each circle. Use separation stirring rods. Combine and mix the two drops in each circle. . Manually rock the test card in such a manner that liquid swirls around in each circle. Continue rocking the card for 2 to 3 minutes. Compare the agglutination pattern of each circle with those of the negative and positive controls (Reagents3&4).About Ultrasound Imaging technique include,. Starting at the level of the groin, the common femoral vein is imaged in transverse section and will be seen to lie medial to the common femoral. The common femoral vein should be compressed to demonstrate patency and is, followed distally beyond the saphenofemoral junction, to the junction of the superficial femoral vein and profundafemoris vein. The proximal segment of the profundafemoris vein should also be assessed for patency if possible. With the transducer turned into the longitudinal plane, the flow pattern in the common femoral vein should be assessed with color flow imaging and spectral Doppler. Flow should appear spontaneous and phasic at this level if there is no outflow obstruction. A calf squeeze can provide evidence of good flow augmentation in the proximal superficial femoral vein, which is a useful indirect indicator of probable superficial femoral and popliteal vein patency. Alternatively, strong foot flexion will also normally augment flowthe popliteal vein is examined by scanning the popliteal fossa in a transverse plane with supine or standing position. Starting in the middle of the popliteal fossa, the vein is followed proximally as far as possible to overlap the area scanned from the medial lower thigh. The popliteal vein will be seen lying above the popliteal artery when imaged from the popliteal fossa. The below-knee popliteal vein and gastrocnemius branches are then examined in the transverse plane. The popliteal vein can also be duplicated.The calf veins are often easier to identify distally. They are then followed proximally to the top of the calf. The posterior tibial and peroneal veins can be imaged in a transverse plane from the medial aspect of the calf

From this imaging plane the peroneal veins will lie deep to the posterior tibial veins. It can sometimes be difficult to compress the peroneal veins from this position. Color flow imaging in the longitudinal plane may be useful for demonstrating patency. The peroneal veins can frequently be examined from the posterolateral aspect of the calf. The common trunks of the posterior tibial and peroneal veins can also be very difficult to image, and medial and posterolateral transducer positions may be needed to examine this region at the top of the calf .Examination of the anterior tibial veins is often not requested, as isolated thrombosis of these veins is rare. However, assessment of the anterior tibial veins is usually easier with color flow imaging, in the longitudinal plane, as the veins are small and frequently difficult to identify, with B-mode imaging. When requested, the examination of the calf is completed with an assessment of the soleal veins and sinuses located in the soleus muscle. These veins are imaged from the posterior calf in practice, they can be very difficult to identify, especially in the normal subject. The iliac veins are examined with the patient lying supine, as the iliac veins lie behind the bowel. The iliac veins lie slightly deeper and medial to the iliac arteries. Compression of these veins is not possible, and patency should be confirmed using color flow imaging. In addition, spectral Doppler can be used to examine flow patterns with flow augmentation maneuvers. The main limitation of examining this area is incomplete visualization due to overlying bowel gas and the potential to miss partially occluding thrombus.In some cases the vena cava may need to be examined. This vessel lies to the right of the aorta when imaged in transverse section. Color flow imaging can be used in the transverse plane to look for filling defects, but some transverse tilt may have to be applied to the transducer to produce a reasonable Doppler angle. Flow should also be assessed in longitudinal section with color flow and spectral Doppler ultrasound Examination of this area should be undertaken with a considerable degree of experience. Other imaging modalities are generally preferable. The data of patients obtained from work sheet is used to collect data on more than fifty clinical items These items were divided into main categories, namely age, sex, nationality, referring department, affected limb, signs, risk factors, probability of DVT, complications, patients' group, patient status, diagnostic tests, affected vein, vein status, alternative, Types and sites of DVT The data analyzed by software program SPSS.16.

3. Results

The study consisted of 300Saudi patients were 121 males (40.3%) and 179 females (59.7%)their age groups as ≤

20years 3 (0.1%), ≤ 30years 06 (2.0%), ≤ 40years 13 (14.3%), ≤ 50years 76 (25.3%), ≤ 60years 126 (42.0%), ≥ 60years 76 (25.3%).with symptoms and signs suggestive of DVT. obese 246 (82 %), over 40 years 295 (98.3%), hypertension 161 (53.7%) smoker 108(36.0%), hormone therapy o oralcontraceptive131 (43.7%), Pregnancy or post-partum7 (2.3 %) and coagulation disorders, Patients with major joint replacement 34 (11.3%), and H-risk patients, not received anticoagulant 34 (11.3%)among patients for whom deep-vein thrombosis had been ruled out by the initial diagnostic strategy, there were 274 (83%) is confirmed venous thromboembolic in the D-dimer group and in 20 patients (87%) is confirmed by Color Duplex Imaging. Ultrasound testing can be safely omitted in such patients. In our study proximal DVT 14(64%), Distal DVT 8(36%).

Table 1: Clinical Signs of DVT

Clinical Signs	*Sex of Patients*		*Total*	*Percentage %*
	Male	Female		
Swelling	118	156	274	91
Calf pain	106	157	263	88
Erythema	73	99	172	57
Warmth	44	64	108	36
Total	121	179	300	

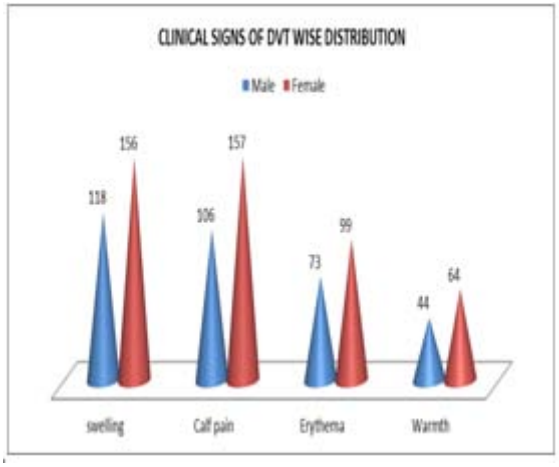

Figure 3: Clinical Signs of DVT

Table 2: Patients Status

Patients' Status	*Sex of Patients*		*Total*	*Percentage %*
	Male	*Female*		
Obese	103	143	246	82
over 40 years	119	176	295	98
Hypertension	59	102	161	54
Smoker	105	03	108	36
Hormone Therapy or Oral .contraceptive	01	130	131	44
Pregnancy or p. partum	00	07	07	2
Coagulation disorders	13	21	34	11
Total	**121**	**179**	**300**	

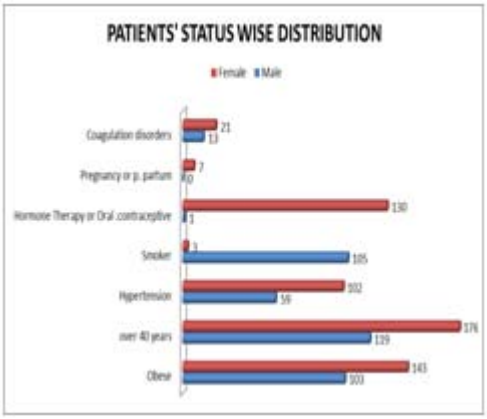

Figure 4: Patients Status

Table 3: Risk Factors of DVT

Risk Factors	*Sex of Patients*		*Total*	*Percentage %*
	Male	*Female*		
Active cancer	11	32	43	14
Paralysis, plaster lower limb	5	12	17	6
Recent bedridden, surgery	11	13	24	8
localized tenderness	96	135	231	77
Leg Swelling	95	149	244	81
Calf swelling (10 cm)	99	135	234	78
Pitting edema	85	135	220	73
collateral superficial vein	96	136	232	77
Previous document DVT	48	79	127	42
Family History	57	62	119	40
Total	**121**	**179**	**300**	

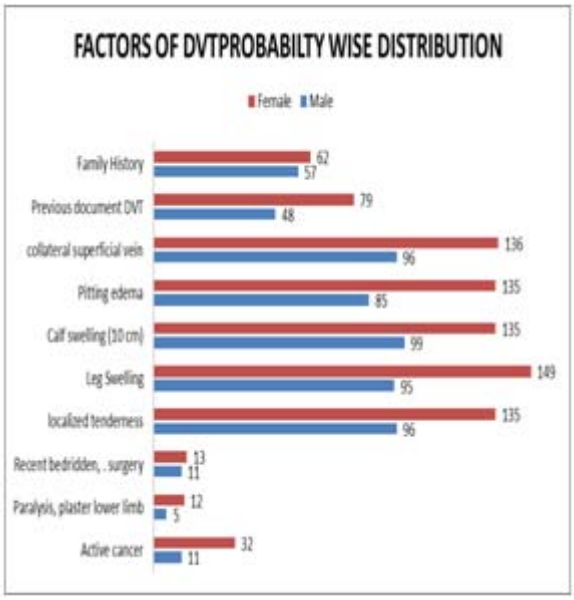

Figure 5: Risk Factors of DVT

4. Discussion and Conclusion

In our study D- Dimer test was positive in 286 (95.3 %) with sensitivity (95.3%) and specificity (83.3%). comparison with Color Duplex Imaging (CDI) showed that 274 positive patients 91.3 % had sensitivity (91.7%) and specificity (97.1%).Current diagnostic strategies for VTE diagnosis almost all include an assessment of the pre-test clinical probability, in order to enable the interpretation of diagnostic tests and to select low-risk patients in whom a less intensive work-up can safely rule out the diagnosis without any imaging test. Clinical prediction rules are

decision-making tools that provide a reliable and reproducible estimate of the clinical probability. They are built and validated following methodological standards. They use combinations of simple available clinical predictors to define a probability of disease which leads to a diagnostic or therapeutic course of action. Several clinical prediction rules are available for VTE diagnosis; all have completed required validation steps. The safety and usefulness of their use in diagnostic strategies have been demonstrated. Their implementation in local guidelines for VTE diagnosis has been shown to be associated with better patients' out- comes. Their use should be encouraged; further research efforts are required to ease their use in daily clinical practice. So, our recommendations are that the diagnosis for DVT is mainly based on complementary examinations. Among the available examinations, the most widely used is the (CDI), due to its accuracy, low cost, availability and patient's tolerance.

References

[1] Caggiati A, Bergan J J, Gloviczki P, et al 2002 Nomenclature of the veins of the lower limbs: an international interdisciplinary consensus statement. Journal of Vascular Surgery 36(2):416-422.

[2] Naess IA, Christiansen SC, Romundstad P, Cannegieter SC, Rosendaal FR, HammerstrømJ.Incidence and mortality of venous thrombosis: a population-based study. J ThrombHaemost 2007; 5:692 – 9.

[3] Cushman M, Glynn RJ, Goldhaber SZ, et al. Hormonal factors and risk of recurrent venous thrombosis: the prevention of recurrent venous thromboembolism trial. J ThrombHaemost 2006; 4:2199 – 203

[4] Spencer FA, Emery C, Lessard D, et al. (2006). "The Worcester venous thromboembolism study: a population-based study of the clinical epidemiology of venous thromboembolism". J Gen Intern Med 21 (7):722–7.

[5] Murin S, Romano PS, White RH. Comparison of outcomes after hospitalization for deep venous thrombosis or pulmonary embolism. ThrombHaemost 2002; 88:407 – 14.

[6] .Nijkeuter M, Sohne M, Tick LW, et al . The natural course of hemo dynamically stable pulmonary embolism: clinical outcome and risk factors in a large prospective cohort study. Chest 2007.

[7] Chapman CS, Akhtar N, Campbell S, et al. The use of D-dimer assay by enzyme immunoassay and latex agglutination techniques in the diagnosis of deep vein thrombosis. Clin Lab Haematol 1990; 12:37 – 42.

[8] Sie P. The value of laboratory tests in the diagnosis of venous thromboembolism. Haematologica 1995; 80:57 – 60.

[9] D'Angelo A, D'Alessandro G, Tomassini L, et al. Evaluation of a new rapid quantitative D-dimer assay in patients with clinically suspected deep vein thrombosis. ThrombHaemost 1996; 75:412 – 6.

[10] Hager K, Platt D. Fibrin degeneration product concentrations (D-dimers) in the course of ageing. Gerontology 1995; 41:159 – 65.

Author Profile

Nadia A. Salih received the B.S. and M.S. degrees in Diagnostic Radiology & Ultrasonography from Sudan University 1998 and 2007.Since 2010 to 2011 she has a lecturer in king Khalid University (Abha, K.S.A) She now as A lecturer of diagnostic radiology in University of Hail .College of Applied medical Sciences ,K.S.A.